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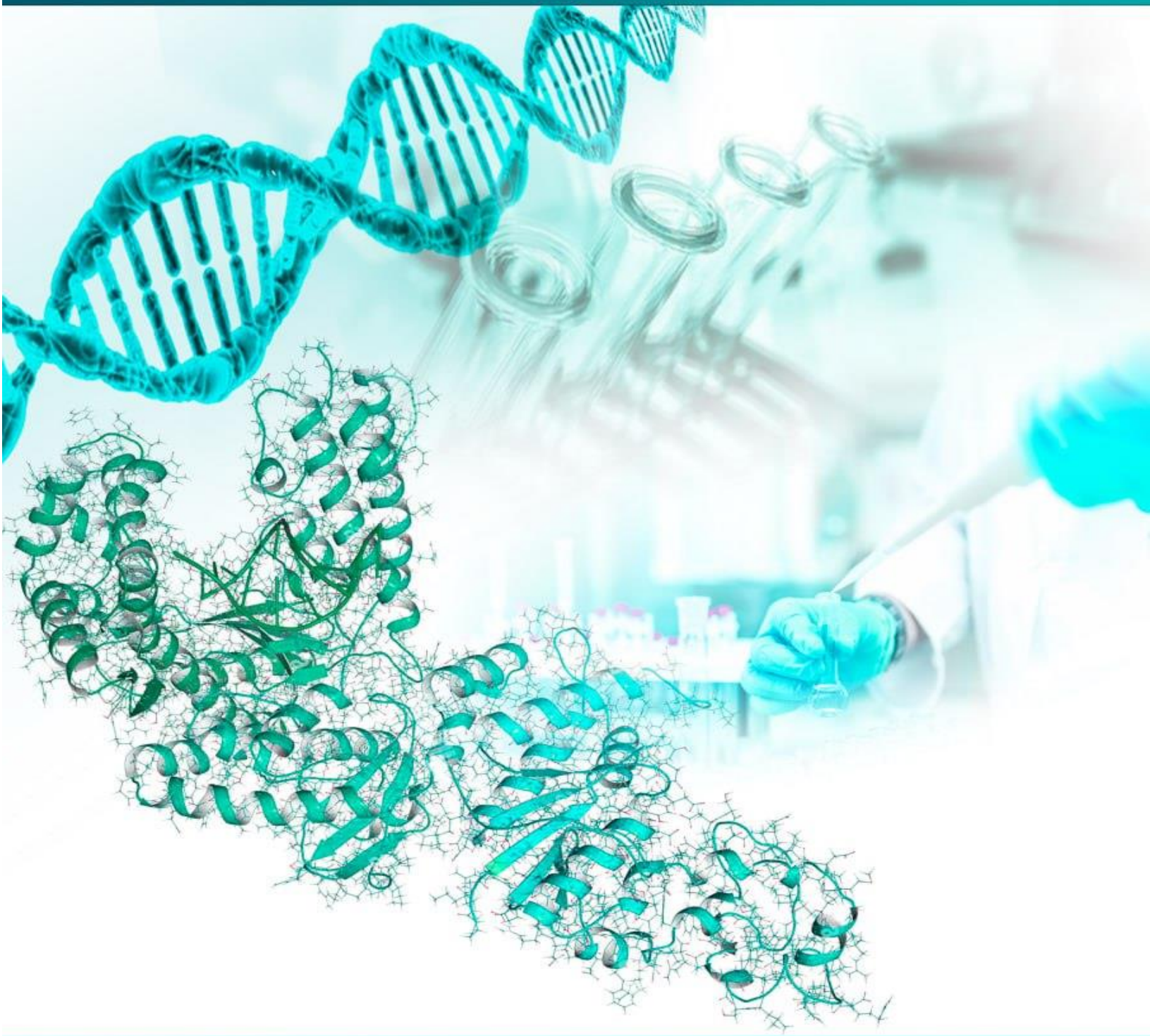

Tehran University of Medical Sciences

ICBMB 2024
Abstracts Book

18th National Congress of Biochemistry
& 9th International Congress of
Biochemistry & Molecular Biology

Tehran - Iran

23-25 October 2024

Acta Biochimica Iranica 2 (2024) supplement

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‘In The Name of God’

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Dear Esteemed Colleagues,

On behalf of the Board of the Biochemical Society of Iran, it is my distinct pleasure and honor to welcome you to the 9th International and 18th National Congress of Biochemistry and Molecular Biology (ICBMB), jointly hosted by the Biochemical Society of Iran and Iran University of Medical Sciences in Tehran from October 23 to October 25, 2024. This congress will be held under auspices of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC).

This event promises to be a paramount event in the field, fostering collaborative exchanges and showcasing cutting-edge advancements in the field of Biochemistry and Molecular Biology. Also, in this congress, we will have a special overview of the latest achievements in the field of clinical chemistry. Our congress aims to provide a dynamic platform for professors, researchers, practitioners and students to share insights and discuss the challenges. With a diverse range of keynote speeches, interactive workshops, and scientific sessions, attendees can expect a rich and enlightening experience. We encourage you to submit your latest research findings and breakthrough innovations for presentation and publication, contributing to the collective knowledge and driving progress in our field. Moreover, the congress offers invaluable networking opportunities, allowing you to connect with peers and create new collaborations.

Your participation and companionship will make this congress more fruitful and we look forward to welcoming you to this enriching scientific gathering.

Prof. Reza Meshkani
President of the Biochemical Society of Iran

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In the name of God

It gives me great pleasure to announce the 18th National Congress of Biochemistry and the 9th International Congress of Biochemistry and Molecular Biology, scheduled to take place from October 23 rd to 25 th , 2024, in the dynamic city of Tehran. This congress presents a unique opportunity for participants to engage in discussions on key research topics within the field. The Iran University of Medical Sciences is privileged to host this esteemed event, with invaluable support from the Biochemical Society of Iran and The International Federation of Clinical Chemistry. The realm of biochemical and laboratory sciences is undergoing rapid transformation propelled by advances in technology, artificial intelligence, and machine learning. This expansive domain continues to yield profound discoveries each year. Notably, significant breakthroughs have been achieved in clinical biochemistry, leading to the development of novel diagnostic strategies and the revision of diagnostic guidelines, thereby profoundly impacting healthcare outcomes. The congress this year promises a comprehensive and pioneering scientific program, crafted through fruitful collaboration between basic and clinical scientists. With a primary focus on human health and well-being, the Congress will feature specialized sessions dedicated to clinical biochemistry, discussions on laboratory-related sessions, presentations showcasing cutting-edge research in biochemistry and molecular biology, sessions organized by young biochemists, and a unique symposium orchestrated by the Iranian Society for Trace Element Research. The program also includes a diverse array of educational workshops and opportunities for industry presentations highlighting the latest advancements in commercial instrumentation.

I am optimistic that with the help of the chancellor of the Iran University of Medical Sciences, president of the Iran Biochemical Society, and all the organizers, the conference will offer three days of informative, productive, and enjoyable discussions. We eagerly anticipate welcoming you to this congress, where you will not only have the opportunity to delve into the latest discoveries, techniques, and developments in basic and clinical biochemistry but also take part in the promotion and establishment of the importance of biochemistry in Iran.

Dr. Mitra Nourbakhsh
Scientific Secretary of the Congress

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Big Data Analytics in Laboratory Medicine: Real-World Application in Reference Interval Harmonization Across Clinical Laboratories

Khosrow Adeli. PhD, FCACB, DABCC, FADLM

Professor and Head, Clinical Biochemistry, and Senior Scientist, Molecular Medicine, The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada.

Past-President, International Federation of Clinical Chemistry & Laboratory Medicine

Professor Adeli is the Head of Clinical Biochemistry in the Department of Paediatric Laboratory Medicine as well as a Senior Scientist in the Molecular Medicine Program of the Research Institute at the Hospital for Sick Children. He is also Vice-Chair of Quality and a Full Professor in the Department of Laboratory Medicine & Pathobiology at the University of Toronto in Toronto, Canada. He is very well known for his extensive national and international contributions over the past 30 years to clinical laboratory service, research, and education. Now, as President of the IFCC, his focus is on continuing the IFCC's journey towards global leadership in laboratory medicine by directly impacting healthcare and patient outcomes through efforts such as global newborn screening, directly contributing to global lab quality, becoming the largest provider of free eLearning, and ultimately continuing to promote the value of laboratory medicine worldwide.

He served as President of IFCC (2020 - 2023), Past Chair (2013 - 2018) and Vice-Chair (2006 - 2012) of IFCC Communications & Publications Division.

Harmonization in laboratory medicine from specimen collection to result reporting is critical to ensure consistent and accurate clinical decision-making. Harmonized or common RIs refer to using one interpretative recommendation for an analyte across several laboratories, regardless of analytical assay or patient population. Harmonized or common RIs should therefore only be considered for assays that demonstrate minimal bias across considered methodologies. Several national surveys have reported wide variation in reference intervals across healthcare centres in certain regions, even those using the same analytical platform for test measurement. There is a high risk of inappropriate test result interpretation when reference intervals are not appropriately harmonized. The Canadian Society for Clinical Chemistry (CSCC) Working Group on Reference Interval Harmonization was established in 2015 to develop evidence-based harmonized/common reference intervals (hRIs) and support their implementation in laboratories across Canada. Harnessing the power of big data, laboratory results were collected across populations and testing platforms to derive common adult RIs for 16 biochemical markers. A novel comprehensive approach was established, including: (1) analysis of big data from community laboratories across Canada; (2) statistical evaluation of age, sex, and analytical differences; (3) derivation of hRIs using the refineR method; and (4) verification of

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proposed hRIs across nine laboratories with different instrumentation using serum and plasma samples collected from healthy Canadian adults. Harmonized RIs were calculated for all assays using the refineR method, except free thyroxine. Derived hRIs met proposed verification criterion across nine laboratories and five manufacturers for alkaline phosphatase, albumin (BCG), chloride, LDH, magnesium, phosphate, potassium (serum), total protein (serum). Further investigation is needed for select analytes due to lower verification in one or more laboratory (albumin (BCP), calcium, total CO2, total bilirubin, sodium) or concern regarding too wide hRIs (alanine aminotransferase, creatinine, TSH). In this presentation, we will discuss the work completed by the Working Group on Reference Interval Harmonization in Canada, challenges encountered, and future plans to support implementation.

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IFCC's Global Leadership in Clinical Laboratory Standardization and Harmonization

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Past-President, International Federation of Clinical Chemistry & Laboratory Medicine

The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) plays a pivotal role in advancing global leadership in clinical laboratory standardization and harmonization. With a mission to enhance the scientific and clinical practice of clinical chemistry and laboratory medicine, the IFCC is committed to establishing universally accepted standards that ensure accuracy, reliability, and comparability of laboratory results worldwide. Through its extensive network of national societies, scientific divisions, and working groups, the IFCC drives initiatives that focus on the development and implementation of reference measurement procedures, calibration materials, and guidelines. These efforts are critical in reducing variability in laboratory measurements, which is essential for patient safety, diagnosis, treatment, and monitoring of diseases.

A cornerstone of IFCC's leadership is its collaboration with international organizations such as the World Health Organization (WHO) and the International Organization for Standardization (ISO). These partnerships strengthen global efforts to harmonize laboratory practices, promoting the adoption of best practices across diverse healthcare settings.

Moreover, the IFCC actively supports education and training initiatives to ensure that laboratory professionals are equipped with the latest knowledge and skills necessary to implement standardized practices. Through conferences, workshops, and publications, the IFCC disseminates valuable information that fosters a global culture of quality and excellence in laboratory medicine.

Overall, the IFCC's global leadership in standardization and harmonization is instrumental in improving patient outcomes by ensuring consistent and reliable laboratory testing worldwide.

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Global Horizons in Newborn Screening: Bridging Gaps and Developing Synergies for Universal Health Advancements across Regions

Aysha Habib Khan

Haiderali R Charania Professor, Consultant Chemical Pathologist, Department of Pathology & Laboratory Medicine, Aga Khan University, Karachi, Pakistan

Prof Aysha Habib Khan is Haiderali R Charania Professor of Chemical Pathology at Aga Khan University. She is founding head of biochemical genetics lab and chair of newborn screening committee at AKU and Vice President Pakistan Society of Chemical Pathology. She Co- Chair the IFCC/ISNS global taskforce of newborn screening committee and serves as treasurer and executive council member of international society of newborn screening and Academic Council member representing Pakistan in Society of Study of Inborn Errors of Metabolism (SSIEM).

Newborn screening (NBS) is critical in early detection and management of treatable childhood non-communicable diseases (NCDs). While high-income countries have well-established NBS programs, low and middle-income countries (LMICs) still face challenges in universally screening all newborns, leading to preventable adverse outcomes. Significant global disparities exist in NBS policies, largely due to variations in healthcare infrastructure and strategic priorities.

To address these gaps and enhance global health equity, the International Federation of Clinical Chemistry (IFCC) and the International Society for Neonatal Screening (ISNS) have established a task force aimed at supporting the development of NBS programs in resource-limited settings. This task force has facilitated networking among local advocates, health policymakers, and engaging experts from high-income countries to guide the implementation of NBS programs in LMICs. A needs assessment survey conducted in 2021, with responses from 84 countries, highlighted the existing NBS activities and identified congenital hypothyroidism, phenylketonuria, congenital adrenal hyperplasia, and cystic fibrosis as the most commonly screened disorders.

Key successes of the task force include legislative advancements in the Dominican Republic and the development of a national action plan for NBS in South Africa, and many other countries including Indonesia, Kazakhstan etc. The task force has also emphasized the importance of multidisciplinary engagement, infrastructure development, and improving access to treatment.

To further support NBS efforts, ISNS is developing an interactive world map that visualizes global NBS coverage, promoting best practices, and encouraging collaboration among stakeholders. This tool aims to enhance newborn healthcare access, support public health initiatives, and improve infant health outcomes globally. Through these initiatives, the global community is making strides towards achieving universal NBS and advancing the United Nations Sustainable Development Goals by 2030.

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The role of newborn screening in the early detection of rare disorders: doing good and avoiding harm

James R Bonham, Sheffield Children's Hospital, S10 2TH, UK

Dr. Bonham is currently the National Laboratory Lead for the Newborn Screening Blood Spot Program in the United Kingdom on behalf of Public Health England. He is also president of the International Society for Neonatal Screening, which includes more than 500 members in 40 countries. In 2012, he led a study to introduce additional inherited metabolic disorders into the national newborn screening program in the UK. Four of these were incorporated as part of the program in England and Wales, starting in 2015. He has interests in the organization, quality, and effectiveness of newborn screening and how this might be optimized and extended to benefit patients and families in the UK and Europe, and more recently to low- and middle-income countries as part of the Task Force on Global Newborn Screening. His efforts in these areas were generously recognized by the award of an MBE in 2020.

In 1963, Dr Robert Guthrie helped introduce newborn screening for phenylketonuria in the USA. Since that time more than 60,000 children have benefitted from this life changing intervention. Of course, it did not end with PKU but in subsequent years other disorders were added.

A breakthrough came in the mid-1990s due to the work of Millington and Chace who described a method using MS/MS capable of detecting up to 50 additional conditions. To date around 500,000 babies have benefitted from rapid and effective asymptomatic treatment.

Despite these successes, newborn screening can cause harm as well as benefit. Approximately 400,000 families may have received a false positive result with increased parental anxiety and increased vigilance during childhood. In addition, uncertainty for the parents of asymptomatic children with a mild form of the disease is not uncommon and requires great care to avoid overtreatment.

Alongside these benefits and challenges, genomic screening has now become a reality, at least as part of pilot studies and research. This brings opportunities to include conditions where no biochemical marker is available. It does though pose ethical and practical issues.

The key messages will include the imperative to consider newborn screening as a program and not just a test. The need for clear case definitions and a means to assess the long-term outcome before screening begins. The importance of improving the positive predictive value of screening by the use of second tier tests and other means. When considering the introduction of genomic testing we will emphasize the importance of protecting the reputation of screening and the need to use genomics, proteomics and metabolomics as complimentary techniques.

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The role of Laboratory Professionals in managing AI applications in the routine laboratory

Sergio Bernardini, (MD, PhD), is a full professor of Clinical Biochemistry and Clinical Molecular Biology at the Department of Internal Medicine of The University of Rome Tor Vergata, and the head physician of the Clinical Molecular Biology Unit at the Tor Vergata University Hospital.
He received his degree in Medicine in 1986 and the PhD in Paediatric Sciences in 1995. He has specialized in Paediatrics (1990) and in Clinical Chemistry and Biochemistry (1998).
2018-2019: President of the Italian Society of Clinical Biochemistry and Clinical Molecular Biology (SIBioC)
2012-2017: Secretary of the International Federation Clinical Chemistry and Laboratory Medicine (IFCC)

The Total Testing Process is changing too because some Digital Assistants start to be implemented in the pre-preanalytical phase (Intelligent ordering system), in the pre-analytical phase (Intelligent manager) and in the post-analytical Phase (Intelligent Interpreting and reporting system).
Artificial Intelligence raised many concerns from humanists but, at least to date, there is nothing really artificial and then we prefer talk about “Augmented Intelligence” because any process has still its roots in human work. AI is the science of making machines do things that would require intelligence if done by human.
Indeed, human and machine intelligence can interact in a continuum from assisted intelligence, to augmented intelligence and finally autonomous artificial intelligence also called strong, broad or general, but this kind of intelligence is very far from being real.
In 1989 the term “Machine learning” was introduced to apply statistical methods in extracting information, knowledge, useful patterns, actionable insights from large amounts of data (data set) usually to solve a specific problem. Then ML was applied in Health Care where a big amount of Data is produced from clinical notes, images (X-ray, CT, MRI…), clinical laboratory results, pathology images and reports, medication, genome and family history and, in the next future, omics patterns report. Then, these clinical Data are usually merged with other Data obtained from Recommendations, Guidelines, Best Practice, Current Research, Ongoing clinical trials, new drugs Discovery and Doctors experiences.
The application of augmented Intelligence tools in Medicine is growing very fast because it can be useful to face new evolutions in the health care Systems all over the world: increase in request for care and life expectancy, multi-chronicity, patient’s empowering, reduced time with Doctors, Limits in governments investments for Health Care and Increased expenses out pocket.
Recently also Laboratory Medicine start to implement Augmented Intelligence tools in Hematology, Autoimmunity, Mass Spectrometry and Cancer diagnosis.

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Artificial intelligence in laboratory medicine: challenges and opportunities

Mario Plebani
President, European Federation of Clinical Chemistry and Laboratory Medicine
Full Professor of Clinical Biochemistry and Clinical Molecular Biology
Chief Department of Laboratory Medicine, University Hospital –University of Padova, Italy

Dr. Plebani is professor of clinical biochemistry and clinical molecular biology at the University of Padova School of medicine and chief of the department of laboratory medicine at the University Hospital of Padova in Italy. He served as president of the International Society of Enzymology for four years, president of the Italian Society of Clinical Biochemistry and Molecular Clinical Biology for five years, and president of the Federation of Italian Societies of Laboratory Medicine for three years. Dr. Plebani is editor-in-chief of *Clinical Chemistry and Laboratory Medicine* and co-editor-in-chief of *Diagnosis.*

Laboratory medicine is a constantly progressing field with novel tests and techniques being developed and incorporated into the repertoire of clinical laboratories at an astonishing rate. As a central part of the healthcare system, clinical laboratories have been coping with incremental improvements in informatics for decades, and have been pioneers in digitization and computer-assisted tools as software. This fact, in addition to the central role of clinical laboratories in patient healthcare, highlights the importance of improving timely and accurate diagnosis and patient care through Artificial Intelligence (AI). As a result, the laboratory medical profession may now be facing a big transformation due to disruptive technologies, namely digitalization, Big Data, AI and machine learning (ML). In particular, the adoption of AI tools seems to receive increasing interest in improving the pre-analytical phase -namely appropriateness in test request- and the post-analytical phase (laboratory report). In addition, AI tools have been found to potentially reduce errors in the total testing process, thus improving quality and patient safety. The potential application of AI and ML models to laboratory data could be relevant, but to manage the change and uncover additional benefits to patient care, there is an urgent need to adapt expertise within laboratories and to improve the cooperation between laboratories and AI experts. Current challenges in the right adoption of Ai in laboratory medicine require many efforts, including: a) Guidelines for the development and regulation of AI models for clinical laboratories must be further implemented and improved; 2) willingness to change existing clinical structures and attitudes toward this new technology, and thus there is a need to educate a variety of stakeholders; 3) selection of the most appropriate model for patients, namely those with more complex conditions; 4) Focus on validating the clinical validity and generalizability of AI models. In addition, clinical laboratories must ensure that

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laboratory data are accurate and reliable to avoid the risk of sophisticated systems such as ML and AI using inaccurate results which in turn can lead to inaccurate and potentially harmful information. This concept has been well summarized in the mantra “garbage in, garbage out”.

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Induction of multiple mechanisms of programmed cell death by natural products

Thomas Efferth

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Professor Dr. Prof. h. c. mult. Thomas Efferth is Director of the Institute of Pharmaceutical and Biomedical Sciences and chair of the Department of Pharmaceutical Biology, Johannes Gutenberg University, Mainz, Germany. He is biologist by training (Technical University of Darmstadt, Germany). Ph.D.thesis: German Cancer Research Center (DKFZ), Heidelberg, Germany (1990).

Awards: Prize of the Southwest German Association for Medicine (1991), Willmar-Schwabe-Award of the German Society for Medicinal Plant Research (2006), citizen medal of the City of Heidelberg, Germany (2008), CESAR Award for Translational Oncology (2011), SCENTEDdrop Award on medicinal and fragrant herbs (2015), Qihuang International Award of the Chinese Association of Chinese Medicine (2017), SFE Outstanding International Ethnopharmacologist Award (2021). High Impact Paper Award of the journal Engineering (Chinese Academy of Engineering; 2021)

He is a member of the Academia Europaea and of the World Academy of Sciences. In 2020 (and update in 2022), he was ranked in the Stanford University Citation Ranking among the top 2% of all scientists and scientific disciplines (https://data.mendeley.com/datasets/btchxktzyw/2).

Furthermore, he holds five honorary professorships and is visiting professor (“professional visitor”) .at the McLean Hospital, Harvard Medical School, Boston, MA, USA.

Thomas Efferth published 850+ PubMed-listed papers in peer-reviewed journals in the field of cancer research, pharmacology, and natural products (Hirsch-factor: 115; citation rate: 67,000; acc. to Google Scholar) and a textbook on ‘Molecular Pharmacology and Toxicology’ (Springer Publisher). He is editor-in-chief of “Phytomedicine” and “Phytomedicine Plus” as well as associate editor of several other pharmaceutical journals and scientific advisory board member of several organizations.

Eighteen of his former lab members were promoted to leading academic positions (full professors, associate/assistant professors).

The focus of Efferth's research is on the pharmacology of cancer and viral infections, molecular and cell biology, systems biology and bioinformatics.

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Programmed cell death (PCD) is a complex machinery of diverse molecular mechanisms that finally decide on a cell's fate. After the epoch-making discovery of apoptosis as a genetically driven mode how cells die by Kerr and colleagues in the year 1972 (1), apoptosis research dominated many fields of biomedicine for decades. PCD represents a critical process to maintain homeostasis in healthy organisms. On the other side, PCD is involved in a plethora of pathophysiological processes. During this time, it became clear that other modes of PCD independent of apoptosis exist (2), and research on non-apoptotic cell death came into the focus worldwide. Due to the complexity, different classifications and nomenclatures, there is some confusion on cell death determination. In this presentation, we introduce the hallmarks of different cell death modes and describe a classification system with the categories programmed versus on-programmed cell death as well as apoptotic versus non-apoptotic cell death. Recently, non-apoptotic forms of PCD became hot topics in biomedical research, including vacuole-presenting cell death (autophagy, entosis, methuosis, and paraptosis), mitochondrial-dependent cell death (mitoptosis, partanathos), transition metal-dependent cell death (ferroptosis, cuproptosis), immune-reactive cell death (pyroptosis, NEToptosis, immunogenic cell death), and others (necroptosis, calcioptosis) (3-6). Like synthetic drugs, natural products and herbal mixtures also induce diverse modes of PCD. We give an overview with emphasis to herbal mixtures from traditional Chinese medicine (TCM). Herbal medicine is known to maintain the balance in the body and prevent diseases and also to treat diseases, if this body balance got lost. The influence of TCM on PCD represents an important role in this context (7).

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Diagnosing resistance to adrenal steroids: Overcoming clinical obstacles

Mona Nourbakhsh
Assistant professor of pediatric endocrinology, Aliasghar Children Hospital, School of Medicine, Iran University of Medical Sciences.

Primary adrenal insufficiency occurs when the adrenal gland is unable to produce adequate glucocorticoid and/or mineral corticoid hormones. High or low levels of androgenic hormones may also be present. Primary adrenal insufficiency can have multiple causes. Familial glucocorticoid resistance and familial glucocorticoid deficiency (FGD) are two uncommon hereditary causes of primary adrenal insufficiencies.
FGD Type 1 occurs because of the mutations in the gene that encodes the adrenocorticotropic hormone (ACTH) receptor (MC2R), a hormone that stimulates cortisol production, so the adrenal will not be able to respond to ACTH. The disease is characterized by isolated glucocorticoid deficiency and patients therefore exhibit low or often undetectable serum cortisol with high plasma ACTH levels.
FGD Type 2 is often due to mutations in the gene encoding the steroidogenic factor 1 (SF-1) or other transcription factors involved in adrenal gland development and function. Resistant Forms of Glucocorticoid Deficiency are generally a result of receptor resistance with adequate levels of glucocorticoids in the blood, the body's tissues may not respond to cortisol or enzyme resistance which defects in enzymes involved in the metabolism or action of glucocorticoids might lead to reduced effectiveness of these hormones. Hyperpigmentation, hypoglycemia, seizures, and low blood pressure are the disease's clinical manifestations. If untreated, the disease may be fatal, and recurring hypoglycemia can cause learning disabilities as well as other neurological consequences over time. The course of treatment frequently needs high dose glucocorticoid replacement. Careful monitoring of growth and clinical status is crucial, and the dose must be modified based on clinical response.

Keywords: Adrenal steroids, Familial glucocorticoid resistance

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Alterations of gonadal hormone levels through sexual development

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Gonadal hormones are produced by the human gonads. These hormones are divided into two major groups: steroid hormones, particularly testosterone, estradiol, and progesterone, and peptide hormones, especially activin/inhibin and AMH. Both groups play distinct roles in human physiology and exert their effects within the gonads and beyond. Testosterone is the primary androgen and plays a critical role in the development of primary and secondary male sex characteristics, as well as in spermatogenesis.
Estradiol and progesterone are the main female hormones responsible for the development of secondary sex characteristics and reproductive functions. From fetal life to adulthood, the circulating levels of these hormones and peptides fluctuate. In early fetal life, testicular hormones drive the masculinization of the genitalia. During the first 3–6 months after birth (also known as 'mini-puberty'), gonadotropin and gonadal endocrine functions remain active. During the remainder of infancy and childhood, gonadotropins and gonadal hormones become dormant, though some hormones continue to be secreted by the gonads. Puberty marks the end of childhood and is characterized by fluctuating reproductive hormones that drive physiological and psychological changes, leading to sexual maturation and fertility. This presentation will focus on the types of gonadal hormones and peptides, as well as their roles and changes during sexual development.

Keywords: Sexual development, gonadal hormones

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Apparent Mineralocorticoid Excess; From Discovery to Treatment

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Apparent mineralocorticoid excess (AME) is a rare autosomal recessive disorder caused by mutations in the 11β-hydroxysteroid dehydrogenase type 2 gene (HSD11B2), leading to a deficiency of the HSD11B2 enzyme. While the disorder was first identified in 1977, the mutation responsible for the enzyme deficiency was not known, until the first mutation was discovered in our patients in 1995 through our collaboration with Prof. Maria I. New. Since then, approximately 40 causative mutations have been identified. HSD11B2, part of the short-chain alcohol dehydrogenase family, catalyzes the NAD+-dependent dehydrogenation of cortisol. In the kidneys, this enzyme converts cortisol into its inactive form, cortisone, protecting the mineralocorticoid receptor from cortisol's effects, despite the receptor having an equal affinity for cortisol and aldosterone in vitro, and cortisol being present in the bloodstream at much higher levels. Without HSD11B2, excess cortisol activates the mineralocorticoid receptor, resulting in hypertension without elevated aldosterone or renin levels.

Patients with AME exhibit low birth weight, failure to thrive, low-renin hypertension, and hypokalemia. The impaired conversion of cortisol to cortisone results in a characteristic elevation in the urinary ratio of tetrahydrocortisol (THF) plus allo-THF to tetrahydrocortisone (THE), [(THF+alloTHF)/THE].

Hypertension is a key clinical feature in this disorder; thus, early organ damage affecting the kidneys, nervous system, muscles, heart, and eyes may occur due to chronically elevated blood pressure, metabolic alkalosis, and severe hypokalemia, potentially leading to renal failure.

Our Patients were effectively treated with Spironolactone, a potent antagonist of the mineralocorticoid receptor, which normalized potassium levels. In some cases, antihypertensive medications like furosemide and captopril were also required to control blood pressure. Treatment resulted in catch-up growth, and long-term follow-up demonstrated it to be successful in the management of the patients.

Keywords: Apparent mineralocorticoid excess, 11β-hydroxysteroid dehydrogenase type 2

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Challenges of sex determination in disorders of sex development

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Sex determination in humans involves the interaction of molecular structures, chromosomes during egg formation, transcription factors, and hormones. Any disruption or confusion in these factors can undoubtedly lead to significant challenges in accurately determining gender. Additionally, the treatment team, which may include a pediatric endocrinologist, surgeon, psychiatrist, and forensic medicine specialist, must also consider other factors such as religious beliefs, misinformation, and incorrect advice from those around the patient, making the process of determining a person's identity even more complex.

In Iran, where schools are segregated by gender, individuals experiencing gender confusion may not have the opportunity to make fully informed decisions, unlike in many Western countries. It is crucial that the individual's gender and name are largely determined before starting school. I would like to share an interesting case that I hope will be helpful in deciphering the intricate clinical and paraclinical features in these disorders.

Keywords: heme oxygenase-1, calorie restriction, thioredoxin, quercetin,

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Applications of Artificial Intelligence in Molecular Diagnostics and Genomics

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Artificial Intelligence (AI) is revolutionizing molecular diagnostics and genomics by enhancing accuracy, efficiency, and personalization in disease detection and treatment. Key applications of AI include the followings:

1. **Genomic Data Analysis:** AI processes large genomic datasets to identify genetic variants associated with diseases. This application leads to early diagnosis and personalized plans for treatment and management.
2. **Image-Based Diagnostics:** AI-powered imaging techniques improve the interpretation of molecular imaging, such as morphologic diagnosis and of genetic disorders at chromosomal, cellular and even clinical levels. These techniques enhance image reconstruction, segmentation, and denoising, leading to more precise diagnostics.
3. **Predictive Analytics**: AI models predict disease progression and patient outcomes by analyzing historical and real-time data which is vital for managing chronic diseases and tailoring interventions.
4. **Automated Workflows**: AI also automates routine tasks in molecular diagnostics, such as sample processing and data entry, reducing human error and increasing throughput.
5. **Natural Language Processing (NLP)**: NLP algorithms extract meaningful information from electronic health records (EHRs), leading to the identification of disease patterns and patient stratification.

Challenges, limitations and Future Directions:
Despite its potential, AI in molecular diagnostics faces challenges which include data privacy concerns, the need for large annotated datasets, and the integration of AI systems into currently active clinical workflows.

Keywords: Artificial Intelligence, Molecular Diagnostics, Genomics

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Biochemical Parameters in Infertility

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Infertility is defined as the failure to achieve a clinical pregnancy after 12 months or more of regular, unprotected sexual intercourse. Infertility is a common medical condition that affects up to 15% of couples and affects approximately 186 million people worldwide. It has been raised as a reproductive health problem all over the world. Based on the other studies the prevalence of infertility in different regions of the world is different, and its prevalence in Iran is higher than the global average.
Diagnostic evaluation of infertility is crucial to achieving improvements in targeted prevention and treatment outcomes. Routine measurement of biochemical parameters reflecting thyroid dysfunction, immunological disorders, autoimmune mechanisms, insulin resistance and malabsorption of selected micro- and macronutrients are required to assess infertility. Hypothyroidism may cause menstrual disturbances, infertility as well as heighten the risk of miscarriage by causing an increase in thyrotropin-releasing hormone levels (TRH).
Immunological infertility is diagnosed in cases of spontaneous production of antibodies which interact with antigens occurring on either male or female gametocytes. Therefore, routine measurements of biochemical parameters are required in diagnosis and treatment of infertile couples.

Keywords: Biochemical Parameters, Infertility, Iran

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The role of molecular and biochemical biomarkers in infertility practice

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Infertility is a global public health problem with a huge impact on individuals, families, societies and countries worldwide, which affects about 15% of couples at reproductive age. Basically, Human reproduction is a complex biological process with low-efficiency, so therapeutic interventions become necessary due to Failure following one year of continuous efforts to conceive. Identification the causes of infertility and treatment options are very complex, time consuming, strenuous, expensive and frustrating. According to current evidences, the role of male and female is the same in occurrence of infertility. Diagnosis and treatment of infertility is performed using functional biomarkers of the reproduction system in men and women, whose numbers and their efficiency have been improved over time. in spite of development in our knowledge and data on fertility process and infertility diagnosis, it is still unknown the causes of infertility in about 20 to 25% of infertile couples, despite their normal fertility parameters and continuous efforts to conceive. The problems of couples with unexplained infertility is not obvious with available tools, techniques and biomarkers, so we need more accurate tools and newer biomarkers. the success rate of assisted fertility treatments is relatively low, which is due to lack of knowledge on molecular details of critical reproduction processes such as spermatogenesis, oogenesis, sperm and oocyte selection, fertilization and early development of the embryo, implantation, early abortion and many other obscure. Therefore, the identification of new biomarkers for the above processes is an inevitable necessity for success in diagnosis and treatment of infertility. the high throughput techniques are powerful tools for identification of new biomarkers. Currently, the discovery of new biomarkers has gone beyond the genome and protein level, current research has expanded to the transcriptome, metabolome, glycome, epigenome and thousands or even millions of other cellular compounds and products. After identifying a new biomarker, its characteristics should be evaluated in terms of sensitivity, specificity, changes in health and disease, easy and cheap tracing and measurement, its value in prognosis, diagnosis, treatment, follow-up and recurrence of the disease in order to obtain the necessary approval for using in the clinic and treatment of infertile patients.

Keywords: Biochemical biomarkers, Infertility, Molecular biomarkers

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The Role of the Urologist in a Reproductive Endocrinology and Infertility Practice

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Endocrinopathies are uncommon etiologies of male factor infertility but the hormonal assessment is a vital component of male fertility evaluation as endocrine disorders are markedly reversible causatives of male infertility. Precise hormonal regulations are prerequisites to maintain normal male fertility parameters. The core male reproductive event, spermatogenesis, entails adequate testosterone concentration, which is produced via steroidogenesis in the Leydig cells. Physiological levels of both the gonadotropins are needed to achieve normal testicular functions. The hypothalamus-derived gonadotropin-releasing hormone (GnRH) is considered the supreme inducer of the gonadotropins and thereby the subsequent endocrine reproductive events. This hypothalamic–pituitary–gonadal (HPG) axis may be modulated by the thyroidal or adrenal axis and numerous other reproductive and nonreproductive hormones. Disruption of this fine hormonal balance and their crosstalk leads to a spectrum of endocrinopathies, inducing subfertility or infertility in men. In this presentation I will discuss the most essential endocrinopathies associated with male factor infertility to aid precise understanding of the endocrine disruptions-mediated male infertility to encourage further research to reveal the detailed etiology of male infertility and perhaps to develop more customized therapies for endocrinopathy-induced male infertility.

Keywords: Reproductive Endocrinology, Infertility, Urologist

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Assay design for large protein complexes formation in programed cell death modalities

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Programed cell death modalities like apoptosis, pyroptosis and necroptosis are crucial for homeostasis in several human disorders like cancer and neurodegenerative diseases. Formation of large protein complexes is a hallmark of all of programmed cell death pathways. Design of new assays which evaluate distinct protein complexes in death pathways is critical to identify potential therapeutic agents that control these cellular responses. Reconstitution of split luciferase fragments have been widely recruited for assessing protein complexes in regulated cell death due to their simplicity, sensitivity, and known chemistry. Split luciferase complementary assays have been used to probe role of native and mutant forms of Apaf-1, Ripk1, NLRP3 structure in regulation of apoptosome, necrosome and inflammasome formation; respectively. Different multiplex bioluminescence and fluorescent assays which simultaneously distinguish between the various cell death phenomena in both in vitro and cell-based assays will be presented.

Keywords: Large protein complexes, Programed cell death

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Photoproteins in drug screening and medical diagnostics

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Photoproteins are bioluminescent proteins that emit light when exposed to specific conditions or stimuli. The Ca2+-regulated photoproteins are a unique class of bioluminescent proteins among those using coelenterazine as a reaction substrate. Thus, part of the function of this category of photoproteins in diagnostic fields is calcium dependent. In drug screening, photoproteins are used as molecular sensors to detect interactions between drugs and target molecules. By coupling these proteins with the molecules of interest, researchers can easily measure changes in light emission, providing a quick and accurate way to assess drug efficacy and safety. In medical diagnostics, photoproteins and cells (cell based biosensors) can be genetically engineered to produce light in the presence of certain biomarkers associated with specific diseases. As mentioned above, the Ca2+ signaling pathway plays a central role in diseases. That's why calcium-regulated photoproteins have been used in this field. This approach offers a promising method for early diagnosis and monitoring of various diseases, enhancing the possibilities for personalized medicine and targeted therapies. Some of recent photoprotein-based biosensors and reporters developed by our research group include hybridoma-based biosensor for rapid detection of V. cholerae, selective reporter for detection of dopamine, rapid and sensitive molecular switch for SARS-Cov-2 detection, bioluminescence measurement of superoxide anion in infertile men with oxidative stress, and rapid screening of drug candidates against EGFR/HER2 pathway. Overall, the diverse applications of Ca2+-regulated photoproteins highlight their importance in advancing our understanding of biological systems and developing novel technologies for various fields.

Keywords: Photoproteins, drug screening, medical diagnostics

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Protein engineering to construction of a truncated XIAP with potential interacting with caspases 3/7/9 based on luciferase complementation assay

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Up-regulation of IAPs (inhibitor of apoptosis proteins) can lead to dysregulated apoptosis and increased the resistance of oncogenic cells. X-linked IAP (XIAP) is a direct inhibitor of cell-death proteases, caspase-3, -7, and -9. The region BIR2 and its segment N-terminal are responsible for binding and inhibiting caspase-3 and -7, and BIR3 binds to caspase-9. In this research, we developed and optimized an in vitro XIAP/caspase interaction method based on a split-luciferase complementation assay. Here, two truncated XIAP consisting of linker-BIR2 region with the different lengths were attached to NLuc domain (BIR2-NLuc and BIR2-BIR3-NLuc) and caspase-3 and caspase-9 fused to CLuc domain, produced in bacterial host, purified, and then their interactions evaluated and compared. According to our results, luminescence signal from the interaction between BIR2-BIR3 with caspase-3 was stronger than BIR2. Moreover, the signal of XIAP construct containing BIR2-BIR3 in interact with caspase-9 was significantly higher than caspase-3. Also, a decrease in caspase-3 activity in the presence of both types of truncated XIAP fusion proteins was observed. Our data demonstrated that the length of truncated XIAP protein influence their ability to better conformational adaptation to affect the function of fusion proteins. Taken together, this study provided the efficient bioluminescent probe for interrogation of a wide variety of compounds on XIAP and caspase-3/7/9 interaction.

Keywords: Truncated XIAP; BIR2-BIR3; Caspase 3; Caspase 9; Split-lucifrrase

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Split Nanoluciferase: Shedding Light on Innovative Cancer Biomarkers Identification

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This study investigates the development of innovative assays for critical cancer biomarkers, specifically alpha-fetoprotein (AFP) and prostate-specific antigen (PSA). Our approach employs a tri-part split-luciferase system in combination with targeted nanobodies. This involves the fusion of nanobodies with the components of the split luciferase. When the nanobodies bind to their respective targets, the luciferase components reconstitute, leading to the generation of a luminescent signal. The findings reveal that these assays demonstrate high sensitivity and specificity, with detection limits that are comparable to those of traditional methodologies. This strategy not only simplifies the detection of biomarkers but also establishes a pathway toward more cost-effective diagnostic solutions in oncology, thus holding the promise of reducing overall healthcare expenses.

Keywords: Split nanoluciferase; Nanobody; Cancer; Prostate-specific antigen; Alpha-fetoprotein.

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Biosensor Based on Renilla Luciferase-Annexin 5 for Early Detection of Apoptosis

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Apoptosis, or programmed cell death, is a critical process in maintaining cellular homeostasis and is implicated in various diseases, including cancer. The early detection of apoptotic cells is vital for understanding disease progression and the effectiveness of therapeutic interventions. Annexin V is a protein that selectively binds to phosphatidylserine, which translocates to the outer leaflet of the plasma membrane in early apoptotic cells. The integration of Renilla luciferase with annexin V in a biosensor allows for high sensitivity and specificity in detecting these early apoptotic events.

In this study Annexin V was linked to Renilla luciferase using the recombinant fusion protein technology. The gene of fusion protein was cloned in pET21a and the recombinant probe expressed as soluble protein with his tag. Subsequent purification was achieved through (Ni-NTA) affinity chromatography followed by size exclusion chromatography. Then the highly purified probe was dialyzed against PBS buffer and the protein concentration was quantified using the Bradford assay. This probe exhibits the ability to selectively bind to apoptotic cells, enabling the detection of Renilla luciferase activity using a luminometer. Furthermore, the probe was evaluated in a preclinical study focusing on apoptosis in neutrophils.

The biosensor utilizing Renilla luciferase and annexin V marks a significant advancement in cell biology, particularly for early apoptosis detection. This innovation promises to enhance diagnostics and treatments for various diseases, emphasizing the need for ongoing research. The RLuc/Annexin V biosensor is distinguished by its use of bioluminescence detection, which offers a novel approach to identifying apoptosis. Additionally, this biosensor enables high-throughput drug screening, broadening its use in biomedical research. It also has great potential for non-invasive in vivo imaging to track apoptosis in small animal models. By leveraging the bioluminescent properties of Renilla luciferase, this approach facilitates sensitive and quantitative measurement of apoptotic stages in cells. In conclusion, this biosensor is a crucial tool for improving our understanding and management of apoptosis-related diseases, deserving further investigation and application.

Keywords: apoptosis, Renilla luciferase, Annexin V, biosensor, translocate

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Medical genetic methods for the management of inherited metabolic disorders in the context of newborn screening

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This lecture explores cutting-edge approaches in medical genetics for managing inherited metabolic disorders, with a focus on newborn screening.
Newborn screening is a crucial tool for the early detection of these disorders, enabling timely interventions that can prevent severe complications or irreversible damage.
With the advent of advanced genetic techniques such as next-generation sequencing (NGS) and whole-genome sequencing (WGS), the scope of newborn screening has broadened, offering faster, more accurate identification of metabolic disorders at birth.
These genetic methods allow for personalized treatment plans tailored to the specific mutations and metabolic pathways involved, greatly improving patient outcomes.
Clinical geneticists play a key role in integrating genetic data with clinical findings to optimize diagnosis and treatment, while also offering vital genetic counseling to families.
This innovative approach not only improves disease management but also highlights the growing importance of genetic testing in the context of early-life interventions, transforming the future of inherited metabolic disorder care.

Keywords: Inherited metabolic disorders, Newborn screening

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Laboratory diagnostic approaches in metabolic disorders

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The diagnosis of inborn errors of metabolism (IEM) takes many forms. Due to the advances in newborn screening (NBS), the diagnosis of many IEM has become relatively easy utilizing laboratory biomarkers. For the majority of IEM, early diagnosis prevents the onset of severe clinical symptoms, thus reducing morbidity and mortality. However, due to molecular, biochemical, and clinical variability of IEM, not all disorders included in NBS programs will be detected and diagnosed by screening alone. The proper use of routine laboratory results in the initial patient assessment is also discussed, which can help guide efficient ordering of specialized laboratory tests to confirm a potential diagnosis and initiate treatment as soon as possible.

In recent years, advancement in technologies such as tandem mass spectrometry (MS/MS) and next-generation sequencing (NGS) employing a massive parallel sequencing strategy, have profoundly expanded our knowledge of IEM and metabolic disorders in general.

Appropriate test selection must be driven by a combination of the patient's clinical presentation and the results of routine first tier laboratory tests, which can help guide more specific testing. When evaluating a patient for a possible IEM, routine laboratory tests can identify underlying patterns suspicious for a metabolic defect. Although biochemical genetic and molecular genetic tests are required to confirm a diagnosis, basic laboratory tests are still important and often provide the first clues to a possible underlying IEM. The field of IEM continues to grow as evolving technologies like NGS and comprehensive metabolomic profiling strategies provide deeper insight into mechanisms.

Keywords: Laboratory, metabolic disorders, Iran

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Applications of Tandem Mass Spectrometry in the Diagnosis of Metabolic Disorders

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Metabolic disorders are medical conditions caused by changes in specific genes that defects the activity of enzymes, transporters, or cofactors, which lead to the accumulation of abnormal metabolites, lack of essential products, or the accumulation of intermediate metabolites.
The goal of newborn screening (NBS) is to detect disorders that threaten life or long-term health, before the infant becomes symptomatic. Early diagnosis and treatment of these rare disorders may significantly reduce mortality and morbidity in affected patients.
In Expanded Newborn Screening, with the help of tandem mass spectrometry we can now readily detect multiple metabolic diseases on a single dried blood spot (DBS). Tandem mass spectrometry is a sensitive, specific and reliable method for screening of inborn errors of metabolism. By this method we able to detect a wide range of amino acids and acylcarnitines, thus enable to screen more than 40 genetic diseases including fatty acid and organic disorders. Liquid chromatography combined with MS/MS (LC-MS/MS) and GC/Mass are employing for second-tier and confirmatory tests.

Keywords: Tandem Mass Spectrometry, Metabolic Disorders, Applications
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Non-metabolic changes of metabolites in the interpretation of diagnostic tests for metabolic diseases

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Inborn errors of metabolism are a heterogeneous group of disorders that may be inherited or may occur as the result of spontaneous mutations. These diseases involve failure of the metabolic pathways. Although any given inborn error of metabolism is very rare, taken as a group, inborn errors of metabolism occur in 1 in 2500 births. They can present at any age, and therefore, awareness of these diseases, their presentations, and their evaluation is critical for interprofessional team members.

Intraindividual variations will occur with respect to the time of sampling, the patient's clinical status, eventual diet management, and whether the sample is collected when the patient is fasted or fed. Sampling during fasting or metabolic decompensation is often considered to be most valuable because, in most cases, metabolites of interest are then excreted selectively or at a higher concentration. On the other hand, metabolic decompensation, such as lactic acidosis, ketosis, or liver failure, gives rise to an abnormal excretion of organic acids that are otherwise involved in particular IEM; this sometimes renders interpretation even more difficult.

Information on diet, drug intake, and clinical symptoms and signs may often be required by the clinical chemist to refine his or her interpretation. The clinical chemist can inform the clinician of pitfalls, the possible origins of abnormal results, and further analyses that can be performed. On the other hand, a final diagnosis can be established only in terms of the patient's history and clinical picture, in addition to results from biochemical and medical examinations.

Keywords: Metabolites, Metabolic diseases, Iran

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Ethical considerations in medical diagnostic laboratories based on the professional code of ethics of the Islamic Republic of Iran

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Background: Medical laboratories are one of the health care delivery environments, whose service providers must be familiar with ethical norms and act accordingly. This study aimed to review and analysis the relevant ethical provisions in the professional code of ethics of the Iran's medical council (IMC).
Methods: In this document analysis, the professional code of ethics for the members of IMC was analyzed from the perspective of ethical considerations in laboratories.
Results: Health professionals who works in medical diagnosis laboratories, like other health professionals, must follow the general tasks explained in this code. The materials of this section are emphasized on establishing an effective and respectful relationship with clients/patients. The provisions/articles that directly refer to the observance of ethical standards in laboratories are: Article 30 on "Considering the priority of the interests of patients when referring them to other medical professionals or para- clinical institutions such as imaging centers, pharmacies, hospitals, and the like". Article 31 on "Prohibition of receiving and granting any reward or privilege, including cash, gift, discount on rent or office fees, request for cross-referral of the patient, and the like, in exchange for referring the patient to other medical professionals, to the diagnostic and treatment centers, including hospitals, laboratories, imaging centers, rehabilitation centers, or medical equipment companies, pharmacies, and the like". Other related items in the bill of rights of clients to medical diagnostic laboratories can be implicitly found in the code.
Conclusion: Health professionals working in medical laboratories should be aware of the provisions of the professional code of ethics as well as the provisions of the bill of rights of clients to medical diagnostic laboratories and act accordingly.

Keywords: professional ethics, clients' rights charter, medical diagnostic laboratories

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A review of professional ethics in the medical laboratory

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Laboratory services are an integral and important part of diagnostic and therapeutic procedures. Providing these services can sometimes be accompanied by ethical challenges. The most important and common issues of professional ethics in the medical laboratory by using professional texts, resources and observations, include: respect for patients' autonomy, confidentiality and privacy, truth-telling, conflict of interest, relationship between the laboratory and other stakeholders, research, providing standard and quality of services, professionalism and new technologies in the laboratory. The development of facilities and technologies has caused new challenges to be added to the previous issues. It is important to pay attention to the mentioned cases because understanding these facts and thinking of a solution in each case can prevent conflict between stakeholders and complaints of clients from the laboratory. In this article, we will analyze a number of cases using the code of ethics of laboratory employees and the general guide of professional ethics for medical professionals and affiliates of the medical council organization.

Keywords: Medical laboratory, Professional ethics

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Code of Bioethics for Medical Laboratory Technologists

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The Code of Ethics, along with the Standards of Practice, defines professionalism in the practice of medical laboratory technology (MLTs). MLTs adhere not only to the guidelines, but also to the underlying spirit and precepts. A medical laboratory technologist's fundamental responsibility is to manage the prescribed medical laboratory services for patients in an effort to improve their health. MLTs have professional obligations to work collaboratively with colleagues and other healthcare providers to deliver professional services.

Ethics in laboratory sciences is one of the branches of professional ethics that tries to apply ethical principles in the field of laboratory sciences and also in the field of ethical decisions in this profession.

The four principles of bioethics include respect for autonomy, the principle of non-maleficence, the principle of beneficence, and the principle of justice.

Considering that medical laboratories as one of the providers of health services have a special responsibility towards patients, paying attention to the rights of patients and respecting their human dignity are among the priorities and necessities that increase the satisfaction of them and the efficiency of laboratory centers.

The Iranian Charter of Patients' Rights states 5 main patients' rights that together aim to guarantee a high level of human health protection. It is the client's right to receive laboratory services appropriately. Information should be provided to the clients in a good and sufficient way. Laboratory services must be based on respecting the privacy of clients as well as respecting the principle of confidentiality.

Keywords: Bioethics, Medical Laboratory

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Management of errors in a clinical laboratory

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Clinical laboratory practice has a leading role in the field of healthcare quality management. There are three phases of laboratory testing: Pre-Analytical, Analytical and Post-analytical. The preanalytical phase is concerned with specimen collection transport and processing. The analytical phase relates to the testing of specimens and the post analytical phase deals with the transmission, interpretation, follow up and retesting. Most errors occur in the pre-analytical phase.

From the results of many researches, we believe that the pre-analytical errors can be reduced by training the laboratory personnel techniques, storage, transport and instrument handling. In an error disclosure, patients want to hear an explicit statement that an error occurred, what happened, and the implications for their health, why it happened and how recurrences will be prevented in the future for themselves and other patients.

Keywords: Pre-Analytical, Analytical and Post-analytical

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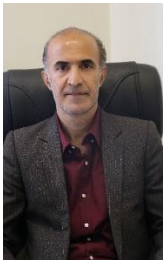

Advanced Tumor Imaging by tumor-targeting peptides

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Enhanced tumor imaging is critical for early cancer detection, precise diagnosis, and effective treatment monitoring. Recent advancements in nanotechnology and molecular imaging have paved the way for the development of innovative imaging agents that offer superior sensitivity and specificity. In this presentation, we explore the potential of tumor-targeting peptides, specifically a peptide targeting both vascular endothelial growth factor receptor 1 (VEGFR1) and VEGFR2 (named VGB3), and an endostatin-derived peptide (denoted as C-peptide), in enhancing tumor imaging across various modalities. These receptors are highly expressed on the surface of tumor cells or tumor microenvironment. The potential of these molecules is investigated by different binding, cellular, and animal studies. Our research focuses on the conjugation of these peptides with different imaging agents to improve their targeting capabilities. We have developed VGB3-DOTA-Gd and VGB3-DTPA-68Ga conjugates for enhanced PET and MRI imaging, respectively, demonstrating their potential for precise tumor localization. Additionally, we have investigated solid lipid nanoparticles (SLNs) decorated with the endostatin-derived peptide (C-peptide), which not only improves the delivery of imaging agents but also enhances their stability and biocompatibility.

Furthermore, we have synthesized superparamagnetic iron oxide nanoparticles (SPIONs) conjugated with the C-peptide for MRI, showcasing their ability to provide high-contrast images of tumor tissues. Our work also extends to gold nanoparticles decorated with the C-peptide, which offer dual-modality imaging capabilities for CT and MRI, thereby providing comprehensive tumor visualization.

Through this lecture, we will present an overview of our lab's innovative approaches and findings in the field of tumor-targeting peptides for enhanced imaging. Our work underscores the importance of integrating targeted peptides with advanced imaging agents to achieve more accurate and efficient cancer diagnostics, ultimately contributing to better patient outcomes.

Keywords: Tumor Imaging, VEGFR1, Peptides

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Application of in vivo Preclinical Imaging in Research

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It is well known that preclinical imaging plays a crucial role in biomedical research, providing a non-invasive means to visualize biological processes in living organisms. This technology is essential for studying disease mechanisms, evaluating therapeutic interventions, and monitoring disease progression in animal models. Various imaging modalities, including magnetic resonance imaging (MRI), positron emission tomography (PET), computed tomography (CT), Single Photon Emission Tomography (SPECT), and optical imaging, offer unique advantages that cater to specific research needs. One of the primary applications of preclinical imaging is in the field of cancer research. Researchers utilize imaging techniques to assess tumor growth, monitor response to treatments, and evaluate metastasis in real time. This capability allows for the optimization of therapeutic strategies and the development of personalized medicine approaches. Additionally, preclinical imaging facilitates the exploration of molecular targets and the evaluation of drug delivery systems, enhancing our understanding of pharmacokinetics and pharmacodynamics.

Beyond oncology, preclinical imaging is also pivotal in neuroscience, cardiovascular research, and regenerative medicine. In neuroscience, imaging techniques enable researchers to visualize brain activity and structural changes associated with neurodegenerative diseases. In cardiovascular studies, imaging helps in assessing heart function and vascular integrity. Furthermore, in regenerative medicine, preclinical imaging aids in tracking stem cell therapies and tissue engineering applications.

Overall, preclinical imaging serves as an invaluable tool in advancing our understanding of complex biological systems and accelerating the translation of research findings into clinical applications. By enabling real-time monitoring and detailed analysis of physiological processes, it significantly enhances the efficacy and safety of new therapeutic approaches.

Keywords: Preclinical Imaging, PET, MRI

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The Development of Diagnostic and Therapeutic Radiopharmaceuticals in Iran

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Over the past three decades, nuclear medicine has evolved into a dynamic and independent medical specialty in Iran. Currently, more than 220 nuclear medicine centers are operational across the country. Radiopharmaceuticals, which form the cornerstone of nuclear medicine, represent one of the most significant peaceful applications of nuclear science in modern healthcare. These radioactive compounds are prepared in specific forms for administration to humans, enabling both the diagnosis and treatment of various diseases. While diagnostic radiopharmaceuticals remain the most widely used globally, therapeutic applications are gaining prominence and continue to expand. In Iran, the domestic production of radiopharmaceuticals commenced several years ago, with the initial development of technetium-99m generators and various cold kits for conventional nuclear medicine. This local production has consistently expanded while maintaining compliance with international standards. In response to increasing national demand and in consideration of international advancements, Iran has extended its production capabilities beyond the Tehran Research Reactor—the oldest active center for the production of medical radioisotopes in the country. At present, two commercial accelerators and over ten hospital cyclotrons are either fully operational or nearing completion. In recent years, particularly over the past decade, significant advancements have been made in the development and clinical application of various radiopharmaceuticals for both diagnostic purposes, using SPECT/PET technologies, and therapeutic treatments involving beta and alpha particles.
The objective of this presentation is to provide a comprehensive overview of the current status of diagnostic and therapeutic radiopharmaceutical development in Iran.

Keywords: Nuclear medicine, SPECT/PET, Radiopharmaceuticals

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Nanoscale Contrast Agents: A Promising Tool for Ultrasound Imaging

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Nanoscale contrast agents have been employed as a versatile platform in biomedical research, demonstrating significant potential for ultrasound imaging and therapy. Various types of these agents have been extensively investigated in preclinical studies to address a wide range of biomedical applications. This lecture will provide a comprehensive overview of the structure and composition of these nanoscale contrast agents, as well as the methods of their preparation and functionalization using chemo-synthetic and biosynthetic strategies. Subsequently, recent advances in the application of these agents for molecular ultrasound imaging will be discussed. Finally, the challenges and future prospects of these agents will be explored to facilitate the development of this innovative nanoplatform in the biomedical field.

Keywords: Nanoscale, Imaging, Ultrasound, Contrast

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Imaging Mass Spectrometry for clinical diagnostic and Guided- Surgery Applications

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Histopathology techniques, initially based on staining methods, have been used for over a century to differentiate healthy cells from diseased ones. Following improvements in microscopy and associated optical detection methods, biomarker-based imaging techniques (immunohistochemistry) introduced to diagnostic society. The common feature of all these microscopy-based methods is that they rely on measuring a unique property (ies) of the analyte, which itself is under the influence of various chemical, physical, and environmental modulators and thus, might lead to biased results. This is not certainly the strategy for the mass-analyzing devices called mass spectrometer or its offspring, Imaging Mass Spectrometer, which both measure the mass of the analyte and its fragment ions. It is worthwhile to mention that in biological mass spectrometers, the molecular ions are formed following the bombardment of the matrix-covered analyte with a variety of suitable lasers as is the case in Matrix-Assisted laser Desorption Mass Spectrometry (MALDI- MS).

Despite the enormous progress in ex vivo surface analyses of biological tissues, the next challenging step for IMS is to move toward in vivo analyses at the level of human beings. In that regard, recently Spider Mass Spectrometry has been introduced which uses endogenous water molecules as the matrix for the generation of ions from the exposed surface of the target organ. In this system, the desorbed ions are collected by aspiration and transmitted to the mass analyzer of the MS instrument. Spider Mass Spectrometry allows for the real-time direct monitoring of the organ surface analysis with preservation of the spatial locations and arrangement of the detected molecules within the tissue with minimal invasive effects. It also works without need and dependency on any sort of Tags, stains, and/or chemical derivatization of the analyte. In other words, and despite the microscopy-based techniques, IMS does not need previous knowledge on the chemical identity of the analyte under investigation.

In this report, we will discuss the principle and the main components of the Spider Mass Spectrometer along with several examples of its wide biomedical and diagnostic applications.

Keywords: MALDI- MS, clinical diagnostic

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Microfluidics for Biomedical Applications

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Advancements in microfluidic devices have led to rapid, reliable performance and high-throughput biochemical analysis with minimal sample use. These devices are applied to bio-applications, from analyzing proteins and DNA to studying living cells. Microfluidic devices minimize inertial and gravitational forces, making shear stress the primary factor in the microenvironment. They offer functionalities like micromixing, separation, and droplet generation, beneficial for medicine and diagnostics (biosensors). In drug delivery and cell culture, microfluidics enables precise concentration gradients and shear stress, essential for Organ-on-a-Chip (OoC) technology.

Keywords: Microfluidics, Biomedical Applications, biosensors

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Point-of-care testing (POCT) for bio-analyte detection, from near-patient tests to wearable technology

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Early and timely diagnosis of diseases is crucial for effective treatment and improved clinical outcomes. However, conventional diagnostic testing is often time-consuming and requires advanced laboratory settings, limiting the potential of point-of-care testing (POCT). Recent research has focused on developing rapid, specific, portable, and economical miniaturized diagnostic tests suitable for various clinical applications. POC assays offer low-cost solutions, particularly in remote and congregate settings, transforming healthcare practices by enhancing accessibility to reliable, and easy-to-use on-site testing. The integration of technologies such as nanotechnology, micro/nanofabrication, the Internet of Things (IoT), and artificial intelligence (AI) is essential for maximizing the impact of these assays on patient care, enabling the miniaturization of laboratory assays into lab-on-a-chip or lab-on-a-body formats. This speech will outline recent advancements in POC diagnostic tools and highlight their utility in detecting clinical bio-analytes, including near-patient tests and wearable on-body testing.

Keywords: Point-of-care testing, artificial intelligence, nanofabrication

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Nanotechnology application in Point of Care Testing (POCT)

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Medicine and nanotechnology have experienced significant progress in the last few years. POC devices have become a critical component of healthcare, diagnostics, and therapy, and with advances in nanotechnology, this field may also receive innovative changes. Various types of biological and non-biological nanomaterials and nanostructures are designed to perform specific functions effectively. Among these functions is point-of-care (POC) diagnostics, which enables the use of portable devices to provide a sensitive, rapid and accurate diagnosis. In this article and lecture, we consider nanomaterials and nanostructures used in POC detection. How nanomaterials have helped in miniaturization and improving the quality of diagnosis. The applications of POCT, especially in the field of cancer, cardiovascular diseases and diabetes, will be further discussed. we will also discuss the future directions and main challenges.

Keywords: Nanotechnology, POCT

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Wearable Electrochemical Biosensors: from Lab to Market

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Wearable electrochemical biosensors are at the forefront of personalized healthcare, offering continuous, non-invasive monitoring of critical biomarkers in real-time. This presentation will explore their path from concept to market, emphasizing recent breakthroughs and challenges. Attendees will learn about the integration of flexible electronics, microfluidic systems, and advanced nanomaterials that allow for the detection of analytes in body fluids such as sweat, saliva, and interstitial fluid. We'll delve into the critical role of high-performance nanomaterial-based sensors, which improve sensitivity, selectivity, and stability, while maintaining biocompatibility and adaptability for long-term use. Another focal point will be the correlation between sweat and blood biomarkers, an essential factor in achieving clinical-grade accuracy. The presentation will also address energy autonomy and the development of self-powered biosensors, which are crucial for continuous monitoring. Beyond the technical aspects, the session will cover the commercialization process, including regulatory challenges, scalability, and the integration of wearable biosensors into existing healthcare frameworks. Additionally, the potential for machine learning to enhance predictive capabilities will be highlighted, showcasing how these sensors can not only track but also forecast health trends and disease progression. Finally, future directions will be outlined, focusing on expanding the biosensors' applications for point-of-care diagnostics, preventive medicine, and personalized treatment. This comprehensive overview aims to inspire further innovation in wearable biosensors, ultimately transforming global health management.

Keywords: Electrochemical Biosensors, Health management

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Current and Future Trends in Gastrointestinal Cancers in Iran

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Gastrointestinal (GI) cancers, including stomach, colorectal, and esophageal cancers, are among the leading causes of cancer-related mortality in Iran. Current trends show that the incidence of these cancers is increasing, partly due to changing lifestyle factors such as diet, obesity, and smoking, alongside genetic predispositions. Stomach cancer remains the most prevalent GI cancer, but colorectal cancer is emerging as a significant public health concern, especially among younger populations. Screening programs are still underdeveloped, contributing to late-stage diagnosis and poor prognosis. Future trends point toward a potential rise in the burden of GI cancers due to population aging and the continued prevalence of risk factors. However, advancements in medical research, including genomics, targeted therapies, and the adoption of personalized medicine, are expected to improve early detection and treatment outcomes. Strengthening public health policies, increasing awareness, and implementing national screening programs will be critical in addressing the growing burden of GI cancers in Iran.

Keywords: Gastrointestinal Cancers, Iran

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The Future of Pancreatic Cancer Screening

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Pancreatic cancer remains one of the most aggressive and challenging cancers to detect early due to its often-asymptomatic nature in early stages and its anatomical location. However, advancements in screening technologies and research offer hope for more effective early detection strategies. Emerging techniques such as liquid biopsy, which detects cancer-related genetic mutations or proteins in blood, show promise in identifying pancreatic cancer at a stage where it is more treatable. Additionally, advancements in imaging technologies, including improved MRI and CT scans, and the use of artificial intelligence to analyze patterns in these images, may enhance screening accuracy. Genetic screening in high-risk populations, particularly those with family histories of pancreatic cancer or associated syndromes, is also likely to play a crucial role in the future. Ongoing research into biomarkers, such as CA 19-9 and novel molecular markers, offers potential breakthroughs in non-invasive detection. Ultimately, the future of pancreatic cancer screening will depend on integrating these innovative approaches to improve early diagnosis, which is key to increasing survival rates. However, challenges remain in ensuring widespread accessibility, affordability, and the reduction of false positives to avoid unnecessary treatments.

Keywords: Pancreatic Cancer, Iran, Screening

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Genomics and Its Role in Colon Cancer Prevention

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Genomics plays a crucial role in advancing the prevention and early detection of colon cancer. By studying the genetic and molecular mechanisms underlying the disease, researchers can identify specific genetic mutations and variations that increase an individual's risk of developing colon cancer. Key genes, such as APC, KRAS, and TP53, are often mutated in colon cancer, and understanding these alterations allows for more personalized risk assessment. Genomic testing can also inform tailored screening strategies, such as earlier and more frequent colonoscopies for high-risk individuals. Additionally, advancements in genomics contribute to the development of targeted therapies and preventative measures, including lifestyle interventions based on an individual's genetic profile. As genomics continues to evolve, it offers a promising path to reduce colon cancer incidence through precision medicine and personalized prevention strategies.

Keywords: Genomics, Colon cancer, Precision medicine

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The Patterns of Calcium Intake and Serum vitamin-D Levels in Iran: The Results of the Iranian Multicenter Osteoporosis Study-2021

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Background: Dietary intake of calcium generally decreases in the elderly. Moreover, Endogenous production of vitamin-D reduces due to both less exposure to sunlight and diminished capacity of cutaneous synthesis of vitamin-D that leads to increased risk of osteoporosis. The dietary calcium intake and serum vit-D were measured in a country-wide population-based study.

Methods: Data from the Iranian Multicenter Osteoporosis Study-2021 was used. Using a multi-stage cluster random sampling method, individuals≥50 years were included from urban and rural areas of eight provinces in Iran. A 168-item food frequency questionnaire was used to define the calcium intake. Serum vitamin-D was measured in a central lab. Insufficient dietary calcium intake was characterized as a calcium intake of <1200mg/day for all women and men>70 years, and <1000mg/day for men aged 50-70 years. Vitamin-D <30ng/mL defined as hypovitaminosis-D.

Results: We included 1450 participants (54.6% women), with a mean age of 60.7±7.9 years. The estimated median dietary calcium intake was 943.5 mg/day (855.2 in women and 1067.2 in men). Insufficient dietary calcium intake in was detected in 75.5%(95% CI:71.9-78.8) of women and 47.8%(95% CI: 43.4-52.3) of men (P<0.001). The insufficient intake was significantly more prevalent in individuals aged ≥65years [69.0%(63.9-74.0)], comparing those <65years[60.3% (56.9%-63.8%)]; however, there was no significant difference between rural and urban populations (P-value=0.325). The prevalence of hypovitaminosis-D was lower in women [26.3%(22.9–30.0)], compared to the men [39.3%(35.0–43.8)]. The statistically significant difference was detected between rural [37.2%(31.7–42.9)] and urban areas [30.4%(27.3–33.7)]. The prevalence was higher in individuals >=65years [32.7(28.0-37.8)], compared to the younger ones [32.0%(28.3-35.2)].

Conclusion: This study showed a high prevalence of insufficient dietary calcium intake and hypovitaminosis-D, with a noticeable increase in elderly. Considering the higher needs in older population, targeted interventions are suggested.

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Association Between Metabolites and Osteoporosis

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Osteoporosis is a significant public health concern characterized by reduced bone mineral density and an elevated risk of fractures, particularly in older adults. Recent research has identified specific metabolites that may play a crucial role in bone health and the pathogenesis of osteoporosis, revealing a complex interplay between metabolic processes and bone integrity.

Key findings indicate that certain amino acids, particularly branched-chain amino acids such as valine, leucine, and isoleucine, are inversely associated with osteoporosis risk. Elevated levels of these metabolites correlate with higher BMD, suggesting their potential as protective factors against bone loss. Conversely, metabolites like phosphatidylcholine and glutamine have shown inconsistent relationships with bone health, indicating that the role of metabolites in osteoporosis is multifaceted and may depend on various physiological contexts.

Additionally, lipid metabolism has emerged as a significant area of interest. Alterations in lipid profiles, particularly the presence of specific fatty acids, have been linked to decreased bone mass. These findings suggest that lipid-derived metabolites may influence osteoblast and osteoclast activity, thereby affecting bone remodeling processes crucial for maintaining skeletal health.

Emerging evidence also highlights the potential of metabolomic profiling as a predictive tool for osteoporosis. By integrating metabolite levels with traditional risk factors, clinicians may enhance the accuracy of osteoporosis risk assessments and early interventions.

Overall, the association between metabolites and osteoporosis underscores the importance of metabolic health in maintaining bone integrity. Continued exploration of these relationships may pave the way for novel biomarkers and therapeutic strategies aimed at preventing and treating osteoporosis, ultimately improving patient outcomes and quality of life.

Keywords: Metabolites, Osteoporosis, BMD

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Epidemiology of Osteoporosis and Its Related Fractures in Iran

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Osteoporosis affects more than 200 million people worldwide. Osteoporotic fractures are considered the most common and severe consequence of osteoporosis. One in every 2 women and 1 in every 4 men over the age of 50 worldwide will experience an osteoporotic fracture. Osteoporotic fractures are associated with disability, social isolation, impaired quality of life, and death. According to the results of the Iranian multicenter osteoporosis survey, the prevalence of osteoporosis in the population over 50 years old in Iran is estimated at 31% (37.5% in women and 23.5% in men). Based on a meta-analysis of original studies conducted in Iran, the incidence of hip fractures, which are considered the most severe type of fracture, is estimated at 157 and 138 per 100,000 people in women and men over 50 years old, respectively. A study conducted at Shafa Yahyaiyan Hospital in Tehran showed that the one-year mortality rate in patients with hip fractures is 17.7% (20% in men and 16% in women). A study estimating the economic burden of osteoporosis and its related fractures in 2020 showed that the cost of this public health issue in the country amounts to over 2 billion dollars annually. The high prevalence of osteoporosis, the high incidence of related fractures, and the significant economic burden it imposes on families and the health system, along with the rapid growth of the elderly population in the country, highlight the necessity of designing and implementing effective interventions for its prevention and control.

Keywords: Epidemiology, f Osteoporosis, Iran

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Sarcopenia: an overview on definition, epidemiology and its related biomarkers

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Sarcopenia is a geriatric disease, characterized by loss of skeletal muscle mass, muscle strength and function, leading to adverse effects such as physical disability, falls, fracture, metabolic disorders, poor quality of life and increased mortality. Sarcopenia has high personal, social and economic burdens. The average of its prevalence is 10–13% worldwide and it has been estimated about 23% among both genders in Iran.
Moreover, individuals with sarcopenia are not aware of the disease in the earlier stage but gradually, critical events in physical and functional disability occur. Therefore, early detection of sarcopenia and finding specific biomarkers forms the basis for primary prevention in order to reduce the progress of sarcopenia and prevent its severe outcomes.
Some studies suggested the effects of inflammatory cytokines in reducing muscle mass and strength. In SARIR study, we found a significant difference in hs-CRP for muscle strength (P = 0.04). Furthermore, we did not observe any remarkable association between inflammatory biomarkers including IL-6 (OR 1.15; 95% CI 0.31-4.28), TNF-α (OR 0.68; 95% CI 0.17-2.77), and hs-CRP (OR 2.39; 95% CI 0.87-6.55) and the presence of sarcopenia.
A strong inverse association was shown between sarcopenia and minerals such as Calcium, Iron, Magnesium, Phosphorus, Potassium, Zinc, and vitamins (A, E, C, Biotin, B2, B3 and B6). Participants with the higher daily protein, carbohydrate and total calories intake revealed a significant reduced risk of sarcopenia in older Iranian adults. In addition, vitamin D insufficiency is linked with muscle weakness and atrophy of type II fibers and sarcopenia.

Keywords: Sarcopenia, Epidemiology, Biomarkers

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The Role of Laboratory in Osteoporosis Diagnosis and Management

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Osteoporosis is a prevalent skeletal disorder characterized by reduced bone mineral density (BMD) and compromised bone microarchitecture. While dual-energy X-ray absorptiometry (DXA) remains the gold standard for diagnosing osteoporosis, laboratory evaluations are indispensable for understanding the underlying pathophysiology, identifying secondary causes, and monitoring treatment efficacy.

Key laboratory tests include biochemical markers of bone turnover markers (BTMs) such as procollagen type 1 N-terminal propeptide (P1NP), osteocalcin, C-terminal telopeptide of type 1 collagen (CTX) and urinary N-telopeptide. It is suggested that a bone formation marker (serum PINP) and a bone resorption marker (serum CTx) could be used as reference analytes for BTM measurements in clinical studies. Although BTMs are influenced by various pre analytic and analytic variables, they can help clinicians to assess response to treatment and follow-up sooner than BMD.

Laboratory workup also helps exclude secondary causes of osteoporosis, such as metabolic bone diseases, endocrine disorders, and nutritional deficiencies. Serum calcium, phosphate, parathyroid hormone (PTH), and 25-hydroxyvitamin D are routinely assessed to identify hyperparathyroidism, vitamin D deficiency, or malabsorption syndromes, all of which contribute to bone demineralization. In addition, testing thyroid function, renal function (creatinine, glomerular filtration rate), and liver enzymes is critical, as both hyperthyroidism and chronic kidney disease can exacerbate osteoporosis and influence treatment choices. Furthermore, tests for serum alkaline phosphatase and bone-specific alkaline phosphatase can provide additional insights into bone turnover, particularly in cases of Paget's disease or osteomalacia.

The laboratory's role in managing osteoporosis extends beyond diagnosis, as ongoing monitoring of biochemical markers and metabolic parameters supports individualized, evidence-based management strategies, improving patient outcomes and minimizing fracture risk.

Keywords: Laboratory, Osteoporosis Diagnosis, Management

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The Effect of Small Molecules and Natural Products on Aggregated Proteins Related to Alzheimer's Disease and Other Neurodegenerative Diseases

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Aggregated proteins, such as Amyloid Beta (Aβ) and Tau proteins, play critical roles in the symptoms and progression of neurodegenerative diseases like Alzheimer's Disease (AD). Scientists in research laboratories worldwide are exploring therapeutic approaches to prevent the formation and promote the disaggregation of these aggregates. Small molecules like Congo Red were among the first candidates to affect the aggregated proteins. Then, other chemicals from different families have been studied and even introduced as drugs to treat these harmful diseases. Peptides, antibodies against aggregated proteins, and natural products have also been researched extensively as potential disaggregating compounds. In my presentation, I will provide a comprehensive review of these various classes of compounds, their mechanisms of action, and the compelling reasons for their limited success in treating the disease. Additionally, I will delve into the research conducted in my lab, including insights from in vitro and in vivo studies on AD. Finally, I will expound on my efforts during my sabbatical at Professor Eisenberg's Lab at UCLA.

Keywords: Natural Products, Alzheimer's Disease, Neurodegenerative Diseases

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Psychotropic properties of saffron in different neurological and psychiatric diseases: Experience from Roozbeh Psychiatric Hospital

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Saffron is the dried stigma of a plant named Crocus sativus L. and has been known as the world's most expensive spice and a widely used medicinal plant. Indeed, saffron is a Persian herb with a history as long as Persian Empire. Saffron could be found throughout the world; however, Iran accounts for 90% of the world's whole saffron and is the origin of the most researches conducted on the potential medical utilities of this expensive spice. Beyond the traditional uses of saffron for treating some conditions such as stomachache or impaired digestion, this spice has shown hypolipidemic, hypotensive, anti-inflammatory, antioxidant, neuroendocrine, and neuroprotective effects. Moreover, it has been exhibited that saffron and its active constituents can increase the reuptake inhibition of dopamine and norepinephrine, antagonize N-methyl-D-aspartate (NMDA) receptors, and agonize Gamma Aminobutyric Acid (GABA) receptors. There is mounting evidence proposing psychoprotective properties of saffron in different neurological and psychiatric settings. over the last 25 years, we investigated on psychotropic effect of saffron at Roozbeh psychiatric hospital. I present my experience from Roozbeh Hospital.

Keywords: Roozbeh Psychiatric Hospital, Saffron, Psychiatric diseases

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Drug Repurposing and Metabolic Syndrome

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Metabolic syndrome includes a range of conditions, such as obesity, hypertension, dyslipidemia, and insulin resistance, that significantly elevate the risk of cardiovascular disease and type 2 diabetes. This syndrome arises from a complex interplay of genetic, environmental, and lifestyle factors, making it a pressing public health issue due to its increasing prevalence and related health complications. The biochemical mechanisms behind metabolic syndrome involve the dysregulation of glucose and lipid metabolism, resulting in chronic inflammation and oxidative stress. Drug repurposing, which identifies new therapeutic uses for existing medications, presents a promising strategy for managing metabolic syndrome. This approach accelerates drug development by utilizing established safety profiles and reduces the costs typically associated with introducing new treatments. Several drugs initially created for other conditions have shown potential in addressing various aspects of metabolic syndrome. For example, metformin, commonly prescribed for type 2 diabetes, has proven effective beyond glycemic control. It aids in glucose regulation and improves lipid levels, thereby supporting weight management and reducing inflammation—key factors in metabolic syndrome. Another notable example is statins, primarily used for hyperlipidemia, which have shown beneficial effects in reducing cardiovascular risk and systemic inflammation associated with metabolic syndrome. These biochemical insights highlight the value of drug repurposing as a strategic approach to combat metabolic syndrome. By leveraging established drugs with known safety profiles, we can potentially address the complex biochemical disturbances associated with this condition, offering new hope for effective management.

Keywords: Metabolic Syndrome, Drug Repurposing, Diabetes

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AI-Driven Decision Support System for Diagnosing Genetic Disorders in the Iranian Population through NGS Data Analysis

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Next-generation sequencing (NGS) technology, a cornerstone in modern genetics, offers a precise and economical means to identify genetic disorders. It rapidly and accurately maps genetic mutations within predisposed genes across diverse populations. Integral to medical genetics and personalized medicine, NGS is poised to become routine in clinical diagnostics. Leveraging artificial intelligence (AI) and machine learning, researchers extract profound insights from NGS data, enhancing the ability to predict disease severity, estimate disease onset, and forecast patient survival based on genetic profiles.

NGS data analysis is pivotal for elucidating the etiologies of both common and rare genetic diseases, as well as previously uncharacterized syndromes. It is instrumental in early detecting hereditary cancers, such as thyroid and colorectal cancers, by identifying susceptibility-inducing genetic mutations. Furthermore, NGS facilitates the diagnosis of genetic disorders linked to intellectual disabilities, developmental delays, hereditary deafness, and conditions impacting the nervous, integumentary, cardiovascular, endocrine, and reproductive systems.

Our interdisciplinary team at the Health Technology Incubator of Mashhad University of Medical Sciences, comprising medical genetics, computer science, and medical informatics experts, has developed an innovative decision-support system, SMART.DX.GEN. This AI-enabled platform utilizes NGS to compile and analyze clinical and genetic data specific to the Iranian population, employing machine learning algorithms to map phenotype-genotype correlations. SMART.DX.GEN substantially improves the precision in diagnosing genetic anomalies and hereditary cancers prevalent in the Iranian demographic. Accessible via http://www.SMARTDXGEN.com, this platform serves medical geneticists, clinicians, researchers, genetic laboratories, healthcare facilities, and academic institutions, markedly enhancing diagnostic capabilities.

Keywords: Next-generation sequencing, Artificial intelligence, Genetic Disorders, Iran

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Big Data Application and Challenges In Clinical Laboratory

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The integration of Big Data into clinical laboratory medicine represents a transformative shift, offering unprecedented opportunities for enhancing patient care and precision medicine. As clinical laboratories generate vast amounts of data from diverse sources such as laboratory results, electronic medical records, and imaging informatics Big Data technologies can facilitate the analysis and interpretation of this information, leading to improved diagnostic accuracy and personalized treatment strategies.

However, the application of Big Data in this field is not without challenges. Key issues include data heterogeneity, the curse of dimensionality, and the need for robust computational methods to manage and analyze complex datasets. Additionally, concerns regarding data privacy, standardization, and regulatory compliance pose significant barriers to the effective utilization of Big Data technologies in clinical settings.

To harness the full potential of Big Data in laboratory medicine, it is essential to develop frameworks that ensure data are findable, accessible, interoperable, and reusable (FAIR). This requires innovative approaches to data governance, automated processes for data integration, and the implementation of artificial intelligence (AI) tools that can derive meaningful insights from large datasets. Addressing these challenges will be crucial for advancing clinical laboratory practices and ultimately improving patient outcomes in an increasingly data-driven healthcare landscape.

Keywords: Big Data, Clinical Laboratory

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Amythist: The first Iranian Karyotyping software

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Karyotyping software is a common software in medical genetics laboratories that can detect chromosomal abnormalities by evaluating the images of chromosomes. Karyotyping test is used to check the health of the fetus through screening tests and also to diagnose some cancers.
In a karyotyping process, the computer is first connected to a digital camera mounted on an optical microscope. Then the software receives the slide image as input. Then, after cleaning and separating the chromosomes, the software arranges the chromosomes in their correct position as 23 pairs. In this software, artificial intelligence is used to arrange the chromosomes in the correct position.
This software is the first and the only Iranian karyotyping software and is used in some genetic laboratories. This product is developed by Aqeeq Biotech Co., which belongs to Zitagene Afarin Holding.

Keywords: Amythist, Karyotyping software, Iran

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Artificial Intelligence in Biochemistry

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The potential of AI to advance Biochemistry is vast and largely untapped. Machine learning, a type of AI, enables computers to learn from data to make predictions and decisions without explicit programming. Some of the main applications may be mentioned such as accelerating drug discovery, the use of AI in predicting the outcomes of enzyme-catalyzed reactions, is a core aspect of Biochemistry. For instance, deep learning neural networks have been used to predict protein secondary structure from amino acid sequences with high accuracy. Solving the enigma of protein folding, it can aid in drug discovery by predicting how potential drug molecules will interact with their targets in the body. AI can also help in understanding genetic diseases by predicting the effects of mutations on protein function. It can also assist in environmental Biochemistry by predicting how pollutants might interact with organisms and ecosystems. It holds the promise of personalized medicine, where treatments are tailored to the individual's genetic makeup, heralding a new era of healthcare. Researchers developed an AI model that accurately predicted patient responses to various cancer treatments based on genetic data. The model was trained on a dataset of over 2,000 cancer patients and was able to predict treatment responses with an accuracy of over 80%. This is a significant improvement over traditional methods and could have profound implications for the future of cancer treatment. Oxidative stress usually refers to the generation of reactive oxygen species such as superoxide, peroxides, hydroxyl radical or singlet oxygen, some neurological degenerative disorders such as Parkinson's and Alzheimer's disorder may in certain conditions be associated with the generation of reactive oxygen species. Prediction and classification of oxidative stress in cells and tissues are hence the important research performance in the area. Supervised machine learning can successfully automate the process of evaluation and quantification of oxidative damage in biological samples, as well as extract useful data from the abundance of experimental results. Last but not the least, is the application of AI in education. AI can provide interactive learning tools, making the complex concepts of Biochemistry more accessible to students. In summery it is worth to mention that AI may be used in different areas of clinical and basic research of Biochemistry which should be taken into account by the scientist’s and students active in the field individually.

Keywords: Artificial Intelligence, Biochemistry

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Artificial Intelligence Application in Business

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Artificial Intelligence in business is considered as applying tools such as machine learning, natural language processing, and computer vision to optimize and boost business functions, data analysis, decision-making and drive business value. Accordingly, we established a website with the address rojanphahub.ir to record information related to bacteriophages in the country with the aim of using these data to develop programs related to the use of artificial intelligence. Recording the data related to native phages of Iran is important, especially because of the increasing growth of antibiotic resistance and the frequent warnings of WHO. Moreover, It was previously reported that the annual death rate directly caused by AMR is predicted to rise to 10 million by 2050. The use of phages is considered a possible replacement to decrease the use of antibiotics. Hence, having a phage bank inside the country is particularly necessary. The discovery of phages controlling the growth of Salmonella pathogenic bacteria in poultry will be considered as a practical example in this project. To create this dataset, phages are isolated and sequenced. Safe checking in terms of not having antibiotic resistance genes and toxic genes is done with programs derived from artificial intelligence and machine learning. Eventually our aim is to design a program based on machine learning to prepare the most suitable phage cocktail as an alternative to antibiotics in poultry.

Keywords: Artificial Intelligence, Application, Business

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AI in Clinical Biochemistry: Transformative Opportunities and Key Challenges

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The integration of Artificial Intelligence (AI) in clinical biochemistry represents a transformative shift in the landscape of diagnostic medicine. AI technologies, including machine learning algorithms and deep learning models, offer significant opportunities to enhance the accuracy, efficiency, and speed of biochemical analyses. These advancements promise to improve patient outcomes through personalized medicine, predictive diagnostics, and automated workflows that minimize human error and reduce turnaround times. AI-driven tools can analyse vast datasets to identify subtle patterns and correlations, providing insights that are beyond human capabilities. However, the implementation of AI in clinical biochemistry also presents several key challenges. These include concerns about data privacy and security, the need for large, high-quality datasets for training robust models, and the potential for algorithmic bias, which can lead to misdiagnosis or health disparities. Additionally, there are regulatory and ethical considerations regarding the integration of AI into clinical decision-making processes, as well as the need for collaboration between clinicians, data scientists, and regulatory bodies to ensure safe and effective use. This abstract will explore the transformative potential of AI in clinical biochemistry, highlighting both the opportunities it presents and the challenges that must be addressed to fully realize its benefits.

Keywords: Artificial Intelligence, Clinical Biochemistry, Challenges

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Cardiac tissue regeneration by modulating mitochondrial biological activity in rat heart infarct model

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Background: Today, ischemic heart diseases are considered one of the main problems in the field of human health. The development of new cellular product methods has brought new hopes to treating patients with cardiac ischemia. This study aims to investigate the effect of mitochondria activated with dichloroacetate and metformin drugs extracted from mesenchymal stem cells (MSCs) on the infarcted rat model. With the hypothesis that the transplantation of activated mitochondria improves the potential of angiogenesis and regeneration in the repair and function of the infarcted heart.

Methods: For this purpose, male Wistar rats were divided into six groups (control and treatment) and examined at a time interval of 14 days. After induction of acute infarct, mitochondria activated by metformin and dichloroacetate drugs were extracted from MSCs and injected into groups with or without hydrogel in 3 areas (around the infarct or border). After 14 days, the heart was removed and to evaluate angiogenesis by vWF and α-SMA factors, the immunohistochemical method and evaluation of fibrotic areas with Masson trichrome staining, evaluation of ischemic tissue quality with H&E staining, evaluation of heart function, blood enzymes were examined.

Results: In this study, the findings indicate that the injection of active mitochondria extracted from mesenchymal stem cells can restore and improve heart function in the infarcted area. According to Masson's trichrome staining, the thickness of the anterior wall of the left ventricle was significantly increased in groups with mitochondrial injection (Mito), hydrogel (Alg/Gel), and Mito + Alg/Gel compared to the stroke group (MI) ($p < ۰.۰۰۰۱$). The increase of angiogenic factor (vWF) and the density of capillaries (α-SMA) showed a similar trend, in which the number and density of capillaries in the Mito + Alg/Gel group was the highest compared to the other groups, especially the MI group ($p < ۰.۰۰۰۱$). AST, ALT, and LDH enzymes were examined in different groups, 14 days after MI, but no significant difference was observed between the groups that received Mito + Alg/Gel and the other groups ($P>۰.۰5$).

Conclusions: Injection of activated mitochondria with DCA/Met drugs led to an increase in angiogenic capacities at the infarct site, which improved the function of heart tissue.

Keywords: Mesenchymal stem cells, hydrogel, infarct, angiogenesis

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Exosomes and Their Therapeutic Applications

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Exosomes are small extracellular vesicles that play a crucial role in intercellular communication. These membrane-bound structures are released by cells into the extracellular space and have emerged as a promising field for therapeutic applications, particularly in the context of our recent study on the intraprostatic injection of exosomes isolated from adipose-derived mesenchymal stem cells for the treatment of chronic non-bacterial prostatitis. Exosomes possess unique properties that make them attractive for drug delivery. They are stable, biocompatible, and can traverse biological barriers. By engineering exosomes to carry specific cargo molecules, such as therapeutic proteins, small interfering RNAs (siRNAs), or anti-cancer drugs, researchers can enhance drug stability and improve targeted delivery to specific cells or tissues. This approach has the potential to minimize off-target effects and increase therapeutic efficacy, offering a more precise and effective treatment strategy. In our study, we demonstrated that exosomes derived from adipose-derived mesenchymal stem cells can be utilized as therapeutic agents in various diseases, including chronic non-bacterial prostatitis. For example, exosomes loaded with anti-inflammatory compounds have shown promise in protecting against inflammation. In cancer treatment, tumor exosomes carrying chemotherapeutics effectively transport drugs to target tumor tissues while reducing adverse effects. Furthermore, exosomes can be engineered to carry antigens, serving as sources of specific stimuli for immune responses against cancer. The therapeutic potential of exosomes extends beyond drug delivery. Our findings indicate that stem cell exosomes have immunomodulatory, anti-inflammatory, anti-fibrotic, and angiogenic properties, making them promising candidates for tissue repair and regeneration. Additionally, exosomes isolated from tissues can accurately reflect disease pathology and permit analysis of the spatial and temporal heterogeneity of the tissue microenvironment. As our understanding of exosome biology and their therapeutic applications continues to expand, we can expect remarkable advancements that will revolutionize the field of medicine and lead to more personalized and effective therapies. The unique properties of exosomes, combined with their ability to transport various therapeutic substances, make them a captivating and rapidly evolving field with significant therapeutic implications, particularly in the context of chronic non-bacterial prostatitis treatment.

Keywords: Exosomes, Applications, Inflammation

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Role of Extracellular vesicles (EVs) in inflammation

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Extracellular vesicles (EVs) propose great opportunity for the diagnosis and treatment of Alzheimer disease. They are lipid membrane vesicles that by transferring of pTau proteins and Aβ peptides have vital role in the pathogenesis of Alzheimer disease. EVs also involved in neuroinflammation and oxidative stress. These vesicles are secreted by different cell types, such as pericytes endothelial cells, oligodendrocytes, microglia, astrocytes, and neurons. EVs has significant role in the physiological conditions, including immune regulation, intercellular signaling, cell migration, angiogenesis, neuronal communication, and cell growth. In AD, exosomes can induce apoptosis and inflammation, and consequently lead to neuronal death, by diffusing pTau and Aβ between cells. EVs offer a significant cell-to-cell communication approaches by carrying their cargo to recipient cells, hence participating in the progression of Alzheimer disease by transferring inflammatory factors and pathologic agents. We isolated EVs and then characterized them. Our results showed that EVs reduced the activity of antioxidants enzymes ($P<0.05$), oxidative stress markers($P<0.05$), and inflammatory factors ($P<0.05$), as compared to control groups ($P<0.05$). In this study, we showed that EVs participate in inflammatory process.

Keywords: Extracellular vesicles, inflammation, oxidative stress

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Iron-Deficiency Anemia: Symptoms, Causes, and Differential Diagnoses

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Significant reduction (at least 10%) in circulating red cell mass or their hemoglobin (Hb) content appropriate for the age and sex, leading to corresponding decrease in the oxygen- carrying capacity of blood and anemia. Based on WHO criteria anemia characterized by Hb lower than 13 and 12 g/dl in men and women, respectively. Human iron metabolism is the set of chemical reactions that maintain human homeostasis of iron at the systemic and cellular level. It is also necessary for cellular respiration (cytochromes), oxygen transport. Iron deficiency anemia (IDA) is the most common hypoproliferative anemia, followed by anemia of chronic inflammation and renal disease. Pathogenesis of IDA is defined by poor iron stores, poor dietary intake of iron, overdevelop and chronic bleeding. IDA is categorized to 3 stages including prelatent, latent and marked IDA. In each stage, the laboratory findings are variable and help to diagnose the stages of IDA. When there is a suspicion of IDA, the following tests are helpful, ferritin, serum iron, total iron-binding capacity (TIBC), transferrin saturation (T.Sat). Diagnosis of IDA is not based on clinical manifestations, and is based solely on laboratory findings, although clinical manifestations can help in diagnosis. Angular cheilitis and koilonychia are the two main clinical manifestations of severe IDA. Finally, IDA Should be differentiated by Hb electrophoresis and mentzer index, level of serum lead, soluble transferrin receptor (sTfR) protein and ferritin from thalassemia, lead poisoning, and anemia of inflammation. Anemia of inflammation, also called anemia of chronic disease (ACD), a type of anemia that affects people who have conditions that cause inflammation. In response to inflammatory cytokines, increasingly IL-6, the liver produces increased amounts of hepcidin.

Keywords: Iron-Deficiency Anemia, Symptoms, Differential Diagnoses

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Interdisciplinary discourse of geometry, art and biochemistry

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Interdisciplinary and transdisciplinary studies in the common areas of geometry, art and biochemistry are the promise of new horizons and new landescapes in education, research, technology, diagnosis and treatment. Topics such as symmetry, chirality, fractals, tensegrity, fullerene, penrose mosaics tessellation, photography, design, music, animation, bionic and architecture are common in the interdisciplinary discourse of geometry, art and biochemistry. A brief look at some parts of this discourse explains, and for the eager searchers, guide references are introduced.

Keywords: Interdisciplinary, Geometry, Biochemistry

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Applications of Clinical Biochemistry in Treatment of Recalcitrant diseases

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Background: Clinical biochemistry has wide applications in medicine such as diagnosis, treatment, prevention and monitoring of disease. The knowledge of biochemical mechanisms in recalcitrant diseases could help to design a protocol for treatment. In this study, clinical biochemistry is used for the treatment of refractory diseases such as chylothorax, pneumothorax, plural effusion, diabetic chronic wound, deep second and third burns.
Methods: PRP-fibrin glue had been prepared by biochemical methods and had been used for treatment of 117 patients which had refractory chylothorax, pneumothorax, plural effusion after cardiothoracic surgery. A new repairing gel had been prepared and used for treatment of 10 diabetic patients with chronic wounds and 10 patients with deep burns.
Results: 95 percent of patients which had refractory chylothorax, pneumothorax, plural effusion were rescued. The wound of 7 diabetic patients and deep burns of 10 patients were healed by using the repairing gel.
Conclusion: The knowing the deep knowledge of clinical biochemistry mechanisms involved in recalcitrant diseases could turn on a light to invent compositions to treat these diseases.

Keywords: Clinical Biochemistry, Applications, Recalcitrant diseases

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Emerging role GLP-1 Receptor Agonists in Obesity

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GLP-1 agonists, initially developed for type 2 diabetes, are increasingly recognized for their role in obesity management. These drugs promote significant weight loss, achieving placebo-adjusted reductions of 12% to 18% in clinical trials, surpassing previous obesity medications. They enhance insulin secretion, reduce gastric emptying, and improve insulin sensitivity, contributing to their effectiveness. Additionally, GLP-1 agonists may provide cardiovascular benefits and are considered the gold standard for treating overweight patients with diabetes. However, concerns about accessibility and high costs remain significant barriers to widespread use.

Keywords: GLP-1 Receptor Agonists, Obesity

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Role of the CTRP family in diseases development and progression

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C1q tumor necrosis factor-related proteins (CTRPs), which are members of the adipokine superfamily, homologs of adiponectin with numerous functions and are closely associated with metabolic diseases, such as cardiovascular, abnormal glucose and lipid metabolism and diabetes.

Structurally, CTRPs are predominantly homotrimers. This highly conserved and novel family contains more than 13 structural and functional adiponectin paralogs from CTRP1-CTRP15 and expanding. Apart from CTRP4, all CTRPs consist of an amino-terminal signal peptide, a short variable region, a collagen-like domain and most importantly, a globular carboxy-terminal domain homologous to the complement protein C1q, which is crucial for their biological functions. Most CTRPs are expressed in adipose tissue, and other tissues such as heart, placenta, mesenchyme, testis. CTRPs are also highly involved in the regulation of numerous physiological and pathological processes, including glycolipid metabolism, protein kinase pathways, cell proliferation, cell apoptosis and inflammation. CTRPs also play important roles in the development and progression of numerous types of tumors, including liver, colon and lung cancers. Various CTRPs through diverse signaling pathways could have either anti/inflammatory, carcinogenic or anti-tumor effects depending on the type of disease. Although the roles and underlying mechanisms of CTRPs in tumor genesis are not known completely, but the results of some studies suggested that CTRPs have the potential to be considered as therapeutic targets in metabolic diseases and numerous types of cancer, which offers glimmer of hope for potential treatment strategies.

Keywords: CTRPs, adiponectin paralog, signaling pathways, metabolic diseases, cancer

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Bilirubin, once a toxin but now a life-saving endogenous metabolite. A bench-to-bedside approach

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Background: Metabolic intermediates are often portrayed as minor components that play no fundamental role in health or disease, merely mediating the end goal of metabolism. Recent studies have shown that many of these intermediates are so important that they may overshadow the health of the body. Meanwhile, bilirubin, a tetrapyrrole compound generally known as a toxic excretory compound, can sometimes have life-saving effects. Bilirubin, an endogenous metabolic byproduct of heme catabolism, was initially considered a useless and potentially toxic compound at high levels. Recent evidence suggests that mildly elevated bilirubin levels may provide potent protection against oxidative stress-associated diseases, including cardiovascular disease, diabetes, metabolic syndrome, and certain cancers potentially leading to a lower overall risk of mortality.

Methods: We investigated the role of bilirubin in histopathological changes, gene expression, and biochemical markers, considering various approaches such as inflammation mechanisms, tumorigenesis, autophagy, apoptosis, and endoplasmic reticulum (ER) stress. The effects of bilirubin were examined in vitro and in vivo using quantitative real-time PCR, western blot analysis, and histological studies.

Results: Our results in various projects showed that bilirubin alters the expression of autophagy/apoptosis-related genes such as Mdm2, Bcl-2, BECN1, LC3, and Atgs, and improves disease symptoms in cancer cell lines and fatty liver models. Furthermore, we observed an improving effect of bilirubin on the expression of ER stress-related genes in type 2 diabetes models. Moreover, bilirubin has a positive effect on inflammation and metabolism by altering the expression of genes such as PPAR-α, TIGAR, SIRT1, and NF-kB.

Conclusion: Therapeutic strategies aimed at inducing a controlled state characterized by mild non-pathological hyperbilirubinemia may represent a novel approach to the prevention and amelioration of oxidative stress-related and inflammatory diseases. Bilirubin can be considered a therapeutic metabolite due to its endogenous antioxidant properties and therapeutic effects against various diseases.

Keywords: Bilirubin, Oxidative Stress, Metabolic Diseases, Cancer

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Securigera Securidaca ameliorated diabetic complications in streptozotocin-induced diabetic rats

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Background: Chronic complications of diabetes are linked to metabolic disturbances, causing significant morbidity and mortality. Researchers are exploring safer alternatives to synthetic antidiabetic drugs, with herbal materials gaining attention. Securigera securidaca seeds are rich in flavonoids and phenolic acids with powerful biological effects. The current study was undertaken to evaluate the effects of hydroalcoholic extract of S. securidaca seeds (HESS) on anti-oxidant and anti-inflammatory capacity, fertility power, tissue changes of the pancreas, liver, and testis, hepatic and pancreatic Local Renin-Angiotensin System (RAS), cardio-protective properties, and cardiovascular risk indices in streptozotocin (STZ) induced diabetic rats.

Methods: Twenty-five male Wistar rats were randomly separated into five groups equally, which consisted of healthy and diabetic control groups, as well as three groups receiving different doses of HESS treatment, for 35 days. Serum and tissue samples were taken, and analyzed for biochemical profile and histopathological changes. Furthermore, the total amounts of phenolic and flavonoid substances in the herbal extract were measured. Statistical analysis was done using SPSS and GraphPad Software. one-way analysis of variance (ANOVA-1) followed by the post hoc Tukey test was used for data analyses.

Results: The herbal extract contained a high amount of flavonoid and phenolic compounds. the HESS decreased glucose and insulin resistance, as well as increased insulin sensitivity, and insulin secretion. In addition, The HESS mitigated oxidative and nitrosative stress, as well as inflammation, dose dependently. Administration of high doses of HESS, significantly ameliorated lipid profiles, reinstated PON1 activity, and diminished cardiovascular risk indices. HESS made ameliorate sperm parameters in diabetic rats but appeared small remedial impact on harmed testicular tissue. Herbal extract, demonstrated minimal influence on the angiogenic and anti-angiogenic biomarkers (except TGF-β), even at the maximum dosages. HESS demonstrated a dose-dependent alleviation of oxidative stress in tissue, along with alterations in the levels of local renin-angiotensin system (RAS) components in both pancreatic and hepatic tissues, when compared to the diabetic control group.

Conclusion: HESS may be regarded as an appropriate herbal adjunct in the pharmacological management of diabetes.

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The importance and method of measuring metals in the diagnosis of diseases

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Background: Trace elements are essential for the proper functioning of the body and some of them can be toxic and may disrupt the balance of essential nutrients. It can be assessed in urine, blood, feces, and hair. The comparison of urine element concentrations before and after administration of a chelator can be used to estimate net retention of potentially toxic elements which is useful for monitoring the efficacy of metal detoxification therapy. Whole blood is a suitable sample to assess the status of essential elements such as Mg, Cu, Zn, and also metal toxicities. Analysis of the elements in stool and hair provides a means to assess the detoxification of potentially toxic metals. Deficiencies or excesses of these essential elements affect numerous metabolic processes.

Methods: Clinical reference laboratories around the world can measure these elements using Inductively coupled plasma mass spectrometry (ICP-MS) and High-resolution ICP-MS. We were one of the laboratories to employ ICP-MS and ICP/OES techniques for elemental analysis.

Results: Results of urine element analyses, following the administration of a chelator, are expressed within 24 hours after correcting the creatinine amounts. For several toxic elements such as Mercury, Cadmium, Lead, Antimony, and Uranium, biliary excretion of metals into feces is a primary natural route of elimination from the body. Hair elements analysis provides information regarding recent and ongoing exposure to potentially toxic metals, especially methylmercury and arsenic, and the time-averaged status of specific nutrient elements. This noninvasive screening test requires only 0.25 grams of hair.

Conclusion: Our mission will be to research, develop, and offer innovative specialty tests that help physicians identify health risks and improve outcomes for patients with chronic conditions. Also, we could educate support healthcare professionals to take more consideration to estimate trace elements status in biological samples.

Keywords: ICP technique, ICP-MS, Noninvasive screening tests

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The biological activities of trace elements, Angiogenesis, Immunity and anticancer effects: New approaches

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Background: Many inorganic elements are recognized as being essential for the growth of all living organisms. Transfer of nutrients and waste material from cells and tissues in the biological systems is accomplished through a functional vasculature network. Maintenance of the vascular system is vital to the well-being of organisms, and its alterations contribute to the pathogenesis of many diseases. The recent aspects of the relationship between different elements and their role in angiogenesis and production of pro- and anti-angiogenic factors were assessed. Many essential elements exist in nature with significant influence on human health. Angiogenesis is vital in developmental, repair, and regenerative processes, and its aberrant regulation contributes to the pathogenesis of many diseases including cancer. The angiogenic activity can act as a double-edged sword. It can lead to better regeneration and healing, or result in necrosis of biological tissues that might jeopardize the dental treatment outcomes. The addition of inorganic ions leads to enhanced angiogenesis and immune responses, which holds promise for the development of functional tissue-engineered constructs to repair and regenerate damaged tissues and organs.

Case presentation: For example, the effect of chromium, silicon, zinc, copper, and sulfur on different aspects of angiogenesis, with critical roles in healing and regeneration processes, and undeniable roles in tumorigenesis and malignancies. In dentistry, angiogenesis plays a great role in the regeneration of dentin and dental pulp tissues after injuries. It has utmost importance in the revascularization of traumatic premature teeth, which results in radicular dental pulp survival and continuity of root formation.

Conclusion: The angiogenesis, immunogenicity, or pathogenicity of trace elements, especially concerning oral and dental pathology and their use in all kinds of prostheses, has opened new horizons for us, which will undoubtedly increase their use in the mentioned fields.

Keywords: Angiogenesis, Trace elements, Micronutrients, Revascularization, Immunity

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Comprehensive Analysis of Heavy Metals and Essential Elements in Colorectal Cancer

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Background: Colorectal cancer (CRC) is the third most common cancer globally. The role of heavy metals (HMs) in the progression and inhibition of CRC is complex. HMs may replace essential elements in the body, disrupting cellular and enzymatic mechanisms. Therefore, to accurately study the role of HMs in malignancies, it is important to examine changes in the profiles of HMs and essential metals.

Methods: We conducted a 3.5-year case-control study (322 participants), including CRC, advanced adenoma (AA), and control groups, at Poursina Hakim Gastroenterology Research Center, Isfahan, Iran. The serum levels of 18 metals were measured using Inductively Coupled Argon Plasma Optical Emission Spectroscopy. These metals included: essential metals (nutritional elements): calcium, zinc, copper, magnesium, manganese, Iron, boron, and sodium; heavy/toxic metals: nickel, lead, cadmium, arsenic, aluminum, antimony, Tungsten; and trace elements including selenium, cobalt, and chromium.

Results: The results revealed that the levels of arsenic and cadmium were significantly elevated in the CRC group compared to the AA and control groups. Additionally, lead and antimony levels were higher in CRC compared to the control group. Conversely, zinc levels were higher in the AA group than in the CRC group. The trend of serum copper changes was similar to zinc in the three groups but the difference was not statistically significant (p=0.084).

Conclusion: The study demonstrates a clear association between elevated levels of certain HMs, such as arsenic, cadmium, and lead, with CRC. These findings suggest that alterations in the homeostasis of HMs may contribute to the development and progression of CRC. Understanding these metal profiles could provide valuable insights for developing targeted diagnostic and preventive measures to reduce the incidence of CRC. Further research is warranted to explore the mechanisms underlying these associations and to evaluate the potential for clinical applications in cancer prevention and management.

Keywords: Colorectal cancer, heavy metals, essential elements, advanced adenoma

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Common and different roles of Zn and Cu in various types of cancer

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Background: Zn and Cu are both essential trace elements in different tissues of the human body and take part in several cellular metabolisms, and enzyme activities. Those are catalytic cofactors for the superoxide dismutase (Zn/Cu SOD). The biological action of both has been demonstrated to have antioxidant and anti-inflammatory properties. Any alteration of intake of only one of them may cause an imbalance in their levels. Excessive dietary Zn can cause Cu deficiency. An increased Cu/Zn ratio was noted in many different malignancies including breast, ovarian, endometrial, and cervical cancer. The aim of this study was to estimate Zn and Cu levels in tumor and its margin tissues in patients with breast cancer.
Methods: 40 women with a histologically confirmed diagnosis of invasive ductal carcinoma who had not received any treatment such as chemotherapy, surgery and/or radiation therapy were enrolled. The tissue levels of Cu and Zn were measured by an atomic adsorption spectrophotometer equipped with a graphite furnace.
Results: Our data showed that both Zn and Cu levels in tumor tissues were significantly higher in patients with breast cancer compared to tumor marginal tissue. A correlation was found between tissue concentration of Zn and tumor location, lymph node involvement, and HER2 receptor. Oxidative stress enzymatic markers including SOD, CAT, and GPX showed that the
enzymatic activity of SOD ($p=0.005$), CAT ($p=0.0001$), and GPX ($p=0.003$) in the tumor tissue of breast cancer patients was significantly reduced compared to the tumor margin tissue.
Conclusion: Increasing intracellular Zn activates Zn-dependent metalloproteinases, which catalyze the breakdown of extracellular matrix and are involved in angiogenesis and tumor proliferation. Numerous studies have reported increased Cu concentrations in breast cancer tissue, which can induce breast cancer through angiogenesis. The maintenance of homeostasis of antioxidant trace metals represents a potential way to reduce the chances of carcinogenesis.

Keywords: Zinc. Copper, Breast cancer, Tumor tissue.

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Interrelationship between aluminum and iron metabolism in patients with chronic renal failure maintained on hemodialysis

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Background: The relationship between aluminum toxicity and iron metabolism has been investigated in our lab during the past 40 years, particularly in those patients with chronic renal failure maintained on hemodialysis. Aluminum is used to purify the water supply and prepare dialysis fluid for patients. During dialysis aluminum transfers across the dialysis membrane, blood circulation binds to human serum transferrin and causes several diseases including anemia, neurological disease, and bone diseases. Aluminum competes with iron metabolism and causes hypochromic microcytic anemia. The exact points of interference of aluminum are at mitochondria which is a major site of the Heme synthesis.
Case presentation: For the estimation of those trace elements, atomic absorption was used. Several experiments have been done on patients with chronic renal disease; I will discuss them in detail in the congress. Aluminum enters the brains of these patients and causes neurofibrillary degeneration interferes with neurotransmitters and produces dementia and Alzheimer's disease.
Discussion: Aluminum not only interferes with Iron but also with calcium metabolism and causes bone disease which is completely different from regular osteomalacia in renal patients. These bone diseases do not respond to vitamin D and calcium therapy. This bone disease is called Newcastle bone disease as recently has been cited in textbooks.

Keywords: Aluminum, renal disease, iron metabolism, anemia, dementia, Alzheimer's disease

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The importance of elements in food chain

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Background: Elemental analysis of food is currently gaining in importance because of growing concern about food quality and consumer's health. Food chain is the way of element transfer from basic natural sources to plants, animals, and humans as the final link. Elements are categorized to macro, micro, and toxic elements. In comparison to macro/micro elements which are vital for life, toxic elements have detrimental effects on organisms. The long and uncontrolled use of elements (specially metals) has led to their ubiquity in various environmental compartments. Therefore, monitoring of elements is important in food chain links such as soil, water, air, feed and food.

Case Presentation: Different types of foods are assessed with new methods and instruments in our well-equipped laboratories. In this regard I am trying to discuss some basic sources of them. All soils naturally contain trace levels of metals. The concentration of metals in soil is related to the geology of the parent material from which the soil was formed. Metals may be transported to ground water. Elements can be taken up by plants if they are present in the soil as soluble ions in the forms of organic or inorganic complexes. Element accumulation in food plants depend on concentration of ions and chemical character of complexes form. Elements can also be transferred to animals by digestive system of animals and are accumulated in lipid-rich tissues, which are used as food for human nutrition, including milk, eggs, or even honey.

Conclusion: Essential nutrients play a crucial role in various metabolic processes. In contrast, toxic elements tend to accumulate in animal or human organs. So, monitoring of the level dose in food chain could be an effective strategy to reduce human health risk.

Keywords: Food chain, Metals, Toxic elements, Nutrients

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Importance of measurement and speciation of trace elements in medical geology

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Background: All living organisms for biological functions need some naturally existing trace elements such as iron, zinc, copper and selenium; however, excessive amounts of toxic trace elements specially in certain forms such as lead, mercury arsenic and cadmium can be harmful to health. Determination and speciation of these kinds of trace elements are surveyed in medical geology field. Medical geology represents a multidisciplinary approach, that reveals the complicated relationships between the earth (geological factors), health, and life sciences.
Case Presentation: The measurement of trace elements is important for the following reasons: Identification of pollution, prevention of diseases and management of natural resources. There are many advanced instrumental methods used for trace elements analysis, including advanced techniques for speciation that allow for the differentiation of chemical forms and their bioavailability. Some case studies which have been done on dispersion of some disease and trace elements in some part of Iran illustrate the role of geological sources in elemental contamination will be discussed.
Conclusion: These results highlight the significance of geochemical mapping in identifying at-risk populations.

Keywords: Medical geology, Geological factors, Natural elements

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Molecular Mechanism of Action of Targeted T Cell Therapies

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Adoptive transfer of targeted T cell therapies has thrived as a promising curative modality for various cancers. Four targeted T cell therapy categories have been identified: endogenous antigen-reactive T cells, tumor-infiltrating lymphocytes (TILs), antigen-directed engineered TCR T cells, and chimeric antigen receptor (CAR) T cells. Exceptfor CAR T cells that can recognize tumor antigens independent of the expression of major histocompatibility complex (MHC) molecules, the three other targeted T cells exert their anti-tumor effects on tumor cells in an MHC-dependent manner. Recognition of molecular mechanisms of action of these effector cells helps better understand their efficacy. To date, several mechanisms of action of targeted T cells have been described, which are as follows: the binding to a targeted antigen present on tumor cells and subsequent activation of anti-tumoral effects through the secretion of inflammatory cytokines (e.g., IL-1, IL-2, IL-6, IFN-γ, and TNF-α), cytolytic effector function via perforin and granzyme, and TNF-related apoptosis-inducing ligand (TRAIL) pathway. In addition, apoptosis of tumor cells can be elicited via the activation of caspase 8 and the formation of death-inducing signaling complex (DISC) mediated by mature caspase-3 following initiation of Fas and Fas ligand (FasL) pathway.

Keywords: T Cell therapy, chimeric antigen receptor (CAR) T cells, inflammatory cytokines

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History and perspective of cell therapy in the world and Iran

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Cell therapy, or cytotherapy, utilizes living cells, particularly stem cells, to treat various diseases. This innovative approach has evolved significantly since the 19th century when scientists first recognized the differentiation capabilities of cells. The term "stem cell" was introduced in the early 20th century by Russian doctor Alexander Maximo, who hypothesized the existence of hematopoietic cells. Subsequent research led to the identification of various stem cell types and methods for their cultivation and differentiation. The therapeutic potential of stem cells was first demonstrated in 1956 when Dr. Edward Donnall Thomas successfully transplanted bone marrow stem cells into a leukemia patient. This was followed by Dr. Robert Good's successful transplant for a non-cancerous immune disorder in 1968. Since then, over 30 million cell therapies have been performed globally, with 38 cell and gene therapy products receiving FDA approval for conditions such as leukemia, skin disorders, and prostate cancer. In Iran, stem cell treatment began in 1990 with Dr. Ghavamzadeh establishing the first bone marrow transplant department at Shariati Hospital in Tehran. Iran has since conducted over 8,000 transplants, expanding the application of stem cells to non-blood disorders, such as heart lesions and corneal repairs. The country has positioned itself as a leader in stem cell research, establishing numerous academic and private institutes dedicated to this field. To support this growth, Iran's Department of Biological Medicines launched the "Cell, Gene, and Tissue Products Unit" in 2009-2010 to oversee the development of cell-based medicines. In 2011, the academic field of Applied Cell Sciences was introduced to train specialists in clinical-grade cell production. Recent advancements include the addition of three new cell therapy drugs to Iran's drug list: DestroCell for GVHD, Rooinsheet for burn repair, and RooinGraf for chronic wound treatment. These developments reflect Iran's commitment to advancing regenerative medicine and cell therapy services.

Keywords: Cell therapy, Iran, cytotherapy

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Mechanisms of action of stem cells in the treatment of neurodegenerative diseases

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Mesenchymal stem cell (MSC) therapy is a valued therapeutic strategy for neurodegenerative diseases. A lot of studies on animals and human patients have shown that MSC transplantation is safe, possible, and effective in neurodegenerative diseases like Alzheimer's, Parkinson's, ALS, and Huntington's. The desired outcome mediated by MSCs is mostly achieved through the secretion of immunomodulatory molecules in conjunction with the release of several neurotrophic factors, including glial cell line-derived neurotrophic factor (GDNF) and brain-derived neurotrophic factor (BDNF). MSC therapy primarily facilitates the destruction of pathogenic protein aggregates, a characteristic feature of chronic neurodegenerative diseases, by producing protein-degrading chemicals. These chemicals reduce neuroinflammation while also providing neuroprotection, thereby mitigating disease clinical symptoms and facilitating cognitive and functional recovery. Furthermore, the differentiation of MSCs into neural-like cells in vivo has been partially demonstrated. We have reviewed and discussed the mechanisms and functions of mesenchymal stem cells (MSCs) in the treatment of neurodegenerative diseases such as AD, HD, PD, and ALS.

Keywords: Mechanisms of action, Stem cells, neurodegenerative diseases

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CAR T-Cell Therapy: Mechanism of Action Against Malignant Cells

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CAR-T cell therapy has been approved for various blood cancers, including lymphoma and leukemia, and more recently, multiple myeloma, but not for solid tumors. The approach involves modifying a patient's T cells (autologous CAR T cells) to fight cancer. Scientists are working on allogeneic CAR T cells that come from donors and could be manufactured in advance and administered “off the shelf.” However, challenges exist, such as the risk of rejection or graft-versus-host disease. CAR T-cell therapy involves several key steps. Initially, T cells are extracted from a patient's blood and genetically engineered in the laboratory to express a chimeric antigen receptor (CAR) on their surface. These CARs are synthetic molecules designed to recognize and bind to specific antigens present on cancer cells. Once engineered, the CAR T cells undergo large-scale expansion and reintroduction into the patient. The CAR structure is composed of an extracellular antigen-recognition domain, usually derived from an antibody's single-chain variable fragment (scFv), allowing it to target specific proteins on cancer cells. The most common target is CD19, found on B-cell malignancies. When the CAR T cell comes across a cancer cell that expresses the target antigen, it binds to the antigen and sets off a series of signaling events inside the cell. The CAR binding to the target antigen on malignant cells triggers the activation of the CAR T cell through the intracellular signaling domains attached to the CAR structure. These signaling domains often include the CD3ζ (zeta) chain, which is a key component of the T-cell receptor (TCR) complex, along with co-stimulatory domains like CD28 or 4-1BB (CD137). These co-stimulatory domains enhance the activation, proliferation, and survival of CAR T cells upon antigen engagement. When the CAR T cell binds to its target, the CD3ζ signaling domain initiates a series of phosphorylation events, activating downstream signaling pathways such as the PI3K/AKT, MAPK/ERK, and NF-κB pathways. These pathways promote the release of cytotoxic granules containing perforin and granzymes from the CAR T cells. Perforin creates pores in the target cancer cell's membrane, allowing granzymes to enter and induce apoptosis (programmed cell death) in the malignant cell. Additionally, CAR T cells secrete pro-inflammatory cytokines like interferon-gamma (IFN-γ) and tumor necrosis factor-alpha (TNF-α), which further enhance the immune response against cancer cells and can recruit other immune cells to the tumor site. Here, the mechanisms involved have been discussed and explained.

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Biochemical potential of Exosomes derived from Mesenchymal Stem Cells

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Extracellular Vehicles (EVs) derived from MSCs, including Exosomes and shed microvesicles (50–1000 nm diameter), have significant biochemical potential as they play crucial roles in intercellular communication, and transporting proteins. Exosomes can mimic the biological activity of MSCs by horizontally transferring many functional molecules including mRNAs, miRNAs, and lipids to the cellular microenvironment. Exosomes target cells communication and possess restorative processes. MSC-exosome effects are elicited by modulating inflammation, angiogenesis, cell proliferation, and matrix synthesis. They have been shown to reduce apoptosis in various epithelial tissues and protect cartilage and bone by suppressing inflammatory cytokines and macrophage activation. This allows them to exert anti-inflammatory and tissue-protective effects, making them valuable for therapeutic applications. Also, their ability to reflect the biochemical state of their originating cells makes them valuable in research for biomarkers and diagnostic settings.

Keywords: Exosomes, Mesenchymal Stem Cells, Biomarkers

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Application of mesenchymal stem cells in disease treatment: molecular and biochemical mechanisms

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Mesenchymal stem cells (MSCs) are among the types of stem cells that are found in both embryonic tissues and in various adult body parts. These cells act as the body's soldiers, circulating throughout the body via the bloodstream so that wherever the body needs repair and restoration, these cells assist in the healing and rebuilding process. Mesenchymal stem cells have two essential characteristics that make them suitable candidates for treating many diseases: 1) Their suppressive action on the immune system and anti-inflammatory effects; 2) Their property of regeneration and their ability to reconstruct, which can regenerate many organs, including cartilage, fat, and bone. These cells have several applications in the treatment of many diseases, including slow-healing wounds, most inflammatory diseases such as IBD and CP, GVHD, and pain management. Mesenchymal stem cells stimulate this anti-inflammatory property and the ability to proliferate, grow, and regenerate through certain molecular and biochemical pathways, which we intend to explain in this discussion.

Keywords: mesenchymal stem cells, Disease treatment, Biochemical mechanisms

Oral Presentations

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Abstract: A-10-2871-1

Investigating the Role of Microbiome-Derived Short-Chain Fatty Acids as Early Markers of Metabolic Syndrome: Insights for Clinical Diagnostics

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Background: Metabolic syndrome covers a group of disorders that raise the risk of developing heart disease, stroke, and type 2 diabetes and have been related to gut health, possibly due to dysbiosis. In this work, the researchers aimed to find whether Short-Chain Fatty Acids (SCFA)-mediated gut bacterial metabolism and inflammation could be an early predictor of metabolic syndrome.
Methods: This study analyzed the gut bacterial composition and SCFA levels in 65 patients, both with and without metabolic syndrome. The authors used GC-MS technology to assess specific gut bacteria species or metabolites associated with metabolic syndrome, aiming to investigate changes in gut bacteria that could potentially influence metabolism and the development of metabolic syndrome.
Results: Metabolic syndrome in patients was associated with reduced levels of the fatty acid butyrate and an increase in acetate. Butyrate is a SCFA with anti-inflammatory properties that is favorably connected with enhanced metabolic health. Acetate has been positively linked with greater markers of obesity. The ratio of acetate to butyrate was strongly connected with body mass index, waist circumference, fasting blood glucose, triglyceride levels, and blood pressure (all $r = 0.45$, $p < 0.01$). Inflammatory indicators were low in people with higher levels of butyrate; this link was statistically significant ($r = –0.35$, $p < 0.05$). By ROC curve analysis, the accuracy in predicting metabolic syndrome by measuring this ratio of short-chain fatty acids by clinical indicators was substantially raised from 0.70 using only clinical markers to 0.85 utilizing additional AUC measurement of the ratio of short-chain fatty acids.
Conclusion: With an emphasis on the inclusion of microbiome-related metabolites in clinical assessments, this study suggests that measuring short-chain fatty acids (SCFAs) could serve as an early diagnostic tool for metabolic syndrome. Additionally, it implies that researchers could explore novel treatment options through the manipulation of gut bacteria.

Keywords: Metabolic Syndrome, Biomarkers, Metabolomics, Gastrointestinal Microbiome, Fatty Acids analysis

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Abstract: A-10-2812-1

Indole-3-Carbinol Promotes M2 Macrophage Polarization Via Ahr Pathway and Glucose Transporter Regulation in Thp-1 Macrophage-Like Cells

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Background: Macrophages, essential for innate immunity and highly adaptable, respond to pathogens or tissue damages by altering their phenotype between pro-inflammatory M1 and anti-inflammatory M2 types. Disruption in macrophage polarization is linked to inflammatory diseases and metabolic disorders. Glucose metabolism, crucial for macrophage function, is regulated by glucose transporters. The Aryl hydrocarbon receptor (AhR) modulates immune responses, with diverse ligands influencing macrophage phenotypes and function. Our study aimed to investigate how AhR activation by I3C and TCDD could impact glucose transporters and macrophage phenotypes and functions in THP-1 cells.

Methods: THP-1 cells were differentiated into macrophage-like cells and treated for 24 hours with 100 ng/mL LPS, 100 nM TCDD, and 10 ng/µL I3C. Real-time PCR was performed with primers targeting CYP1A1, CYP1B1, ARG-1, IL-12B, AHRR, NOS2, IL10, GLUT1, GLUT3, and GLUT6. Flow cytometry assessed CD86, CD16, and CD163 expressions. Cytokines TNFα and TGFβ were measured using ELISA.

Results: CYP1A1 and CYP1B1 expression was significantly increased in I3C and TCDD treatments, with CYP1B1 showing a higher fold change in I3C compared to TCDD. AhRR expression was highest in the TCDD group. For macrophage polarization, I3C significantly elevated CD163 expression while reducing CD16 and CD86, indicative of M2-like polarization. Additionally, I3C promoted Arg1 expression and reduced NOS2 levels, while TCDD increased NOS2. Cytokine analysis revealed I3C-induced upregulation of IL-10 and TGF-β, while TCDD significantly elevated TNF-α and IL-12. I3C upregulated glucose transporter genes (GLUT1, GLUT3, GLUT6), in contrast to the downregulation observed in TCDD-treated cells.

Conclusion: Our findings demonstrated that I3C distinctly modulates AhR activation genes, macrophage polarization, cytokine expression, and glucose transporter levels in THP-1 cells compared to TCDD and LPS treatments. Our results suggest that I3C favors an anti-inflammatory M2-like macrophage polarization, coupled with enhanced metabolic activity.

Keywords: Aryl hydrocarbon receptor (AhR), Indole-3-carbinol (I3C), TCDD, LPS, Macrophage polarization, M2 macrophages, Glucose transporters, Immune modulation

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Abstract: A-10-2162-2

Assessment of A Novel Designed Peptide's Anti-Endotoxin and Hemolytic Activities, and Cytotoxicity: An in Silico and in Vitro Study

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Background: Endotoxin, also recognized as lipopolysaccharide (LPS), is considered the pathogenic factor of septic shock triggered by Gram-negative bacteria and generates inflammatory responses. Synthetic peptides have pulled in expanding consideration from researchers for the blocking of LPS and treatment of sepsis. The aim of the study was to design a novel synthetic anti-endotoxin peptide and assess its effect in vitro.

Methods: To design a new peptide, anti-endotoxin peptides were extracted from the APD3 site. The physicochemical features, secondary structure content, and tertiary structure type of each residue were determined by ProtParam, GOR IV, pep-fold, and I-TASSER. Hemolytic activity and cytotoxicity of the peptide on RAW264.7 cells were assessed by human RBC hemolysis test and MTT assay, respectively. Real-time PCR and western blot were utilized to assess the gene expression of IL-1β, TNF-α, IL-6, IL-10, iNOS, and TLR4, as well as the protein expression of NF-KB(P65), correspondingly. The designed peptide has 13 amino acid residues (GRRWWRFKKWWKF). The second structure of the peptide had 46.15% random coil and 53.85% extended strand.

Results: The results of the prediction of the tertiary structure demonstrated the peptide forms an alpha helix structure. It possesses low hemolytic activity and low cytotoxicity against RAW264.7 cells. This peptide remarkably restored LPS-induced TLR4 overexpression, and decreased gene expression of IL-1β, IL-6, iNOS, and TNF-α, whereas increased IL-10. This peptide significantly decreased the protein expression of NF-KB (p65).

Conclusion: These findings infer that this peptide with low toxicity, hemolytic activity, and LPS-neutralizing activity, merits more research as a possible anti-LPS agent for managing septic shock.

Keywords: Endotoxin, Lipopolysaccharide, Cytotoxicity, Peptide, Septic shock

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Abstract: A-10-2258-1

The Effect of Omega-6 and Recombinant NMP Protein on Endoplasmic Reticulum Stress of Liver Tissue of Non-Alcoholic Fatty Liver (NAFLD) Rats

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Background: Endoplasmic reticulum stress (ERS) plays an important role in the development of non-alcoholic fatty liver disease (NAFLD). This study investigated the effect of consuming omega-6, and recombinant NMP protein alone or in combination with omega-6, on ERS in NAFLD Rats.

Methods: NMP recombinant protein, the enhanced product of the human SHIP2 gene, was synthesized by genetic engineering method in the Pichia pastoris host according to the Ecallantide method. In this experimental study, 80 male Wistar rats (weight 156.19 ± 7.82 g) were divided into five groups, including control-healthy (CN), patient (NAFLD), patient+omega-6 (OMG6NAF), patient+NMP recombinant protein (NMPNAF) and NMP+Omega 6 patient (OM6NMPNAF). The supplement groups received 2 grams of omega-6 (per kilogram of body weight) orally during the intervention period. Also, at the same time, 2 ml of NMP recombinant protein was injected intravenously with selenium adjuvant to establish a better balance of Immune System Response.

Results: Induction of NAFLD increased GRP78, PNPLA3, ALT, and AST($p<0.0001$). The expression of GRP78 and PNPLA3 in OM6NMPNAF ($p<0.0001$ and $p<0.001$, respectively) and OMG6NAF ($p<0.0001$ and $p<0.001$, respectively) groups had a significant decrease compared to NAFLD. ALT and AST also decreased significantly in OM6NMPNAF ($p<0.00001$ and $p<0.0001$ respectively) and NMP NAF ($p<0.0001$ and $p<0.001$ respectively) groups. The combined intervention of NMP protein with omega-6 supplement was also significant compared to the effect of each intervention alone on GRP78, PNPLA3, ALT, and AST($p<0.005$). The amount of tissue inflammation decreased by about 94 and the balance of the immune system response was successfully achieved. The purity percentage of NMP recombinant protein in the yeast host was about %88.5($p<0.0001$). Also, the kidney GFR index was measured in the direction of excretion of excess omega-6 and NMP recombinant protein, which confirmed insignificant and successful excretion ($P<0.001$).

Conclusion: NMP recombinant protein and omega-6 consumption inhibited ER stress in liver tissue by decreasing the expression of GRP78 and PNPLA3. Nevertheless, this may represent a promising new treatment method for non-alcoholic fatty liver disease.

Keywords: NAFLD, Omega-6, NMP Recombinant Protein, Liver Pathobiology, Rats.

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Abstract: A-10-2770-1

Enhancing Hesperidin Delivery Via Niosomes: Effects on Locomotor Activity and Proenkephalin Protein Expression in Depressed Rats

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Background: Depression is a disorder linked to cognitive deficits, locomotor activity, and protein expressions. Hesperidin has shown promise in treating depression. However, its poor water solubility limits its use. In this study, we loaded hesperidin into niosomes to enhance its delivery. We investigated locomotor activity in Wistar male rats using open-field and assessed proenkephalin protein levels in the hippocampus.

Methods: 36 male rats were used and divided into six groups: control (saline for 14 days), depressed (reserpine (0.5 mg/kg) for 14 days), hesperidin (hesperidin (20 mg/kg) for 14 days), depression-hesperidin (reserpine (0.5 mg/kg) for 14 days+ hesperidin (20 mg/kg) for 14 days), nano (niosome-hesperidin (20 mg/kg) for 7 days), and depression-nano (reserpine (0.5 mg/kg) for 14 days+ niosome-hesperidin (20 mg/kg) for 7 days). Open field test was taken on the 7th and 14th day. Then the hippocampus tissue samples were extracted and the proenkephalin protein levels were assessed using the western blot method.

Results: The results indicate significant changes in proenkephalin protein levels in the depressed ($p<0.01$), hesperidin ($p<0.0001$), depression-hesperidin ($p<0.001$), and depression-nano ($p<0.001$) groups compared to the control group. Additionally, the protein levels were significantly higher in both the depression-hesperidin group and the depression-nano group compared to the depressed group ($p<0.0001$). Also, it was shown that the locomotor activity in the open field test during the 7th and 14th days was significantly different between the control group and the depression group on day 14 ($p<0.05$), and the hesperidin group had significantly increased levels compared to the depressive group on day 7 ($p<0.001$). We observed a significant increase between the hesperidin group on day 7 and the depressive on day 14 ($p<0.01$), hesperidin and niosome-hesperidin ($p<0.01$), and depression-nano and hesperidin on day 7 ($p<0.05$).

Conclusion: The results of this study demonstrated the nanoparticles loaded with hesperidin influenced locomotor activity, proenkephalin protein expression, and improved depressive-like behavior within a shorter timeframe.

Keywords: Depression, Niosome-hesperidin, Proenkephalin, Open field test, Locomotor activity

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Abstract: A-10-2831-1

Microfluidic Biosensor for the Troponin I Detection Based on Immunoassay

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Background: Troponin I, a cardiac-specific protein, is crucial for heart muscle contraction. As a biomarker, it excels in diagnosing heart injuries. Its sensitivity and specificity make it superior to other markers like CK-MB. Elevated troponin I indicates heart damage severity. Beyond initial diagnosis, it aids in post-injury monitoring and predicting complications. Microfluidic biosensors rapidly and accurately detect Troponin I using microchannels and biological components.

Methods: In the current microfluidic biosensor, a biological sample containing Troponin I protein is passed through microfluidic channels. This movement binds Troponin I to immobilized capture antibodies on the PMMA surface and is subsequently detected by an HRP-conjugated antibody; to set up the conditions, a pilot ELISA-based model was generated on a PMMA surface to detect the mentioned signal.

Results: In the first step, laser-cut PMMA channels were bonded together. Then capture antibodies immobilized on the surface. For generating a pilot model, a sandwich ELISA was carried out according to a standard ELISA protocol. Different concentrations of Troponin I were prepared. A calibration curve of Troponin I concentration versus wavelength is plotted and the concentration of unknown samples is determined from this curve. The detection limit of the ELISA model was at least 0.01 ng/ml.

Conclusion: The microfluidic biosensor presented in this study provides a precise and sensitive tool for Troponin I measurement. This technology can be used in early detection, monitoring of cardiovascular disease treatment, and other clinical applications. Future studies can explore the ability of this biosensor in clinical samples and the development of simultaneous detection of multiple biomarkers at the same time.

Keywords: Keywords: Microfluidic, Biosensor, Troponin I, cardiovascular disease

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Abstract: A-10-2824-3

Cell Therapy Using Co-Treatment Mesenchymal Stem Cells with Exosomes Obtained from the Umbilical Cord in Infertile Women Due to Asherman Syndrome

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Background: Asherman syndrome (AS), characterized by intrauterine adhesions, is a significant cause of infertility and menstrual irregularities. Traditional treatments have shown limited success, prompting the exploration of regenerative therapies. This study investigated the potential of co-treating mesenchymal stem cells (MSCs) and exosomes derived from umbilical cords (UC) as a novel therapeutic approach for AS-related infertility.
Methods: Twelve patients with AS were randomly allocated into four groups: (1) single injection of MSCs, (2) two exosome injections, (3) co-treatment with MSCs and exosomes, and (4) phosphate-buffered saline control. Endometrial gene expression, thickness, adhesions, pregnancy, and live birth rates were assessed.
Results: The co-treatment group exhibited significant upregulation of genes involved in endometrial regeneration (TGF-β1, ADAM15, ADAM17, SMAD3, Integrinβ3) and downregulation of SMAD7. This group also demonstrated the highest mean endometrial thickness, reduced intrauterine adhesions, and the highest pregnancy (66.7%) and live birth rates. No severe adverse events were reported.
Conclusion: Co-treatment with UC-derived MSCs and exosomes shows promise as a safe and effective therapy for AS-related infertility, with synergistic effects on endometrial regeneration and reproductive outcomes. These findings warrant further investigation in more extensive clinical trials.

Keywords: Asherman syndrome, Mesenchymal stem cells, Exosomes, Cell therapy

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Abstract: A-10-2825-1

PCLO Variations Cause Pontocerebellar Hypoplasia Type 3: A Novel Variant in PCLO and Crispr-Edited Cells Based Wes Results

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Background: Pathogenic variations in the PCLO gene cause Pontocerebellar Hypoplasia type 3 (PCH3), an extremely rare autosomal recessive disorder, characterized by seizure, intellectual disability, developmental delay, and microcephaly. PCLO encodes the Piccolo protein, which plays a critical role in synaptic function and neurological disorders. Hitherto, only one pathogenic variant in PCLO causing PCH3 has been reported in the literature. Research on PCH3 is ongoing, but due to its rarity, there are relatively few studies on the condition.

Methods: A novel homozygous (NM_033026: c.458T>C, p. Met153Thr) variant in PCLO was detected by whole-exome sequencing and confirmed by Sanger sequencing. Furthermore, explaining the pathogenicity of PCLO variants was done by functional studies such as the generation of CRISPR-edited cells, Real-time PCR, in-silico analysis, and NGS results.

Results: The proband presented with seizure, microcephaly, mild ataxia, and behavioral issues. Unlike the previously reported cases, she manifested toe walking, loss of tendon reflexes, and paralysis of one side of her body. Then, the PCLO knock-out cell model and molecular analysis provided support for the loss of function of the Piccolo protein in the case of homozygous variants of PCLO. Our investigations also demonstrated that Piccolo deficiency could affect the expression of other genes such as CtBp1 and BSN.

Conclusion: Here, we have identified one novel PCLO variant causing PCH3. A novel CRISPR-based cell model for PCH3 was also designed that will provide an appropriate foundation for further studies on the molecular mechanisms of Piccolo functions. This model will contribute to a better understanding of the disease pathogenesis.

Keywords: PCLO, Piccolo, Pontocerebellar hypoplasia type 3, Mutation, CRISPR/Cas9.

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Abstract: A-10-2807-1

The Effects of Heat-Killed Saccharomyces boulardii on Inflammatory Markers and Intestinal Barrier in Rats with Obstructive Cholestasis

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Background: Saccharomyces boulardii is a unique probiotic yeast known for its anti-inflammatory properties and its impact on intestinal barrier functions. According to some studies, altering the gut microbiota could strengthen the gut barrier and decrease inflammatory responses in liver fibrosis. However, the safety of live probiotics remains a significant concern. This study examined the impacts of heat-killed S.boulardii on inflammation and intestinal barrier disruption in an experimental liver fibrosis model.

Methods: liver injury was induced by Bile duct ligation (BDL) in male Wistar rats. The study included four groups (n=8), two of which were BDL; one group received heat-killed S.boulardii, and another one vehicle daily by gastric gavage. Sham-operated and normal controls either received vehicle. Heat-killed S.boulardii was prescribed 7 days before BDL and then for 21 consecutive days after BDL. Finally, the expression of αSMA, TNFα, IL-6, and IL-10 genes in liver tissues and ZO-1 genes in the terminal ileum were assessed. Also, liver tissues and ileum were histologically analyzed.

Results: After treatment with heat-killed S.boulardii, the expression of αSMA, TNFα, and IL-6 genes were lower compared to the group of BDL rats ($P \leq 0.001$), but gene expression of IL-10 was higher ($P \leq 0.01$) in liver tissue, also the expression of the ZO-1 genes in the ileum was greater than that in the BDL group ($P \leq 0.001$). Moreover, liver tissue fibrosis and bile duct hyperplasia were lower than in the BDL group ($P \leq 0.05$). Also inflammatory, and necrosis cells, were not significantly lower than in the BDL group. Collagen fibers accumulate in the liver tissue in this group lower than the BDL group ($P \leq 0.001$). Additionally, villi shortening and crypt density in ileum tissue were lower than that in the BDL group ($P \leq 0.05$)

Conclusion: Heat-killed S.boulardii has the potential to attenuate liver fibrosis progression.

Keywords: Heat-killed probiotics, Saccharomyces boulardii, Liver fibrosis, Bile duct ligation

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Abstract: A-10-2171-2

Chitosan Nanoparticles as A Vehicle for Enhanced Nephroprotection: A Study on Cisplatin-Induced Nephrotoxicity

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Background: Cisplatin (CP) is a well-known and effective chemotherapeutic drug in cancer treatment, although it may result in nephrotoxicity as a side effect. Melatonin (Mel) has proven strong protective qualities against numerous toxicities due to its free radical scavenging ability. This study aims to investigate the possible nephroprotective effects of melatonin-loaded chitosan nanoparticles (ChitMelNPs) on CP-induced nephrotoxicity in adult male rats.

Methods: Forty male Wistar rats were divided into five groups: Control, CP, Mel (10 mg/kg), ChitMelNPs (10 mg/kg), and ChitNPs (10 mg/kg). The treatments were given by gavage for 15 days, with CP (12 mg/kg) injected intraperitoneally on the 16th day. On the 18th day, the rats were sacrificed to obtain kidney tissue and blood samples. Urea, creatinine, albumin, and total protein levels were evaluated in serum using biochemical tests. In addition, oxidative stress markers MDA and GSH were measured, along with the relative mRNA expression of iNOS and Nrf2.

Results: Following CP delivery, serum urea and creatinine levels increased considerably, while albumin and total protein levels decreased. In addition, histopathological analysis revealed increased inflammatory infiltration, venous congestion, sinusoidal dilatation, and feathery degeneration in the CP group. The CP-treated animals also showed a significant rise in kidney MDA levels and a decrease in glutathione (GSH). In addition, iNOS mRNA levels were notably higher in the CP group's kidneys than in the controls, though Nrf2 expression was reduced. Compared to the CP group, treatment with melatonin and ChitMelNPs significantly lowered serum urea and creatinine levels while enhancing albumin and total protein levels. Additionally, ChitMelNPs provided greater nephroprotective effects than melatonin.

Conclusion: Our findings suggest that oxidative stress and inflammation play an important role in the development of CP-induced nephrotoxicity and that ChitMelNPs might appear as a potential treatment alternative to handle this issue.

Keywords: Melatonin, Cisplatin, Nephrotoxicity, Nrf2, iNOS

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Abstract: A-10-2386-1

Synergistic Effect of Vitamin A and Tryptophan to Induce Tolerogenic Dendritic Cells in Celiac Disease Patient

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Background: Celiac disease (CeD) is a chronic immune-mediated intestinal condition triggered by gluten in genetically susceptible subjects. Some patients continue to have symptoms despite a gluten-free diet (GFD). Researchers are investigating alternative therapies with anti-inflammatory and immune-regulating effects. Tryptophan (Trp) and vitamin A (Retinol, Ret) influence dendritic cells (DCs) and enhance their tolerogenic properties. This study aimed to examine how Ret and Trp together affect the phenotypic and functional maturation of DCs in response to gliadin.

Methods: Monocyte cells from the peripheral blood mononuclear cells (PBMCs) of five celiac disease patients were differentiated into dendritic cells (DCs) using GMCSF and IL-4 for 5 days. The generated DCs (CD11c+, CD14-) were seeded at 0.5 × 106 cells/ml in 24-well plates. These cells were treated with or without 100 µM Trp + 1 µM Ret for 48 hours, followed by stimulation with 500 µg/ml peptic and tryptic (PT) digested gliadin for another 48 hours. Flow cytometry was used to analyze the expression of CD11c, CD14, CD83, CD86, and CD103. Levels of TGF-β, IL-10, IL-12, and TNF-α, were measured by ELISA, while mRNA expression of retinaldehyde dehydrogenase 2 (RALDH2), integrin αE (CD103), and Indoleamine 2, 3-dioxygenase (IDO) were assessed by qRT-PCR.

Results: We found that treatment of monocyte-derived immature DCs of celiac disease with Ret + Trp, followed by PT-gliadin exposure, resulted in significantly reduced expression of maturation markers, including CD83-CD86 and the inflammatory cytokines IL-12 and TNF-α ($p < 0.0001$), while the expression of IL-10, TGF-β and the inhibitory markers CD103, IDO and RALDH2 were significantly increased ($p < 0.0001$) compared to PT- gliadin stimulated DC alone.

Conclusion: The results suggest that vitamin A + tryptophan may provide therapeutic benefits to attenuate the effects of PT-gliadin-stimulated dendritic cells (DCs) in celiac disease. However, further research is needed to fully understand the underlying mechanisms of action in these cells.

Keywords: Celiac disease, Tryptophan, Retinol, Dendritic cells, T regulatory, Immune tolerance

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Abstract: A-10-2426-2

The Antidiabetic Effect of Lysine and a Combination of Lys+Vitc+Zn on Oxidative Stress, Endoplasmic Reticulum Stress, and Parthanatos in Type2 Diabetic (Na+STZ) Rats

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Background: Hyperglycemia leads to aggregation of misfolded proteins and oxidative stress, activating different related apoptosis pathways. In this study, we investigated the effects of L-lysine, as a chemical chaperone, and the co-administration of Lys-Zinc-Vitamin C on oxidative stress, ER stress, and poly [ADP-ribose] polymerase1 (PARP-1) activity (as a Parthanatos parameter) in the skeletal muscle of diabetic rats.

Methods: First, 30 Nicotinamide+Streptozotocin-induced diabetic rats were divided into three groups. Each diabetic group was treated with water (DN), Lys (DL), and Lys+VitC+Zn (DS). After one month, they were sacrificed and tissues were collected. We measured Catalase (CAT), Superoxide dismutase (SOD), Glutathione Peroxidase (GPx) activity, and Total Oxidant Status (TOS) by colorimetric methods. In addition, UPR and autophagy protein expression (eIF2α, p- eIF2α, XBP1s, Beclin1, and LC3) were measured by Western Blotting. Also, the splicing of XBP1 mRNA was evaluated by RT-PCR. In addition, the Colorimetric PARP Assay Kit measured the PARP-1 activity enzyme.

Results: Unlike the DL group, the DS group showed a significant increase in CAT, SOD, and GPx-specific activities as well as TOS compared to DN. In addition, the DS group had significantly different GPx than the DL group. A significant decrease was observed in the XBP1 mRNA splicing of DS and DL groups compared to DN. The expression of XBP1, p-eIF2α, and p-eIF2α/eIF2α ratio was significantly lower than those in the DS group compared to DN. Beclin1 and LC3II expression were significantly reduced in the DS and DL groups compared to DN. Furthermore, PARP-1 activity was significantly decreased in both DL and DS groups compared to DN.

Conclusion: Lysine and Lys+VitC+Zn decreased UPR and autophagy pathways through the reduction of oxidative stress and ER stress, which ultimately reduced the PARP-1 activity as a Parthanatos marker. Notably, Lys+VitC+Zn has more antidiabetic potential than Lysine alone in type 2 diabetic rats.

Keywords: Diabetes, Lysine, Oxidative Stress, ER stress, Parthanatos

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Abstract: A-10-2706-2

Metformin and Morin Combination Therapy Ameliorates Oxidative Stress in Skeletal Muscle of Mice Fed a High-Fat Diet

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Background: Oxidative stress, characterized by increased intracellular reactive oxygen species (ROS) generation, has been reported to be a key factor in the induction of insulin resistance in the muscle. This study aimed to investigate the single and combined treatment effects of metformin (MET) and morin (MOR) on oxidative stress parameters in the skeletal muscle of mice fed a high-fat diet.
Methods: Fifty male C57BL/6 mice were randomized into two dietary groups: the control group received a normal chow diet, and the high-fat diet (HFD) group received a 60 % fat-powered HFD for 15 weeks. Afterward, the HFD group was randomly divided into four groups: HFD, HFD + MET (0.23%), HFD + MOR (0.1%), and HFD + MET + MOR for 10 weeks. Various parameters related to oxidative stress, such as ferric reducing antioxidant power (FRAP), total thiol (–SH) group contents, malondialdehyde (MDA) levels, and protein carbonyl content, were measured in muscle tissue. Nuclear factor erythroid 2–related factor 2 (Nrf2) protein levels were measured by Western blotting analysis.
Results: Treatment with MET and MOR, either alone or in combination with a more significant effect, could restore FRAP and total thiol contents, representing the antioxidant capacities, and MDA and protein carbonyl contents, representing lipid and protein oxidative damages ($p<0.001$). Moreover, the combined treatment was more effective than the single treatments in reversing the reduced Nrf2 protein levels in the HFD groups, a key regulator of the antioxidant defense system ($p<0.001$).
Conclusion: These results suggest that treatment with MOR alone and in combination with MET more effectively might avert HFD-induced oxidative stress in the skeletal muscle via the Ntf2 signaling pathway.

Keywords: insulin resistance, metformin, morin, oxidative stress, skeletal muscle

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Abstract: A-10-2344-1

Exploring the Impact of CAPIRI Regimen on the Biochemical and Histopathological Changes in A Mouse Model of Colon Cancer

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Background: Colorectal cancer (CRC) is a major public health concern, ranking third in global cancer diagnoses and second in cancer-related deaths. Among various treatment strategies, combination chemotherapy regimens along with the monoclonal antibodies have emerged as the milestone of CRC treatment aiming to improve anticancer effects and suppress potential drug resistance. Therefore, the present study aimed at investigating the efficacy of CAPIRI chemotherapy regimen in 1,2 dimethylhydrazine-induced mouse model of CRC.

Methods: Twenty-four BALB/c male mice were randomly assigned into three groups of control, DMH, DMH+ CAPIRI (n=8). CRC was induced through intraperitoneal (i.p.) injection of DMH (20 mg/kg b.w.) once weekly for ten consecutive weeks. Post-induction, mice in the DMH+CAPIRI group received daily oral Capecitabine (CAP, 100 mg/kg body weight) and weekly i.p. Irinotecan (IRI, 25 mg/kg body weight) for eight weeks. At the end of 18th week, colonic polyp count, antioxidant enzyme activities (SOD, GPx), myeloperoxidase (MPO) activity, and malondialdehyde (MDA) levels were measured. Histopathological evaluation was performed using H&E staining, and western blotting assessed colonic BAX and Bcl-2 expression levels.

Results: DMH exposure resulted in a 100% polyp incidence in the colon, while CAPIRI significantly reduced polyp numbers to 8%. DMH also led to the significant elevated levels of colonic MDA and MPO as well as reduced antioxidant activities of SOD and GPx as compared to the control group ($P<0.05$); while, these changes were significantly alleviated in the CAPIRI group. Besides, high grade dysplasia and lymphocytic aggregation in the DMH group were almost resolved following CAPIRI treatment. Furthermore, CAPIRI regimen could significantly reverse the downregulated levels of BAX and upregulated levels of Bcl-2 in the DMH group ($P<0.05$).

Conclusion: CAPIRI regimen could efficiently resolve CRC-associated changes in the mouse colon by regulating redox balance and inducting apoptosis, suggesting its potential as an effective regimen for CRC.

Keywords: Colorectal cancer, DMH, CAPIRI, Combination therapy

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Abstract: A-10-2543-2

Granulosa Cells Isolated from Immature Follicles Are Associated with Restricted Glycolysis and Reduced Energy Production: A Dominant Problem in Polycystic Ovary Syndrome

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Background: We hypothesized that immature oocytes are associated with impaired energy production in surrounding granulosa cells (GCs) in polycystic ovary syndrome. Thus, this study investigated mitochondrial function, determined expression of glycolytic regulatory enzymes, and measured ATP level in GCs of PCOS patients.
Methods: GCs were isolated from forty-five PCOS patients and 45 control women. Intracellular concentration of reactive oxygen species (ROS), mitochondrial membrane potential (Dym), the rate of glycolysis, total antioxidant capacity (TAC), activities of catalase (CAT) and superoxide dismutase (SOD), and ATP level were measured in GCs. The gene expression and protein levels of glycolytic enzymes (hexokinase, muscular phosphofructokinase, platelet derived phosphofructokinase, and muscular pyruvate kinase) were determined. Association of GCs energy level with oocyte maturation was further validated by measuring glycolysis rate and ATP level in GCs isolated from mature and immature follicles from new set of fifteen PCOS patients and 15 controls.
Results: PCOS patients showed higher ROS level, declined TAC, reduced CAT and SOD activities, and lower Dym together with reduced expression of key glycolytic enzymes. ATP concentration and fertilization rate were lower in PCOS compared with control group. ATP level was significantly correlated with ROS and Dym (r=–0.624 and r=0.487, respectively). GCs isolated from immature follicles had significantly lower ATP level and rate of glycolysis compared with the GCs separated from mature follicles in both PCOS patients and control.
Conclusion: Declined energy due to the mitochondrial dysfunction and restrained glycolysis in GCs is associated with the immature oocytes and lower fertilization rate in PCOS.

Keywords: Granulosa cells, Glycolysis, In vitro fertilization, Polycystic ovary syndrome, Reactive oxygen species

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Abstract: A-10-2565-1

Development of Triple-Negative Breast Cancer Organoid Model to Study the Effect of Immune Cells

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Background: Breast cancer is one of the most common malignancies among women, categorized into four molecular subtypes, with triple-negative breast cancer (TNBC) being the most aggressive. Although chemotherapy is the primary treatment, drug resistance often develops over time. Recent evidence highlights the significant role of the tumor microenvironment in contributing to this resistance. To design effective therapies, it is crucial to incorporate factors from the tumor microenvironment into treatment models. However, existing models often fall short of accurately reflecting the precise features of this environment. Organoid models, derived from stem cells, patient tumor cells, or established cell lines, provide a more accurate and human-like representation, capturing the natural heterogeneity and structural complexities of tumors.

Methods: This study was conducted in three phases. First, organoids were created with varying ratios of MDA-MB-231 and human dermal fibroblast (HDF) cells, which were then evaluated for morphological characteristics, metastatic behavior, and drug response. The differentiation of THP-1 cells into macrophages was induced using PMA treatment, followed by evaluation through staining and flow cytometry. Finally, three-cell-type organoids were generated by incorporating THP-1 cells and macrophages, which were subsequently characterized.

Results: The initial phase focused on the impact of fibroblasts on the features of organoids. It was observed that higher percentages of fibroblasts intensified metastatic behavior and drug resistance. Next, THP-1 cells were utilized to enhance the complexity of the microenvironment. Prior to their incorporation into the organoids, THP-1 cells were differentiated into a macrophage state, which was evaluated. The addition of immune cells (both differentiated and undifferentiated THP-1) to fully formed organoids resulted in more cohesive structures and larger sizes. However, simultaneous co-culturing of all cell types led to fragmented structures. Ultimately, all formed organoids exhibited well-defined specialized acini structures and heterogeneity—characteristics typical of organoids—and some bean-shaped nuclei were observed, likely corresponding to infiltrating macrophages.

Conclusion: In this study, we developed TNBC models demonstrating that the presence of stromal cells significantly alters cancer cell behavior, particularly concerning drug response, invasion, and sphere formation.

Keywords: Organoid, TNBC, MDA-MB-231, metastasis, drug response, immune cells

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Abstract: A-10-2557-1

The Link Between FGFR1/FGFR3 and Ras Gene Mutations and the Pathological Tumor Grades in Oral Squamous Cell Carcinoma in Iranian Patients

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Background: Fibroblast growth factor receptors (FGFRs) are key players in the development of various malignancies, including oral cavity squamous cell carcinoma (OSCC). This study aimed to identify mutations in specific exons of the FGFR1, FGFR3, and H-Ras genes in tissue biopsies from OSCC patients and assess the expression of their corresponding protein products. Additionally, the relationship between these gene mutations and the patients' demographic data and tumor pathological grade was investigated.

Methods: Sixty-six surgically excised tumor biopsies from OSCC patients and 32 normal gingival tissue samples were analyzed. DNA was extracted from the biopsies, and mutations in selected exons of H-Ras (exon 2), FGFR1 (exon 13), and FGFR3 (exon 7) were determined using Sanger sequencing. Histological and immunohistochemical (IHC) analyses were performed to evaluate protein expression in the tissue samples.

Results: The study found a mutation rate of 53.2% in H-Ras exon 2, 32.2% in FGFR1 exon 13, and 27.4% in FGFR3 exon 7. High-grade (poorly differentiated) tumors showed a 100% mutation rate for H-Ras and 77% for FGFR1 and FGFR3 combined. The IHC analysis revealed significantly higher levels of H-Ras and FGFR protein accumulation in OSCC tumor biopsies compared to normal tissues.

Conclusion: The findings demonstrate a strong association between the frequency of gene mutations in H-Ras, FGFR1, and FGFR3, and the pathological grade of OSCC tumors. Overexpression of the corresponding proteins was also linked to tumor progression. These results provide valuable insights into the molecular mechanisms driving the development and progression of OSCC, highlighting the role of H-Ras and FGFRs as potential targets for therapeutic intervention in high-grade OSCC tumors.

Keywords: Oral cavity cancer, Tumor grade, Ras gene mutation, FGFRs gene mutation, Smoking, Immunohistochemistry

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Abstract: A-10-2493-2

Auraptene's Protective Role in A Mouse Model of Colorectal Cancer Through Inflammation Regulation

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Background: Chronic inflammation is a recognized risk factor for the development and progression of colorectal cancer (CRC). Auraptene, a natural flavonoid found in citrus fruits, is noted for its anticarcinogenic effects in CRC. This study aimed to investigate the anti-inflammatory properties of Auraptene in a CRC mouse model.
Methods: CT-26 xenograft mice were created and randomly assigned to three groups: (i) the Auraptene group, which received intratumoral injections at a concentration of 200 µM; (ii) the sham control group, injected intratumorally with a mixture of normal saline and dimethyl sulfoxide (DMSO) as the solvent for Auraptene; and (iii) a positive control group, where mice received intraperitoneal injections of 5 mg/kg of 5-FU. After 14 days, the mice were sacrificed, and their tumors were collected for further analysis. The anti-inflammatory effects of Auraptene in the tumor tissue were evaluated through Real-time PCR analysis of NF-κB and TGFB1, along with measuring cytokine levels of TNF-α, IL-6, IL-1α, and IF-γ using the ELISA method.
Results: Auraptene significantly reduced inflammation risk by decreasing the mRNA levels of NF-κB and TGFB1 compared to the control group ($p<0.05$). Additionally, there was a significant decrease in the levels of pro-inflammatory cytokines TNF-α, IL-6, and IF-γ compared to the control group ($p<0.05$).
Conclusion: Given the substantial role of a pro-tumorigenic inflammatory environment in cancer progression, our findings suggest that Auraptene could be a promising option for supplementary treatment. This is attributed to its anti-inflammatory properties, demonstrated through the modulation of essential inflammatory mediators.

Keywords: Colorectal cancer, Auraptene, anti-inflammatory effect

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Abstract: A-10-2532-1

The Combination Effect of B7-H7 Suppression and Docetaxel in Gastric Cancer Therapy

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Background: Despite the high prevalence of gastric cancer (GC), drug resistance is a major problem for effective chemotherapy. B7-H7 is a novel member of the B7 superfamily and is expressed in most of cancers. However, the effects of B7-H7 siRNA-mediated silencing in combination with chemotherapy drug on the cell proliferation, apoptosis, cell cycle, and colony formation rate in GC cells, remained unknown. Therefore, this study was designed to assess the effect of B7-H7 suppression using small interference RNA (siRNA) in combination with Docetaxel on GC cells.

Methods: MTT test was applied to determine the IC50 of Docetaxel and the combined effect of B7-H7 siRNA and Docetaxel on the viability of the MKN-45 cells. To determine B7-H7, BCL-2, BAX, and Caspase-3-8-9 genes expression, qRT-PCR was performed. Furthermore, flow cytometry was applied to evaluate apoptosis and the cell cycle status in different groups. Finally, to evaluate the effect of this combination therapy on colony-forming ability, colony formation test was employed.

Results: B7-H7 suppression increased the chemo-sensitivity of MKN-45 cells to Docetaxel and decreased its efficient dose. Also, the expression of B7-H7 mRNA was reduced after using B7-H7 siRNA and Docetaxel in MKN-45 GC cells. Furthermore, B7-H7 suppression alongside Docetaxel reduced colony formation rate, arrested the cell cycle at the G2-M phase, and induced apoptosis by modulating the expression of apoptotic target genes.

Conclusion: B7-H7 plays a significant role in the chemo-sensitivity and pathogenesis of GC. Therefore, B7-H7 suppression, in combination with Docetaxel, may be a promising therapeutic approach in treating

Keywords: Gastric cancer, siRNA, B7-H7, Docetaxel, Chemo-sensitivity, Combination therapy

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Abstract: A-10-2527-2

Exosomes of Whartons' Jelly Mesenchymal Stem Cells Can Recuperate Hepatic Fibrosis Disease by Reducing the NOXs Genes Expression

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Background: Hepatic fibrosis is a major cause of morbidity and mortality in the world. No definite cure has been found for liver fibrosis yet. NADPH oxidases (NOXs), play an important role in developing hepatic fibrosis by producing ROS. The mesenchymal stem cells (MSCs)-derived exosomes can be used as a remedy. The main purpose of this research was to investigate the effect of exosomes of WJ-MSC on NOX genes expression levels and phosphorylation of Smad3 protein in TGF-β-induced liver fibrosis.

Methods: First, liver fibrosis was induced with TGF-β (2 ng/mL) for 24 hours in LX2 cells. Second, the cells were treated with several concentrations of the exosomes derived from WJ-MSCs (10, 20, 30, 40, and 50 µg/ml) for 24h. Then, RT-PCR and Western blot techniques were used to measure NOX1, NOX2, and NOX4 gene expression and Smad3C phosphorylated protein expression. Finally, detection of ROS production was performed using the fluorimetric method and (H2DCF) probe.

Results: After treatment of LX-2 with TGF-β1 to induce liver fibrosis, it was observed that the expression of NOX1, NOX2, and NOX4 mRNA and ROS production increased compared with the control group. However, their mRNA expressions and ROS production decreased significantly with WJ-MSCs exosomes at 40 and 50 µg/ml concentrations in TGF-β-induced- LX-2. Additionally, the Phosphorylation of Smad3C protein was significantly reduced after exposure to exosomes.

conclusion: In our study, exosomes effectively reduced the NOX1, NOX2, NOX4 mRNA expressions, the phosphorylation of Smad3C protein, and ROS production in TGF-β-treated LX2. This data showed that human exosomes of WJ-MSCs can protect the TGF-β induced hepatic fibrosis by inhibition of the NOXs pathway and may be a new treatment for liver fibrosis. Treatment of hepatic fibrosis via human exosomes of WJ-MSCs is a new achievement and can be used as a clinical remedy in the future.

Keywords: Exosome, hepatic fibrosis, NADPH oxidase

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Abstract: A-10-2379-1

The Significance of Cd44v6 in Primary Bone Tumors: A Study of Malignant and Benign Lesions

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Background: The objective of this study was to assess the expression profile of CD44V6, a potential cancer stem cell marker, and its diagnostic and predictive significance in three distinct types of primary bone tumors.
Methods: This study employed real-time qRT-PCR and immunohistochemistry to analyze the gene and protein levels of CD44V6 in a total of 138 fresh bone tissue samples. We also investigated the circulating levels of CD44V6 by isolating peripheral blood mononuclear cells from 92 blood samples. Among these, 69 samples were obtained from patients diagnosed with primary bone tumors, while the remaining 23 samples were from healthy donors.
Results: In patients with osteosarcoma and chondrosarcoma, both the gene and protein expression of CD44V6 were found to be significantly higher compared to the GCT group. Moreover, the circulating level of CD44V6 was notably elevated in patients diagnosed with osteosarcoma and chondrosarcoma compared to the GCT group and patients with malignant tumor characteristics. A strong correlation was observed between the gene and protein levels of CD44V6 and critical tumor indicators, such as tumor grade, metastasis, recurrence, and size at the tumor site. CD44V6 demonstrated potential in differentiating patients with bone tumors from both control groups and in distinguishing tumor groups with severe and invasive characteristics from those with non-severe features. Importantly, the expression level of CD44V6 also showed predictive value for determining tumor grade and the likelihood of recurrence.
Conclusion: CD44V6 is likely involved in the development of primary bone tumors and has potential as a diagnostic biomarker for bone cancer. However, to achieve more accurate and conclusive findings, further mechanistic investigations involving larger population samples are necessary.

Keywords: CD44v6, Osteosarcoma, Chondrosarcoma, Giant cell tumors, malignancy

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Abstract: A-10-2477-1

Non-Enzymatic Paper Strip Sensor Based on Peroxidase-Like Activity of Prussian Blue-Coated Fe2o3 Nanoparticles for the Detection of H_2O_2

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Background: In this study, a non-enzymatic paper strip sensor based on Prussian blue-coated Fe_2O_3 nanoparticles (PB-Fe_2O_3 NPs) was constructed, and its performance in H_2O_2 detection was evaluated.
Methods: First, γ-Fe_2O_3 NPs were synthesized using the co-precipitation method and then coated with Prussian Blue (PB) NPs. The PB- Fe_2O_3 NPs were characterized by UV-visible spectroscopy, DLS, XRD, TEM, and ICP-OES. The peroxidase-like activities of the γ- Fe_2O_3 NPs and PB- Fe_2O_3 NPs were measured by UV-visible spectroscopy.
Results: These characterization methods showed that the PB-Fe_2O_3 NPs were relatively monodisperse and approximately 71 nm in size. The results demonstrated that the catalytic activity of the PB- Fe_2O_3 NPs was higher than that of the γ- Fe_2O_3 NPs and the K_m values for TMB and H_2O_2 as substrates were 0.018, and 385.4, respectively. The paper strip was fabricated based on PB- Fe_2O_3 NPs. The concentrations of PB- Fe_2O_3 NPs and TMB, which were immobilized on paper strip, were then optimized. Serial dilutions of H_2O_2 in the concentration range of 0-5000.0 µM were prepared in acetate buffer and applied to the paper strips. The detection limit of the paper strip for H_2O_2 in acetate buffer was 50.0 µM. The interference of common components in semen specimens on the performance of paper strip was evaluated, and the results showed that citric acid and ascorbic acid under 1000.0 µM concentration of H_2O_2 interfered with the performance of paper strips. The performance of the paper strips in human semen specimens as a biological sample was assessed, and the detection limit was 750.0 µM.
Conclusion: Nanozymes exhibit a sensitive performance in the detection of H_2O_2. However, their appropriate performance in physiological liquids is challenging because of the presence of a series of antioxidant components in physiological liquids, which can interfere with the performance of nanozyme-based biosensors.

Keywords: Paper strip sensor, Prussian blue nanoparticles, Fe_2O_3 nanoparticles, H_2O_2, Nanozymes, Male infertility

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Abstract: A-10-2500-2

Evaluation of Mesenchymal Stem Cells Derived from Different Tissues on Burn Wound Healing on Diabetic Rats

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Background: Diabetes mellitus is a chronic metabolic disease, which is one of the major contributors to chronic wound healing problems and amputations, particularly related to diabetic microvascular complications. When patients with diabetes develop a burn wound, they are at higher risk to develop major complications. In order to reduce the duration of hospitalization and provide rapid wound healing in burn and trauma wounds of diabetes, it is necessary to use experimental diabetic models and investigate the effect of modern regenerative medicine treatment protocols on burn models.

Methods: In this study, rat adipose tissues (AD) and bone marrow were excised, and isolated mesenchymal stem cells (MSCs) were amplified in cell culture and then transferred to the burn areas in STZ-diabetic rats on which thermal burn model created. Wound areas were measured and biopsy samples were excised from the wound areas of all diabetic rats to analyze gene expression levels of wound healing markers by qPCR. The markers, including VEGF, PDGF, bFGF, EGF, Keratinocyte growth factor (KGF) and TGF-β, which are known to be directly involved in wound healing mechanism, were analyzed.

Results: Biopsy samples were excised from the back of cell-treated/untreated rats on 3rd, 7th, 14th and 21th days after treatment. Wound contraction started earlier in both groups treated with MSCs in comparison to the control group. Also, in both groups treated with MSCs, the gene expression levels of VEGF, PDGF, bFGF, EGF increased, while KGF and TGF- β did not show a significant change compared to the untreated diabetic rats. In addition, the levels of VEGF, PDGF, and bFGF in the group treated with MSCs isolated from bone marrow, were higher than those in the AD-MSCs group, but not significant.

Conclusion: We demonstrated that applying MSCs derived from different tissues has a remarkable potential for treatment of diabetic burn wounds. There were no significant difference between the two groups treated with MSCs.

Keywords: Wound healing, Burn wound, Mesenchimal stem cell, Diabetes, Rats

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Abstract: A-10-2437-1

Hepatocellular Carcinoma Induced by Diethyl Nitrosamine in Mice Is Associated with Progressive Tumor Cell Proliferation and H-Ras Expression

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Background: Hepatocellular carcinoma (HCC) is the most common type of liver cancer, with abnormal activation of the Ras-ERK signaling pathway frequently contributing to its development. However, the specific relationship between H-Ras activation and cell proliferation during HCC progression remains unclear. This study aimed to investigate the expression of H-Ras and Ki67 during the development of HCC in a mouse model of liver cancer induced by Diethylnitrosamine (DEN).

Methods: Seventy-two mice were divided into four groups: a control group, a phenobarbital group, a DEN-alone group, and a DEN + phenobarbital (HCC) group. Treatment began on day 14 after birth. Mice in the phenobarbital group received phenobarbital from day 28 onward (500 mg per liter of water), while the DEN + phenobarbital group was given a single intraperitoneal dose of DEN (50 mg/kg) and phenobarbital treatment similar to the phenobarbital group. Mice were euthanized at 2, 4, and 6 months, and blood and liver tissues were collected for RNA extraction and H-Ras expression analysis using real-time PCR. Liver tissue biopsies were fixed in formalin for immunohistochemical (IHC) and immunofluorescence analysis with antibodies targeting H-Ras and Ki67.

Results: Liver function markers ALT and AST levels increased during HCC progression, and histopathological analysis revealed fibrosis in both the phenobarbital and HCC groups at 4 and 6 months. Atypical cells were detected in the 4-month HCC group, with focal malignancies present in the 6-month HCC group. H-Ras expression in the DEN + phenobarbital group increased after two months, peaking at 6 months—1.5 times higher than the phenobarbital group and 2.5 times higher than the control group. Ki67 expression in liver biopsies gradually increased, with significant elevations seen in the 2-month phenobarbital and 6-month DEN + phenobarbital groups.

Conclusion: The study demonstrates that the overexpression of H-ras and Ki67 is closely associated with liver tumor cell proliferation during HCC progression.

Keywords: Diethylnitrosamine, Markers Gene expression, Hepatocellular Carcinoma, H-Ras, Ki67

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Abstract: A-10-2424-1

Electrospun Silk Nanofibers Improve Differentiation Potential of Human Induced Pluripotent Stem Cells to Insulin Producing Cells

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Background: Diabetes mellitus is a chronic metabolic disorder characterized by insulin deficiency and/or insulin resistance, leading to elevated blood glucose levels. Advances in tissue engineering and cell therapy have provided new hopes for treating diabetes. This study investigates the potential of electrospun silk fibroin nanofibers as a scaffold for differentiating human induced pluripotent stem cells (hiPSCs) into insulin-producing cells (IPCs).
Methods: Silk fibroin nanofibers were fabricated using the electrospinning technique. hiPSCs were cultured on these nanofibers and compared with a 2D control. Cell viability was assessed using the MTT assay. The expression of definitive endoderm and pancreatic genes was evaluated by quantitative PCR. Immunofluorescence staining and flow cytometry were employed to confirm IPC differentiation. Insulin and C-peptide secretion in response to glucose stimulation were measured using an ELISA kit.
Results: Scanning electron microscopy (SEM) revealed smooth, bead-free silk nanofibers with interconnected pores. hiPSCs exhibited higher viability and proliferation on silk nanofibers compared to the 2D control. Quantitative PCR showed significantly increased expression of definitive endoderm markers (FoxA2, Sox-17) and pancreatic markers (Insulin, Pdx1, Glut2, Ngn3, Glucagon) in the 3D silk nanofiber group. Immunofluorescence and flow cytometry confirmed successful differentiation into IPCs. IPCs on silk nanofibers demonstrated enhanced insulin and C-peptide secretion in response to glucose stimulation, especially at 25 mM glucose concentration.
Conclusion: Silk fibroin nanofibers significantly enhance the differentiation of hiPSCs into IPCs, showing promise as a scaffold for pancreatic tissue engineering in diabetes treatment. These findings support the potential of silk nanofibers in improving cell survival, proliferation, and functional differentiation of IPCs.

Keywords: producing cells, Three-dimensional scaffold, Induced pluripotent stem cells, Cell therapy, Silk nanofibers

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Abstract: A-10-2438-1

Differential Gene Expression Patterns in ST-elevation Myocardial Infarction and Non-ST-elevation Myocardial Infarction

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Background: Myocardial infarction (MI) has two types, ST-elevation myocardial infarction (STEMI) and Non-ST-elevation myocardial infarction (NSTEMI), which have progressive prevalence in the world. The objective of this study was to utilize previous clinical studies and high throughput data to propose gene profiles and signaling pathways involved in each of STEMI and NSTEMI diseases.

Methods: The study used the gene expression Omnibus (GEO) database to collect transcriptomic data on myocardial infarction (MI). Also, previous clinical studies and the DisGeNET database were evaluated to make the identified genes more valid, then gene networks were created using the STRING database for STEMI and NSTEMI separately. Pathway analysis was conducted using KEGG, and GO enrichment on genes with high scores in both STEMI and NSTEMI networks. Additionally, expression changes in the suggested gene profile were analyzed over a 30-day period.

Results: The high score gene profiles in the STEMI network (including DUSP1, PADI4, CDA, VNN3, CYP4F3, MMP9, NOV, ARG1, IRS2, DUSP2, CRISPLD2, HMGB2, and TNFRS12A) and NSTEMI network (including FAM46C, HBQ1, CA1, KRT1, XK, BTNL3, FEXH, GLRX5, ACOX2, ZBTB32, IPO11, LDLR, NT5DC2, and CD244) found the distinction between STEIM and NSTEIM. The NSTEMI genes found to be more prevalent in the mitochondrial matrix, and nuclear lumen. The STEMI genes were more abundant in secretory vesicles, and the extracellular matrix.

Conclusion: In the study, it was clearly demonstrated that there are low- and high-fold genes present in STEMI and NSTEMI. The enrichment of high-fold genes indicated the involvement of specific signaling pathways and cellular compartments. Distinct gene profiles with high scores were identified for diagnosing STEMI (consisting of 13 genes) and NSTEMI (consisting of 14 genes). The study also proposed cut-off time points of up to three days for measuring the high-score gene profiles associated with STEMI and NSTEMI.

Keywords: myocardial infarction, STEMI, NSTEMI, gene profile, microarray, Gene network

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Abstract: A-10-2405-1

Sar131675 Exhibits Anticancer Activity on Human Ovarian Cancer Cells Through Inhibition of VEGFR-3/ERK1/2/AKT Signaling Pathway

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Background: Vascular endothelial growth factor receptor-3 (VEGFR-3) plays a key role in tumorigenesis and lymphangiogenesis, making it a promising molecular target for cancer therapies. In ovarian cancer, the involvement of VEGFR-3 and its therapeutic potential are not yet fully understood. This study aimed to investigate the effects of SAR131675, a selective VEGFR-3 antagonist, on ovarian cancer cell behavior.

Methods: SAR131675 is known to inhibit lymphatic cell growth through VEGFR-3 blockade. In this study, we examined the role of VEGFR-3 in ovarian cancer cells and explored the effects of SAR131675 on cell proliferation, cell cycle progression, migration, and apoptosis. OVCAR3 and SKOV3 ovarian cancer cells were treated with VEGF-C Cys156Ser (VEGF-CS), a selective ligand for VEGFR-3, to stimulate the receptor. SAR131675 was then applied to assess its dose-dependent effects on the cellular and molecular processes in these cancer cells.

Results: Both mRNA and protein levels of VEGFR-3 were detected in OVCAR3 and SKOV3 cells, and receptor activation was observed following stimulation with 50 ng/ml VEGF-CS. VEGFR-3 phosphorylation led to the activation of downstream signaling molecules, including ERK1/2 and AKT. SAR131675 treatment inhibited VEGF-CS-induced proliferation, colony formation, and migration of ovarian cancer cells in a dose-dependent manner. Furthermore, SAR131675 increased cell cycle arrest and promoted apoptosis in both OVCAR3 and SKOV3 cells. Mechanistically, SAR131675 effectively suppressed VEGFR-3 phosphorylation and downstream activation of ERK1/2 and AKT pathways.

Conclusion: Our findings demonstrate that SAR131675 exerts anticancer effects on ovarian cancer cells by inhibiting VEGFR-3 activation and its downstream ERK1/2 and AKT signaling pathways. This suggests that SAR131675 could be a potential targeted therapy for ovarian cancer.

Keywords: SAR131675, Ovarian cancer, Vascular endothelial growth factor receptor-3, Anticancer activity, AKT, ERK1/2

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Abstract: A-10-2227-2

Lipoic Acid Can Prevent Microplastic-Induced Contractile Response Change in Rat Trachea

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Background: Microplastics are present in human foods and drinking water. Lipoic acid (LA) is a natural compound with antioxidant properties. The current study aimed to assess the role of LA as a protective agent to inhibit polystyrene microplastic-induced oxidative stress and contractile response changes in the trachea of the rats.

Methods: Rats were divided into five groups: control, control treated with LA 100 mg/kg, polystyrene, and polystyrene treated with LA at doses of 25 or 100 mg/kg. To induce oxidative stress and trachea injury, oral polystyrene was administered daily at a dose of 30 mg/kg for two months. Oral LA was also given daily at 25 or 100 mg/kg doses for seven weeks. The contractile response changes of the trachea to acetylcholine (ACh) and potassium chloride (KCl) were recorded in the isolated bath containing Krebs solution. In addition, the activity of catalase (CAT) and reactive oxygen species (ROS) was evaluated. Data analysis was conducted using one-way ANOVA and Tukey post-test. A $p<0.05$ was considered statistically significant.

Results: The polystyrene administration significantly increased the tracheal smooth muscle contractions induced by KCl and ACh compared to the control group ($p<0.001$). While the 25 mg/kg dose of LA did not significantly decrease the contractions compared to the polystyrene group ($p>0.05$), LA at the dose of 100 mg/kg reduced the tracheal muscle contractions ($p<0.05$). The polystyrene group also exhibited higher amounts of ROS relative to controls ($p<0.001$). However, co-administration of LA (100 mg/kg) decreased ROS compared to the polystyrene group ($p<0.05$). The polystyrene group also demonstrated lower activity of CAT compared to the control group ($p<0.01$), and the CAT activity was retrieved in the LA-treated (100 mg/kg) group ($p<0.05$).

Conclusion: LA administration can prevent oxidative stress and contractile response changes in the trachea following microplastic consumption in rats.

Keywords: Lipoic acid, Polystyrene microplastic, Oxidative stress, Trachea

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Abstract: A-10-2263-1

Blockage of Wnt/β-Catenin Signaling Pathway in Colorectal Cancer Resistant Cells by Nitazoxanide Effects on Peptidylarginine Deiminases Expression

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Background: Multidrug resistance (MDR) is a significant obstacle in cancer treatment, where conventional drugs lose their efficacy. Identifying critical mechanisms behind MDR and developing novel therapeutic strategies is essential for overcoming this challenge. This study is the first to investigate the combination effect and molecular mechanism of nitazoxanide (NTZ) and oxaliplatin (OXP) on LS174T/OXP-resistant colorectal cancer cells.
Methods: The cytotoxic effect of NTZ on OXP-resistant and sensitive LS174T cells was assessed using the MTT assay. Changes in the expression levels of MDR-related genes (MDR1, MRP1, and CTNNB1) and PAD enzymes (PAD2, PAD4) were evaluated through RT-qPCR and western blotting. Apoptosis was quantified using flow cytometry.
Results: LS174T/OXP-resistant cells were identified based on their significantly higher IC50 values compared to sensitive cells (11567 nM vs. 1745 nM for 24 h; 5161 nM vs. 882 nM for 48 h, $p<0.05$). The combination of NTZ with OXP significantly reduced the IC50 of OXP in resistant cells after 48 hours (2154 nM, $p<0.05$). NTZ combined with OXP notably downregulated the expression of MDR1 ($p<0.001$), MRP1 ($p<0.05$), and CTNNB1 ($p<0.001$), while PAD2 and PAD4 expression was significantly upregulated ($p<0.001$). Apoptosis was markedly increased in the combination treatment group, as indicated by a rise in the sub-G1 population.
Conclusion: The combination of NTZ and OXP effectively reversed MDR in colorectal cancer cells by downregulating MDR1 and MRP1 and disrupting the Wnt/β-catenin signaling pathway.

Keywords: Colorectal cancer, nitazoxanide, peptidylarginine deiminase, multidrug resistance, Wnt/β-catenin

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-994-4

Evaluation of the protective effect of Biochanin-A on endoplasmic reticulum stress (ERS) in the liver tissue of type 1 diabetic rats

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Background: Long-term diabetes can lead to liver damage. This study was designed to evaluate the protective effect of Biochanin-A (BCA), an isoflavone, on liver by investigating its antidiabetic and antioxidant properties and assessing its effects on endoplasmic reticulum stress (ERS) in the rat liver tissue.

Methods: Twenty-four Wistar Rats were divided into four groups, with six rats in each: Cnt, Dibt control, Dibt-BCA/10, and Dibt-BCA/15. STZ has been used to induce diabetes. BCA was administered by gavage for 42 days. The expression of ATF6α, PERK, IRE1α, NF-kB, and IL-6 genes was assessed by real-time PCR. The activity of superoxide dismutase (SOD) and levels of malondialdehyde (MDA) and FBG in the liver tissue was measured by biochemistry kit.

Results: The results showed that the levels of FBG in serum and malondialdehyde (MDA) level and expression of ATF6α, PERK, IRE1α, NF-kB, and IL-6 genes in liver tissue were significantly higher in the Dibt control group than in the Cnt group ($P<0.05$). Additionally, the activity of superoxide dismutase (SOD) in liver tissue were remarkably reduced in the Dibt control group compared to those in the Cnt group ($P<0.05$). After 42 days of BCA gavage at doses of 10 and 15 mg/kg, the results showed that BCA dose-dependently and significantly improved all parameters in these groups compared to the Dibt group ($P<0.001$).

Conclusion: These results show that BCA has protective effects against liver damage in diabetic rats. Hence, BCA is a potential phytochemical therapy for diabetes and liver damage, although further studies are recommended to ascertain its role.

Keywords: Biochanin-A; liver damage; Endoplasmic reticulum stress; Oxidative stress

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Abstract: A-10-2586-1

The Association Between Arsenic Levels and Oxidative Stress in Myocardial Infarction: A Case-Control Study

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Background: Cardiovascular diseases (CVDs) are known as the first causes of death throughout the world, and mainly myocardial infarction (MI), lead to 7.4 million deaths annually. Atherosclerosis is the major underlying cause of most CVDs. However, exposure to heavy metals, among other factors, deserves further attention as a risk factor for CVDs. This study was designed to evaluate the levels of arsenic (Ars) in myocardial infarction (MI) patients and healthy individuals as well as assess the association between the incidence of MI and Ars, total antioxidant capacity (TAC), and oxidative stress (OS).

Methods: This case-control study was conducted among patients with MI (n = 164) and normal individuals (n = 61) at Shafa Hospital in Kerman, Iran. Patients were classified into two groups, including coronary artery blocks above 50% (CAB > 50%, n = 83) and coronary artery blocks less than 50% (CAB < 50%, n = 83) based on their angiography findings. The demographic characteristics, clinical history, biochemical parameters, and serum Ars and TAC levels were evaluated.

Results: In the present study, both CAB groups had significantly reduced levels of TAC compared with the control. Furthermore, TAC was lower in the CAB>%50 group compared to the CAB%50 (AUC = 78.29), and cytotoxic levels for both CAB groups (Ars ≥ 0.105 ppm), and no significant differences were found between the two groups.

Conclusion: Our findings suggest that Ars at ≥ 0.105 ppm is able to increase the risk of MI through the increased OS and decreased TAC.

Keywords: Cardiovascular diseases, Arsenic, Oxidative stress, Myocardial infarction

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Abstract: A-10-3153-1

Biological Assessment and Anticancer Effects of Green-Synthesized Selenium Nanoparticles

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Background: The green synthesis of nanoparticles is a safe and cost-effective approach that utilizes extracts from various plant parts, including flowers, leaves, stems, and roots. The aim of this study was to synthesize novel Selenium nanoparticles (Se NPs), by means of plant extract, taking advantage of green synthesis procedure.
Methods: Se NPs were synthesized using an aqueous extract of Melissa Officinalis L. (MO). The plant extract, rich in flavonoids, polyphenols, and alkaloids, served as a reducing agent in the nanoparticle synthesis process. Additionally, the extract functioned as both a reducing and capping agent during the simple and rapid green synthesis of Se NPs. The hydrodynamic size of the nanoparticles was assessed through dynamic light scattering (DLS), and their shape and size were further characterized using scanning electron microscopy (SEM) and transmission electron microscopy (TEM). Elemental composition analysis was performed via Energy Dispersive X-ray (EDX). Human Umbilical Vein Endothelial Cells (HUVEC) and MCF-7 breast cancer cell line were used for the assessment of the biological effects of the Se NPs.
Results: Analyses revealed that the Se NPs were spherical. The particle size was measured at 65 nm and 34 nm through DLS and SEM, respectively. Furthermore, biological evaluation showed that Se NPs ledto a significant increase in pro-oxidant properties; however, no toxicity to normal HUVEC cells was observed. Se NPs also demonstrated anticancer activity against the MCF-7 breast cancer cell line and caused dose-dependent cytotoxicity in these cells.
Conclusion: Selenium nanoparticles (Se NPs) were successfully synthesized using a simple, fast, and eco-friendly method and they demonstrated effectiveness in reducing cancer cell viability.

Keywords: Selenium nanoparticles, Melissa officinalis L., extract, Green synthesis, Anticancer, Breast cancer

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2929-1

Investigating the effect of Methanolic extract of artichole leaf on oxidative stress parameters and TNF-α and IL-10 factors in an experimental model of acute pancreatitis

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Background: L-arginine, a precursor of nitric oxide, can induce pancreatic damage at high doses due to the production of free radicals. Artichoke leaf extract is rich in antioxidant compounds and may protect cells by neutralizing these radicals.

Methods: In this study, 60 male Wistar rats were randomly assigned to five groups. Group one received 1 ml/kg body weight (b.w.) of normal saline intraperitoneally (ip). Group two received two ip doses of L-arginine (2 g/kg b.w.) one hour apart on the first day. In group three, rats were administered 10 mg/kg b.w. of melatonin ip two hours after the final L-arginine dose. Groups four and five received oral doses of artichoke extract (200 and 400 mg/kg b.w., respectively) one hour post-L-arginine, administered daily. Each group was subdivided, and animals were euthanized at 24 hours, 72 hours, and 14 days following L-arginine injection.

Results: Rats in the L-arginine group exhibited significantly elevated serum lipase and amylase levels compared to controls. Treatment with artichoke extract (200 and 400 mg/kg) and melatonin significantly reduced serum lipase levels at all time points (24 hours, 72 hours, and 14 days) and serum amylase levels at 24 hours. Artichoke extract also dose-dependently increased total antioxidant capacity (TAC) and decreased myeloperoxidase (MPO) and malondialdehyde levels, markers of oxidative stress. There were no significant differences in the levels of TNF-α, IL-6, and IL-10 between groups. Histological analysis revealed that artichoke extract reduced pancreatic cell necrosis and interstitial edema compared to the L-arginine group.

Conclusion: In conclusion, the methanolic extract of artichoke demonstrated antioxidant and anti-inflammatory properties in L-arginine-induced acute pancreatitis in male rats, highlighting its potential as a therapeutic agent for managing acute pancreatitis.

Keywords: Artichoke leaves, L-arginine, Acute pancreatitis, Oxidative stress

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Abstract: A-10-3112-3

Investigating the relationship between the expression of miR-153, FFAR-4 and oxidative stress indices with CT angiography data in patients with atherosclerosis symptoms in Kerman

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Background: Atherosclerosis is a multifactorial disease. Inflammation and oxidative stress are the main factors involved in the occurrence and progression of atherosclerosis. Long-chain free fatty acids can affect the inflammation process through their specific receptor, FFAR-4. It has also been found that microRNAs play a major role in regulating gene expression. Therefore, in this study, we investigated the relationship between calcium score, vascular occlusion and plaque volume in heart patients with oxidative stress indicators, FFAR-4 and miR-153 expression.

Methods: Blood samples were obtained from 113 people with symptoms of atherosclerosis who referred for CT-angiography. After centrifugation, the plasma and buffy coat was separated. FFAR-4 expression was measured by qRTPCR. Oxidative stress was evaluated by measuring total antioxidant capacity (TAC) and malondialdehyde (MDA) concentration. With bioinformatics studies, it was found that mir-153 is most related to FFAR-4, therefore miR-153 expression was also measured.

Results: The expression of FFAR-4 in the patient group (0.69±0.05) was significantly lower than the control group (1.01±0.08). On the contrary, the expression of miR-153 in the patients (1.44±0.15) was significantly higher than the control group (1.04±0.07). A negative correlation was observed between FFAR-4 expression level with the number of lesions, the volume of plaques, percentage of blockage and calcium score, while only a positive correlation was observed between the number of lesions and the expression of miR-153. The plasma level of MDA in the patient group (2.105±0.37 µM/l) has significantly increased. TAC level in the patient group (560.10±12.006 µMFe2+) compared to the control group (669.49±15.305 µMFe2+) had a significant decrease.

Conclusion: FFAR-4 has protective effects on plaque calcification severity, plaque size and CAD risk, and probably in patients with atherosclerosis, the expression of this receptor decreases with the increase of miR-153. Also, decreased expression of this receptor is associated with oxidative stress in atherosclerotic patients.

Keywords: Oxidative Stress, Malondialdehyde, FFAR-4, miR-153

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Abstract: A-10-3092-1

The effect of NOSHIN-SHAHD herbal syrup on liver functional factors, inflammation and oxidative stress in patients with non-alcoholic fatty liver disease; A randomized, double-blind, placebo-controlled trial study

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Background: Nonalcoholic fatty liver disease (NAFLD) is a condition in which excess fat accumulates in the liver triggers hepatotoxicity and oxidative stress, released pro-inflammatory cytokines and activation of hepatic stellate cells, which ultimately leads to inflammatory liver damage. In this study, we investigated the effect of herbal syrup formulated by Noushin-Shahed Company Contains the combined extract of ten plants artichoke, barberry, thistle, turmeric, licorice, ginger, chicory, rosemary, Mint and anise on improving liver functional factors, inflammation and oxidative stress in NAFLD patients.

Methods: This study was conducted on 80 NAFLD patients. Serum FBS, Chol, TG, HDL, LDL, AST, ALT, ALP, bilirubin and Oxidative stress indicators such as MDA, SOD, carbonylated protein, TAC as well as TNF-α and IL-6 were evaluated. In addition, the percentage of liver steatosis, CAP and fibrosis was also evaluated using the fibro-scan imaging technique. All the measurements have been carried out on two occasions before and after the intervention, in two drug and placebo groups.

Results: The statistical findings for TNF-α and IL-6 showed a significant reduction in the drug group compared to placebo (for both factors $p<0.001$). On the other hand there was a significant increase in the TAC factor ($p=0.03$) and for other indicators MDA, SOD and carbonyl protein despite significant differences Within the groups (comparing the state before with after the intervention) no significant differences were found between the groups.The results of the liver fibro-scan showed the improvement of the steatosis, fibrosis and CAP, within the groups while no significant differences between the groups.

Conclusion: The results showed a significan decrease in serum levels of LDL, TNF-α and IL-6, as well as a significant increase in TAC which is evidence for the potential anti-inflammatory and antioxidant effects of this herbal syrup in improving inflammation, oxidative stress, and lipid metabolism in NAFLD patients.

Keywords: NAFLD, herbal syrup, Oxidative stress, Inflammation, steatosis

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Abstract: A-10-2963-1

MiRNA19a-3p as a promise biomarker in Breast cancer treatment in 2D and 3D cell culture in a microfluidic device

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Background: Due to the high mortality rate associated with Breast cancer (BC), there is a pressing need for a non-invasive biomarker to aid in treatment. Our objective was to assess the potential of miR-19a-3p as a BC biomarker and to develop a novel approach for BC treatment using both 2D and 3D cell cultures within microfluidic devices.
Methods: In our study, we used advanced PPSF (smart PEI-PBA-SAP-F15) polymeric nanoparticles to effectively deliver anti-miR19a-3p to breast cancer (BC) cell lines. We evaluated the advantages of combining miR19a-3p antagonist therapy with Doxorubicin (DOX) in BC using both 2D and 3D cell culture models. Given that 3D culture studies yield more physiologically relevant results, we cultivated spheroids in microfluidic devices, with the molds for these devices created using 3D printing technology.
Results: Analysis using real-time PCR revealed an elevated expression of miR19a-3p in breast cancer (BC) cell lines. The successful transfer of anti-miR19a-3p into these cell lines was achieved. This resulted in an increase in the expression level of the PTEN gene, which is targeted by miRNA-19a-3p. The upregulation of PTEN led to reduced breast cancer cell migration and cell cycle arrest. Additionally, the combination therapy significantly induced apoptosis. Overall, our investigations using 2D and 3D spheroids in microfluidic devices, along with confocal microscopic studies, demonstrated a significantly higher proportion of dead cells in spheroids that were transfected with anti-miR19a-3p-PPSF and treated with DOX in MCF7 cell lines.
Conclusion: This research introduces miR-19a-3p as a BC biomarker. It is also providing an innovative in vitro system for generating, maintaining, visualizing, and evaluating consistent 3D cancer spheroids. The platform enables various biomarker assessments and pharmaceutical testing applications.

Keywords: Breast cancer, biomarker, Polymeric nanoparticles, Anti-miR19a-3p, Doxorubicin, PTEN, Microfluidic devices

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Abstract: A-10-3081-2

Mineral intake patterns are associated with prediabetes regression and progression: Tehran Lipid and Glucose Study

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Background: Dietary minerals have essential roles in insulin and glucose homeostasis. Aim: We investigated the potential association of dietary mineral patterns and longitudinal change of glycemic status in subjects with prediabetes (Pre-DM).
Methods: This study included 1456 subjects with Pre-DM (mean age of 47.2±12.8 and 52.5% men) participated in the third (2006-2008) and fourth (2009-2011) examinations of the Tehran Lipid and Glucose Study that followed up to 2015-2017. The participants' habitual dietary intakes of minerals were assessed using a semi-quantitative food frequency questionnaire (FFQ) at baseline. Principle factor analysis identified three major mineral patterns (with a total variance of 92.3%), including multi-mineral (MM) (characterized by higher loads of phosphorous, zinc, calcium, magnesium, and copper), chromium-selenium (Cr-Se), and iron-magnesium (Fe-Mn) patterns. Cox proportional hazard models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) of developing type 2 diabetes (T2D) and regression to normal glucose regulation (NGR) across tertile categories of mineral patterns score.
Results: After a median of 5.8 years of follow-up, the incidence of T2D and NGR was 23.8 and 46.8%, respectively. After adjustment of the T2D-risk score (i.e., composed of age, sex, family history of diabetes, history of gestational diabetes, body mass index, and physical activity level), Cr-Se and Fe-Mn patterns were associated with an increased chance of returning to NGR by 26% (HR=1.26, 95% CI=1.02-1.55) and 43% (HR=1.42, 95% CI=1.14-1.76), respectively. Fe-Mn pattern was also associated with a reduced risk of developing T2D (HR=0.67, 95% CI=0.49-0.92). MM patterns was not associated with Pre-DM regression and progression.
Conclusion: Subjects with Pre-DM may take more advantages from dietary mineral patterns rich in Cr-Se and Fe-Mn to effectively achieve NGR and prevent progression to T2D.

Keywords: Mineral patterns, pre-diabetes, normoglycemia, type 2 diabetes

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2906-1

Effects of Combined Hydroxychloroquine and Fisetin Treatment on NAFLD Improvement in Mice

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Background: The complex pathogenesis of non-alcoholic fatty liver disease (NAFLD) limits available FDA-approved treatments. Lipotoxicity leads to cellular stress and inflammation, exacerbated by disrupted autophagy that fails to manage lipophagy in the liver. The aim was to evaluate the efficacy of fisetin (FSN) and hydroxychloroquine (HCQ) in animal models of NAFLD.

Methods: Forty-eight male C57BL/6J mice were placed on either a standard chow or high-fat diet (HFD) for 16 weeks. The HFD group was subdivided to receive varying treatments: HFD, HFD + Vehicle, HFD + FSN, HFD + HCQ, and HFD + FSN + HCQ. FSN was given daily via gavage at 80 mg/kg, while HCQ was injected intraperitoneally at 50 mg/kg twice a week for 8 weeks. Assessments, including glucose and insulin tolerance tests, were performed, and liver tissue analysis included evaluations of serum glucose, lipid profiles, oxidative stress markers, and autophagy-related proteins.

Results: Treatment with FSN, HCQ, and particularly FSN+HCQ significantly improved NAFLD through regulation of body weight, insulin response, carbohydrate homeostasis, hepatic lipid metabolism, and inflammation. While the HCQ group showed some improvement in energy balance, it was accompanied by side effects, such as increased oxidative stress. FSN countered these with its direct and indirect antioxidant activity (via increased Nrf2 expression) and by controlling the expression of endoplasmic reticulum stress-related genes (GRP78, eIF2α, ATF4, and CHOP). Moreover, FSN enhanced autophagy via increasing p-AMPK, decreasing mTOR expression, and improving the expression of ULK1, ATG5, and Beclin1, indicated by an increased LC3II/LC3I ratio and reduced p62 protein levels in the liver.

Conclusion: In conclusion, FSN demonstrates significant therapeutic potential for managing NAFLD, and its combination with HCQ represents a promising strategy despite concerns over the long-term side effects of HCQ, aiming to enhance treatment outcomes while minimizing risks.

Keywords: Non-alcoholic fatty liver disease, fisetin, hydroxychloroquine, inflammation, oxidative stress, endoplasmic reticulum stress, autophagy.

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Abstract: A-10-2899-1

Development and Characterization of Chitosan-Sodium Alginate-Calcium Chloride nanoparticles of Acetyl-11-Keto-beta-Boswellic Acid in HT29 colorectal cancer cells

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Background: Colorectal cancer (CRC) is a leading cause of cancer-related morbidity and mortality. Current treatment modalities often face challenges such as limited efficacy. This study aimed to develop a novel drug delivery system using chitosan-sodium alginate-calcium chloride (CS-SA-CaCl2) nanoparticles for acetyl-11-keto-beta-boswellic acid (AKBA), a compound with promising anticancer properties, to enhance its therapeutic efficacy.
Methods: AKBA was extracted from the gum resin of Boswellia serrata using a three-phase partition method. The CS-SA-CaCl2 nanoparticles loaded with AKBA (NBAX) were synthesized by ionic pregelation and characterized for size, encapsulation efficiency, and drug release properties. The cytotoxic effects of NBAX were evaluated against HT29 colorectal cancer cells, and apoptosis induction was assessed using Annexin V staining and flow cytometry. All results were analyzed with GraphPad Prism and the p-values under 0.05 were considered significant.
Results: The extraction efficiency of AKBA was 12.64%. The NBAX exhibited significantly higher cytotoxicity against HT29 cells compared to free AKBA, boswellic acid extract, and the standard chemotherapeutic agent 5-Fluorouracil (5-FU). In particular, the IC50 value for NBAX was significantly lower than that of the other treatments, indicating enhanced potency ($p<0.001$). Flow cytometry analysis showed that NBAX significantly induced apoptosis in HT29 cells, as evidenced by increased early apoptotic cell populations. Annexin V staining results showed a significant increase in the percentage of apoptotic cells treated with AKBA compared to the control and other treatments. In addition, cell cycle analysis indicated that NBAX effectively arrested cell cycle progression, leading to an accumulation of cells in the sub-G1 phase, which is indicative of apoptosis.
Conclusion: NBAX nanoparticles show significant potential as an effective drug delivery system in the CRC cell model. The results suggest that it can enhance the therapeutic efficacy of AKBA, warranting further investigation in preclinical and clinical settings for CRC management.

Keywords: Colorectal cancer, Acetyl-11-Keto-beta-Boswellic Acid (AKBA), nanoparticle drug delivery system, sodium alginate, chitosan, calcium chloride

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Abstract: A-10-2489-1

Pre-treatment with Thymol and Thymol-loaded selenium nanoparticles reduces apoptosis and oxidative damage in SH-SY5Y cells in a 6-hydroxydopamine-induced Parkinson's disease experimental model

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Background: Parkinson's disease (PD) is a neurodegenerative disorder marked by the progressive loss of dopaminergic neurons. Despite various therapeutic options available for symptomatic relief, their efficacy and safety remain in debate, highlighting the need for new neuroprotective agents. Due to potential neuroprotective effects of Thymol and selenium nanoparticles (SeNPs), this study investigates the neuroprotective effects of Thymol, both in its free form and as selenium nanoparticles (SeNPs), using a 6-hydroxydopamine (6-OHDA)-induced PD model in SH-SY5Y cells.

Methods: To synthesize and characterize Nano-Se-Thymol, techniques such as dynamic light scattering (DLS), field-emission scanning electron microscopy (FESEM), Fourier transform infrared (FTIR) spectroscopy, and energy-dispersive X-ray (EDX) analysis were employed. The cytotoxicity of 6-OHDA, Thymol, and Nano-Se-Thymol was assessed through the MTT assay, followed by evaluations for protective effects, apoptosis, cell cycle changes, reactive oxygen species (ROS) levels, and protein expression via Western blotting.

Results: The SeNPs were synthesized and exhibited low toxicity to normal human fibroblast cells and provided superior neuroprotection against 6-OHDA-induced damage compared to free Thymol. It significantly reduced ROS generation and enhanced cell viability. The antioxidant properties of SeNPs contributed to these neuroprotective effects. Additionally, Nano-Se-Thymol decreased the expression of NF-κB inflammatory markers and caspase-3 proteins compared to Thymol alone.

Conclusion: The study suggests that Nano-Se-Thymol is a promising disease-modifying agent with potential therapeutic benefits for PD treatment. Its enhanced efficacy when delivered via SeNPs indicates a need for further preclinical investigations to fully explore its therapeutic potential

Keywords: Selenium nanoparticles, Thymol, Parkinson's disease, 6-hydroxydopamine, Oxidative stress

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Abstract: A-10-2693-1

Strategies for senotherapy-mediated human colon cancer treatment

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Background: Senolytic therapy has garnered significant attention for its potential in combating cancer. This study aimed to investigate the effects of three combinations of chemotherapeutic drugs with well-known senolytic agents (cisplatin+metformin, irinotecan+quercetin, oxaliplatin+caffeine) in K-RAS mutant (HCT-116 and CT26) and wild-type K-RAS-expressing (SW48) colorectal cancer (CRC) cells to assess the impact of K-RAS mutations on the efficacy of these senolytic therapies.

Methods: The optimal combination treatment schedule was determined for each chemotherapeutic drug and adjuvant to maximize their senotherapeutic efficacy. Senescence was evaluated through SA-β-gal staining, p16 and p21 expression, and nuclear morphology. Cell viability and death were assessed using the MTT assay, fluorescent staining methods, annexin V/PI flow cytometry analysis, and RT-qPCR analyses for Bcl-2, Bax, and beclin1.

Results: Cisplatin (5 µM), irinotecan (2.5 µM), and oxaliplatin (2 µM) alone induced multiple senescence hallmarks, including increased SA-β-gal activity, p16 and p21 upregulation, and multinucleation, in all tested cells. The post-treatment of cisplatin-treated cells with 5 mM metformin (cisplatin+metformin), the combined treatment of irinotecan and 25 µM quercetin (irinotecan+quercetin), and the post-treatment of oxaliplatin-treated cells with 2 mM caffeine (oxaliplatin+caffeine) resulted in decreased numbers of SA-β-gal+ cells, reduced cell viability, and lower p16 mRNA expression, alongside increased annexin V-positive cells, Bax/Bcl-2 ratio, and beclin-1 levels compared to drug-alone treatments. Acridine orange (AO)/ethidium bromide and AO staining confirmed the induction of apoptosis and autophagy in CRC cells for all schedules. The senotherapeutic efficacy was ranked as follows: cisplatin+metformin ≥ irinotecan+quercetin > oxaliplatin+caffeine.

Conclusion: Our findings suggest that all tested adjuvants effectively act as senolytic drugs in chemotherapy-induced senescent CRC cells, showing higher efficacy in K-RAS mutant cells by selectively eliminating these senescent cells through the induction of apoptosis and autophagy.

Keywords: Caffeine, Cisplatin, Colorectal cancer, Irinotecan, Metformin, Oxaliplatin, Quercetin, Senolytics

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Abstract: A-10-2815-1

Cyclophilin A increase 1N4R tau protein aggregation, a key factor often overlooked in Alzheimer's disease pathogenesis

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Background: Neurodegenerative disorders, such as Alzheimer's disease (AD), are linked to the abnormal aggregation of tau protein forming toxic oligomers and amyloid deposits. The conformation of tau protein is affected by different proline residues, regulated by peptidyl-prolyl isomerases (PPIases). Nevertheless, the effect of human CypA as a peptidyl-prolyl isomerase on tau protein aggregation remains unexplored.
Methods: We expressed tau protein and various types of cyclophilin A (CypA)—specifically, active CypA with a His- and GST-tagged, and inactive CypA—in BL21 bacteria. Following expression, we purified these enzymes and tau protein using affinity chromatography. Then, we measured the activity of all cyclophilin enzymes. Subsequently, we utilized various spectroscopic techniques to investigate the effects of CypA on the aggregation behavior of tau protein.
Results: We uncovered the pivotal role of CypA's isomerization activity in driving the formation of tau protein amyloid fibrils with characteristic cross-β structures. The 'cistauosis hypothesis' proposes that CypA enhances tau fibril formation in AD by isomerizing specific proline residues from the trans to cis configuration. To validate this theory, we performed refolding experiments using lysozyme as a model protein. Our results showed that CypA boosted lysozyme aggregation and hindered its refolding process, consistent with the notion that correct refolding of lysozyme relies on the proper (trans) isomerization of two critical proline residues."
Conclusion: Our results unequivocally showed that CypA induces the trans-to-cis isomerization of specific proline residues, which ultimately drives increased aggregation. This study underscores the growing importance of isomerization in tau protein pathogenesis in AD, providing new insights into the molecular mechanisms underlying this process.

Keywords: Alzheimer's disease (AD), Amyloid aggregation, Cyclophilin A (CypA), Disaggregation, Refolding

Mini-Oral Presentations

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2167-1

Investigation of the Expression Level of Nlrp3 Inflammasome Complex Genes in Patients with Type 2 Diabetes Consuming Single and Combined Sesame and Canola Oil

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Background: Type 2 diabetes (T2D) is a complex chronic disease characterized by inflammation, with the NLRP3 inflammasome complex playing a significant role in its pathogenesis. Recent studies suggest that unsaturated fatty acids may mitigate inflammation associated with the NLRP3 inflammasome in T2D. Thus, sesame oil (SO), canola oil (CO), and sesame-canola oil (SCO) could potentially reduce inflammation and contribute to T2D management due to their high unsaturated fatty acid content. This study aimed to evaluate the individual and combined effects of SO, CO, and SCO on the expression levels of genes associated with the NLRP3 inflammasome complex.
Methods: This laboratory study involved blood samples from 34 diabetic patients who consumed SO, CO, and SCO during three separate 9-week phases. The expression of NLRP3 inflammasome complex genes was measured using real-time PCR. The correlation between gene expression levels and the intake of SO, CO, and SCO was analyzed.
Results: The consumption of SO, CO, and SCO significantly decreased the expression of caspase-1 and NLRP3 genes in T2D patients ($P<0.001$). Notably, CO intake resulted in a significant reduction in IL-18 and IL-1 gene expression ($P<0.001$), while SO and SCO did not show a significant decrease in these genes ($P=0.121$).
Conclusion: The findings indicate that both individual and combined consumption of SO, CO, and SCO can lower the expression levels of NLRP3 inflammasome complex genes, potentially alleviating inflammatory complications related to T2D. Further research is warranted to expand on these results.

Keywords: sesame oil, canola oil, NLRP3 inflammasome, type 2 diabetes.

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Abstract: A-10-2181-1

Exploring Antimicrobial Potential: in Silico Analysis of Hg-Scorpine-Like Peptide Identified in the Transcriptome of Hemiscorpius Lepturus

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Background: Scorpine-like peptides are known for their dual functionality, exhibiting antimicrobial activity primarily associated with their N-terminal domain and potassium channel inhibitory activity localized within the C-terminal domain. This study identifies an Hg-scorpine-like peptide within the transcriptome of the Hemiscorpius lepturus scorpion.

Methods: To predict the presence of a signal peptide, we utilized the SignalP-5.0 online server. The antimicrobial peptide (AMP) activity of the identified peptide was assessed using several online tools, including AMP Discover, sAMPpred-GAT, and Antimicrobial Peptide Scanner v2. Additionally, we employed ExPASy ProtParam tools, PSIPRED, and SWISS-MODEL servers to evaluate the primary, secondary, and tertiary structures of the peptide. The predicted 3D structure was further analyzed using ProSA-web for protein structure assessment, followed by Ramachandran plot analysis via SWISS-MODEL.

Results: The analysis revealed that the initial 18 amino acids were predicted as a signal peptide with a likelihood of 0.9883. The Antimicrobial Peptide Scanner v2 indicated that the sequence exhibited AMP properties with a prediction probability of 0.9999. Both sAMPpred-GAT and AMP Discover confirmed this classification, predicting the peptide as an AMP with scores of 0.9989 and via the RNN-ABP method, respectively. Key parameters of the primary structure included 75 amino acids, a molecular weight of 8148.55 Daltons, and a theoretical isoelectric point of 9.10, along with various coefficients related to cysteine residues. Secondary structure analysis indicated involvement in helix, strand, and random coil formations. The predicted 3D structure analysis identified three alpha helices with a Z-score within the normal range (-4.13). Ramachandran plot analysis provided insights into conformational angles and percentages of amino acids in allowed and disallowed regions, underscoring stability and structural integrity.

Conclusion: The identified Hg-scorpine-like peptide from Hemiscorpius lepturus demonstrates significant antimicrobial activity. Comprehensive structural analyses support its potential as a multifaceted therapeutic agent.

Keywords: Hg-scorpine-like, Hemiscorpius lepturus, Antimicrobial.

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Abstract: A-10-2181-2

Design, Construction, and Development of an Innovative Targeted Drug Delivery System Utilizing Nrp-1 Peptide

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Background: Targeted cancer therapy is a rapidly evolving approach aimed at overcoming the limitations and adverse effects associated with conventional cancer treatments. In this context, Neuropilin-1 (NRP-1), a transmembrane glycoprotein expressed in both endothelial and tumor cells, plays a pivotal role in stimulating angiogenesis. Diphtheria toxin (DT) is recognized for its potent cytotoxic activity against human cells, making it an attractive candidate for cancer treatment. This study aims to harness the therapeutic potential of DT by designing and constructing a fusion protein, wherein the NRP-1 peptide serves as a targeting moiety fused to DT.

Methods: The synthesis, cloning, and expression of the fusion protein were conducted in bacterial hosts. The purification of the construct was achieved using Ni-NTA chromatography, ensuring the isolation of a pure and functional fusion protein. To evaluate its biological activity, particularly its cytotoxic effects, we employed the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay.

Results: The results demonstrated significant cytotoxic activity of the designed construct, evidenced by a marked reduction in cell viability. This observed cytotoxicity supports the potential of the fusion protein as a targeted therapeutic agent for NRP-1 overexpressing cancer cells. The specificity conferred by the NRP-1 peptide targeting moiety holds promise for minimizing off-target effects, which are common concerns in conventional cancer therapies.

Conclusion: This study lays the groundwork for further exploration and development of targeted cancer therapies utilizing the NRP-1 peptide strategy, with the goal of enhancing treatment efficacy while minimizing systemic side effects.

Keywords: NRP-1, angiogenesis, drug delivery.

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Abstract: A-10-2193-1

Chemotherapy against Colorectal Cancer Cells: Delivery of Pioglitazone Hydrochloride by Polycaprolactone-Polyethylene Glycol Carrier

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Background: Thiazolidinediones, such as pioglitazone hydrochloride (PGZ), have demonstrated antiproliferative effects against cancer cells. The objective of this study was to prepare and characterize nano-encapsulated PGZ and evaluate its cytotoxic and apoptotic effects on HCT-116 and HT-29 colorectal cancer cells, as well as human umbilical vein endothelial cells (HUVECs).

Methods: The PGZ nano-formulation was developed using a triblock (TB) biodegradable copolymer (PCL-PEG-PCL) to enhance the drug's bioavailability as an anticancer agent. Nanoparticles were prepared via the ultrasonic homogenization method. The physicochemical characteristics of TB and TB-PGZ micelles were evaluated using Fourier-transform infrared spectroscopy (FTIR), dynamic light scattering (DLS), and field emission scanning electron microscopy (FESEM). Zeta potential stability, entrapment efficiency, and storage stability were also assessed. Cell viability and apoptosis were determined using the MTT assay and acridine orange (AO) and propidium iodide (PI) staining, respectively.

Results: FESEM analysis revealed that TB-PGZ nanoparticles had a size of ≤ 110 nm, a polydispersity index of ≤ 0.2, and a zeta potential of -17.3 mV. TB-PGZ exhibited higher zeta potential and storage stability at 25°C compared to 4°C after 90 days. The IC50 value for TB-PGZ was approximately twice that of free PGZ due to the slow release of the drug from the micelles. A significant increase in cytotoxic effects was observed in HUVECs, HCT-116, and HT-29 cells ($p < 0.05$). Additionally, TB-PGZ demonstrated a greater cytotoxic effect over time compared to free PGZ. AO/PI staining indicated higher apoptosis rates of 50.33%, 40.66%, and 39% in HUVECs, HCT-116, and HT-29 cells, respectively, compared to PGZ treatment alone.

Conclusion: Targeting human colorectal cancer with TB-PGZ biodegradable copolymer may represent a promising alternative to conventional treatment strategies.

Keywords: Colorectal cancer, Pioglitazone hydrochloride, Micelle, Apoptosis.

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Abstract: A-10-2208-1

Anti-Proliferative and Proapoptotic Potency of Rosmarinus Officinalis L. Extract on Triple Negative Breast Cancer Cells Via Impeding Wnt/β-Catenin Signaling Pathway

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Background: Breast cancer is the most prevalent cancer among women, with triple-negative breast cancer (TNBC) recognized as the most aggressive and metastatic subtype. This subtype is particularly challenging to manage, as it is not responsive to hormonal and targeted therapies. Consequently, finding effective treatment options for TNBC remains a global challenge. Notably, over 60% of anti-cancer compounds are derived from herbal remedies. Rosmarinus officinalis L. (rosemary) possesses a broad range of medicinal properties, including antioxidant, anti-inflammatory, anti-diabetic, and anti-cancer effects. This study investigates the anti-cancer effects of rosemary on TNBC through the suppression of the Wnt/β-catenin pathway.

Methods: Following the preparation of a hydro-alcoholic extract of rosemary, we assessed cell viability and determined the IC50 value by exposing MDA-MB-231 cells to various doses of rosemary extract. Apoptosis induction was evaluated using an Annexin V/PI kit through flow cytometry analysis. Additionally, real-time PCR was employed to measure changes in mRNA expression levels of genes associated with the Wnt/β-catenin pathway in MDA-MB-231 cells following treatment with rosemary extract.

Results: The results indicated that treatment with hydro-alcoholic rosemary extract reduced the viability of MDA-MB-231 cells in a dose- and time-dependent manner. Flow cytometry analysis demonstrated the induction of both early and late apoptosis in TNBC cells. Furthermore, the expression levels of Wnt-10B and β-catenin genes were significantly reduced compared to the control group.

Conclusion: Our findings confirm the cytotoxic and apoptotic effects of hydro-alcoholic rosemary extract on MDA-MB-231 cells by modulating the expression of genes involved in the Wnt/β-catenin signaling pathway. These results suggest that rosemary extract could serve as a promising complementary treatment for triple-negative breast cancer, warranting further investigation through in vivo studies.

Keywords: Triple-negative breast cancer, Rosemary, Antiproliferative, Wnt/β-catenin.

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Abstract: A-10-2186-1

Assessing CCL14 in Adrenocortical Carcinoma: A Potential Diagnostic and Prognostic Biomarker

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Background: Adrenocortical carcinoma (ACC) is a common cancer worldwide, contributing to significant morbidity and mortality each year. While the expression of various genes has been implicated in the pathogenesis of this disease, there is limited information regarding alterations in CCL14 expression in ACC. The aim of this study was to investigate changes in CCL14 expression in adrenocortical carcinoma and to evaluate its potential as a prognostic biomarker.

Methods: To examine alterations in CCL14 expression in ACC, we utilized data from The Cancer Genome Atlas (TCGA) provided by the OncoDB database. We also assessed the association between gene expression, patient mortality rates, and clinical features using TCGA clinical data.

Results: Our findings revealed a significant decrease in CCL14 expression levels in cancerous samples compared to normal tissues (FDR < 0.01, LogFC = -6.23). Additionally, we observed a marked reduction in CCL14 expression levels in TNM T4 samples compared to T1 and T2 stages. Furthermore, Kaplan-Meier survival analysis indicated that decreased CCL14 expression is associated with poor prognosis in patients (LogRank = 0.01).

Conclusion: The results of this study demonstrate a significant decrease in CCL14 expression levels in adrenocortical carcinoma, which correlates with poorer patient prognosis. Our findings suggest that CCL14 expression levels may serve as a valuable prognostic biomarker for adrenocortical carcinoma.

Keywords: Adrenocortical carcinoma, Prognostic biomarker, Mortality rate, CCL14 expression.

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Abstract: A-10-2151-1

Down Expression of Zyxin is Associated with Down Regulation of P53 in Colorectal Cancer

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Background: Colorectal cancer (CRC), as one of the most prevalance cancers in the world, is caused by environmental and genetic factors. It has been shown that the P53 is associated with CRC pathogenesis; moreover, Zyxin (ZYX) may have a role in P53 level and activity. Thus, we aimed to investigate the levels of P53 and ZYX genes and protein in CRC tumor samples.

Methods: The 30 cancerous tissues and 30 matched noncancerous tissues were randomly obtained from 30 patients with CRC. Total RNA was extracted by RNXplus and genes expression were assessed by Real-time PCR. Moreover, Western blot technique was used to investigate ZYX and p53 proteins expression.

Results: Our data demonstrated that the expression of ZYX and p53 genes in cancerous tissues had not a significant difference compared to the matched noncancerous tissues. On the other hand, measuring protein expression by Western blotting technique showed that the ZYX (P=0.0079) and p53 (P=0.0005) expression in tumor tissues showed a significant decrease compared to the matched noncancerous tissues. The correlation analysis indicated the significant correlation between ZYX and P53 proteins (r=0.746, P=0.013).

Conclusion: Based on our findings, the ZYX might has a suppressive function in CRC and be associated with P53.

Keywords: Zyxin, P53, Colorectal cancer.

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Abstract: A-10-2151-2

Comparative Investigation of Pin1 Gene Expression in Tumor Tissue with Tumor Border Tissue and Its Relationship With B-Catenin and Cyclin D1 Gene Expression Levels in Patients with Colorectal Cancer

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Background: Colorectal cancer is one of the most common types of cancer in Iran and the world, and due to the effects of the Pin1 protein on the stability of b-catenin and the expression of the cyclin D1 gene, in this study, it was decided to measure the expression of the Pin1 gene in people with colorectal cancer and the relationship It should be investigated with the level of b-catenin and cyclin D1 gene expression.
Methods: The majority of patients were over 50 years old, without alcohol consumption, non-smokers and without family history of colorectal cancer. Real-time PCR was used to check the expression of Pin1, b-catenin and Cyclin D1 genes.
Results: The results of gene expression showed that the expression level of Pin1 and b-catenin genes in the tumor tissue showed a significant increase compared to the tumor border tissue. On the other hand, it was shown that there is a positive and significant relationship between Pin1 and cyclin D1 gene expression.
Conclusion: The results of this study showed that Pin1 may be important in the pathogenesis of colorectal cancer by increasing the expression of cyclin D1.

Keywords: Colorectal cancer, Pin1, b-catenin, cyclin D1.

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Abstract: A-10-2228-1

Total Antioxidant Capacity in Human Seminal Plasma of Infertile Men and Their Relationship with Sperm Parameters

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Background: Oxidative stress plays a critical role in the pathogenesis of male infertility, yet the adverse effects of oxidative biomarkers on sperm quality remain unclear. This study aimed to investigate the levels of total antioxidant capacity (TAC) in seminal plasma and their relationship with sperm parameters.
Methods: The study included 77 individuals aged 24 to 35 years, classified into two groups: a control group consisting of 40 fertile men and a study group of 37 infertile men. Semen samples were collected in sterile containers, and routine semen analysis was performed within one hour. Following analysis, samples were centrifuged at 4,000 g for 10 minutes and stored at -20ºC for TAC measurement. The TAC biomarker was evaluated using the ferric reducing ability of plasma (FRAP) method.
Results: The mean TAC in seminal plasma was significantly lower in infertile men compared to the control group (1,697.11 ± 708.18 µM/L vs. 2,015.50 ± 670.95 µM/L; p = 0.046). Additionally, we found a positive correlation between TAC and sperm count (p = 0.043, r = 0.232) as well as between TAC and normal sperm morphology (p = 0.025, r = 0.255).
Conclusion: Decreased levels of TAC are associated with infertility in men, with TAC levels being lower in the seminal plasma of idiopathic infertile men compared to healthy fertile men.

Keywords: 8-Hydroxydeoxyguanosine, Infertile men, Nitric oxide, Oxidative stress, Semen, Total antioxidant capacity.

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Abstract: A-10-2225-2

Estimation of Inflammatory Marker Levels Associated with Pfizer/biontech Vaccinated Subjects from Baghdad Hospital

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Background: The introduction of COVID-19 vaccinations has provided a promising opportunity to combat the global pandemic. However, these vaccines have been associated with severe side effects and alterations in blood indicators. This prospective study investigates the impact of the Pfizer vaccine on inflammation markers (IL-1β and IL-10) and various blood markers among vaccinated individuals compared to unvaccinated controls.
Methods: The study included 70 vaccinated individuals and 25 non-vaccinated healthy controls, aged 24 to 35 years. Subjects who received both doses of the vaccine and a booster were studied from December 2022 to April 2023 at Medical City - Baghdad Hospital, Iraq. Blood samples were collected in sterile containers, and routine semen analysis was performed within one hour. Following analysis, samples were centrifuged at 4,000 g for 10 minutes and stored at -20ºC for subsequent measurement of total antioxidant capacity (TAC). Blood glucose levels, triglycerides, HDL, LDL, WBC count, lymphocyte count, hemoglobin, platelet count, cholesterol, and D-dimers were measured using the Cobas c 111® clinical chemistry automated system. IL-1β and IL-10 levels in serum were estimated using ELISA test kits (Cat No: SEA563Hu for IL-1β and SEA056Hu for IL-10 from Cloud-Clone Corp, Iraq).
Results: Our findings revealed that vaccinated individuals exhibited enhanced inflammation and platelet activation. A strong correlation was found between vaccination and both IL-1β and IL-10 levels ($p < 0.01$). Spearman rank correlation analysis indicated that IL-1β levels were directly proportional to the number of vaccine doses ($r = 0.55132$, $p < 0.001$). Additionally, IL-10 levels were significantly elevated in all vaccinated subjects ($p < 0.01$), with no significant differences observed between male and female subjects ($p > 0.05$).
Conclusion: These results suggest that vaccinated individuals may experience increased inflammatory responses and platelet activation following vaccination. Understanding these effects could help optimize vaccine responses in populations at risk of severe COVID-19 clinical courses.

Keywords: COVID-19, Vaccination, Interleukins, Blood markers.

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Abstract: A-10-2217-1

Understanding Biochemical Paraneoplastic Abnormalities and Plasmonic Photothermal Therapy in Female Dogs With Mammary Neoplasms

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Background: Mammary carcinoma is the most common cancer that affects dogs, and in many dogs, it leads to death. As a result, clarifying the pathogenesis and treatment of these diseases is important, so the treatment method can be used and simulated for humans. This study researches the exploration of biochemical paraneoplastic abnormalities and the application of Plasmonic Photothermal Therapy (PPTT) in treating mammary neoplasms in female dogs.

Methods: A comprehensive review of literature from 2015 to 2023 using databases like Google Scholar, PubMed, and Science Direct focusing on the biochemical components of mammary carcinoma in dogs was conducted. Key factors such as interleukins, nitric oxide synthases, and oxidative stress markers were analyzed to evaluate malignancy and treatment response in mammary neoplasms.

Results: In this systematic review article, initially 114 articles were selected from databases including Google Scholar PubMed, and Science Direct. According to the criteria considered and the objectives of the study, out of the initial 100 articles, finally 66 articles were selected and reviewed. These 66 articles include 50 original articles and 16 systematic review articles. The study highlighted the significance of steroid hormones and prolactin in mammary epithelial growth and emphasized their correlation with tumor development in canines. First of all; elevated levels of IL-1, IL-6, and INF-γ were observed in malignant breast tumors, indicating a negative prognosis and predicting malignant tumors. Oxidative stress biomarkers like NOx, AOPP, and FRAP show significant alterations and suggest a link between oxidative stress and cytokine levels in blood. Moreover, this article emphasizes the potential of PPTT and using gold nanorods for tumor apoptosis to treat mammary gland cancer in canines and felines.

Conclusion: This study highlights the significance of biochemical shifts in mammary tumors and promotes innovative treatments, aiming to improve veterinary oncology outcomes.

Keywords: Biochemical, Breast, Cell tumors, Canine, Treatment.

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Abstract: A-10-2235-1

Investigating the Effect of Aqueous Extract of Crocus Sativus on the Expression of Fgf and Vegf Genes in Chicken Embryos

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Background: Fibroblast growth factor (FGF) produced by endothelial cells plays a crucial role in promoting proliferation and survival of these cells. FGFs act as collagenase activators, facilitating the sprouting of new blood vessels and are essential for maintaining and advancing angiogenesis. Vascular endothelial growth factor (VEGF) is believed to initiate the angiogenic process. Crocus sativus, commonly known as saffron, is a prominent medicinal plant used in traditional medicine. This study aims to investigate the effect of aqueous extract of Crocus sativus on the expression of FGF and VEGF genes in chick embryos.

Methods: In this study, 40 Ross spray eggs were randomly divided into eight groups, including a control group, a laboratory control group (PBS), and two experimental groups. After incubation, an egg window was created on the second day, and on the eighth day, gelatin sponges were placed on the chorioallantoic membrane (CAM). Aqueous extracts of Crocus sativus at concentrations of 50 and 100 µg/ml were injected onto the CAM of the chick embryos. Samples were taken from the CAM for RNA extraction and cDNA synthesis to quantitatively measure changes in VEGF and FGF gene expression. The collected data were analyzed using Excel and SPSS 20 statistical software.

Results: The average expression levels of VEGF and FGF genes in the laboratory control group did not show significant differences compared to the control group. However, treatment with 50 and 100 µg/ml concentrations of aqueous extract of Crocus sativus resulted in a significant decrease in the expression of both VEGF and FGF genes compared to the control group.

Conclusion: The findings of this research indicate that the aqueous extract of Crocus sativus has an inhibitory effect on angiogenesis in the chorioallantoic membrane of chick embryos.

Keywords: Gene expression, Crocus sativus, Chorioallantoic membrane, Chick embryo.

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Abstract: A-10-2235-2

Investigating the Effect of Aqueous Extract of Crocus Sativus on the Process of Angiogenesis of the Chorioallantoic Membrane of Chick Embryos

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Background: Angiogenesis refers to the biological process of sprouting new vessels from existing vessels in the tissue. Angiogenesis is a physiological process that is highly regulated and occurs in cases such as wound healing, menstrual cycles, placental growth, and ovulation. Crocus sativus is one of the prominent medicinal plants in traditional medicine. This research was conducted with the aim of investigating the effect of aqueous extract of Crocus sativus on the process of angiogenesis of the chorioallantoic membrane of chick embryos.
Methods: In this research, 40 Ross spray eggs were randomly divided into 4 groups including control, laboratory control (PBS) and 2 experimental groups. After incubation, on the second day of the window, an egg was created and in on the eighth day, after placing the gelatin sponge on the chorioalantoic curve, the aqueous extract of Crocus sativus were injected with doses (50 and 100 µg/ml) onto the chorioalantoic membrane of the chick embryo. On the twelfth day, the corioalantoic membrane was taken and length, the number of vascular splits, weight and height of the embryos were measured. The collected data were analyzed by Excel and SPSS 20 statistical software.
Results: The average number and total length of vascular branches in the laboratory control group did not show any significant difference compared to the control group. The average number and length of vascular branches in concentrations of 50 and 300 µg/ml of aqueous extract of Crocus sativus showed a significant decrease compared to the control group.
Conclusion: According to the methods of this research, the above aqueous extract of Crocus sativus have an inhibitory effect on angiogenesis in the chorioallantoic membrane of chick embryos.

Keywords: Angiogenesis, Crocus sativus, Chorioalantoic Membrane, Chick Embryo.

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Abstract: A-10-2238-1

Characterization of the Structural Properties of Pepsin in the Presence of Caffeic Acid and Quercetin by In Vitro Studies

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Background: The ability of therapeutic compounds to attach to proteins is crucial for understanding their therapeutic effects. In this study, we investigated the behavior of quercetin (QU) and caffeic acid (CA), two common phenolic compounds, on the function and structure of pepsin.

Methods: The effects of quercetin and caffeic acid on the structure and function of pepsin were examined using spectroscopic techniques, including ultraviolet-visible (UV-Vis) and fluorescence spectroscopy.

Results: Absorbance spectroscopy results indicated that pepsin exhibited a maximum absorbance peak at 280 nm. Following treatment with QU and CA, the absorbance intensity of the enzyme changed significantly. In the presence of QU, pepsin's absorbance increased progressively with rising QU concentrations. Conversely, increasing concentrations of CA led to a reduction in absorbance intensity. Fluorescence spectroscopy data further demonstrated that the binding of both phenolic compounds to pepsin resulted in decreased emission intensity.

Conclusion: The maximum absorbance spectrum of pepsin at 280 nm is attributed to the presence of tryptophan (Trp) residues. The observed hyperchromic and hypochromic effects indicate that the microenvironment surrounding the aromatic amino acids in the enzyme was altered. Additionally, the reduced emission intensity upon binding of QU and CA suggests a shift of Trp to a less hydrophilic microenvironment, likely due to changes in the enzyme's tertiary structure. These spectroscopic findings reveal that both compounds can bind to pepsin, thereby altering its structural and conformational properties.

Keywords: Quercetin, Caffeic acid, Pepsin, Structure, Spectroscopic techniques.

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Abstract: A-10-2212-1

Lipase Recombinant from Psychrobacter Sp. C18 Immobilized on Reduced Zinc Oxide-Chitosan Nano Matrix with High Activity

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Background: Lipase is the third most commercially important enzyme, following carbohydrates and proteases. Together with esterases, lipases constitute approximately 10% of the global industrial enzyme market. These enzymes belong to the class of serine hydrolases and do not require any cofactors, as they are part of the hydrolase family.

Methods: In this study, the lipase gene from Psychrobacter c18 was introduced into a suitable host cell using the pET-28 plasmid to facilitate lipase expression. The protein was purified using a nickel agarose column, and the lipase enzyme was subsequently immobilized on zinc oxide-chitosan nanoparticles. Various techniques, including dynamic light scattering (DLS), scanning electron microscopy (SEM), Fourier-transform infrared spectroscopy (FTIR), and energy-dispersive X-ray spectroscopy (EDX), were employed to analyze the substrate composed of chitosan and zinc oxide.

Results: Two methods—physical adsorption and covalent binding—were utilized to stabilize the lipase enzyme. The results indicated that the enzyme retained its catalytic efficiency after both physical and covalent immobilization, with efficiency rates of approximately 90% and 96%, respectively. Furthermore, the stability of the enzyme was enhanced, as evidenced by an increased half-life at 35°C. Physical immobilization resulted in a 7% increase in half-life, while covalent immobilization led to a 15% increase.

Conclusion: The enzyme can be used repeatedly up to 14 times on the substrate, making it a cost-effective option for industrial applications. Additionally, the enzyme can be easily separated from the product using centrifugation.

Keywords: Enzyme, Psychrobacter lipase, Immobilization, Chitosan, ZnO.

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2262-1

Sestrin2, Nfatc1 and Nrf2 in Pbmcs of Patients with Ankylosing Spondylitis Treated with Tnf-A Antagonist Compared to the Without Receiving This Treatment and Control Group

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory autoimmune disease classified as a type of spondyloarthropathy. Sestrin2 plays a critical role in the inflammatory response by protecting cells from injury through the attenuation of reactive oxygen species (ROS) and the inhibition of mammalian target of rapamycin (mTOR) signaling. Sestrin also inhibits ROS by activating NRF2. Additionally, NFATc1 is induced following receptor activator of nuclear factor kappa-B ligand (RANKL) stimulation. This study analyzed the expression of these genes in patients with newly diagnosed ankylosing spondylitis undergoing anti-TNF therapy, compared to a control group.
Methods: In this study, we extracted RNA, synthesized complementary DNA (cDNA), and analyzed the expression levels of these genes using real-time PCR on 60 peripheral blood mononuclear cell (PBMC) samples. The samples were divided into three groups: newly diagnosed AS patients, AS patients receiving anti-TNF therapy, and control individuals. Statistical analysis was performed using SPSS-18, with a significance threshold set at $p < 0.05$.
Results: NRF2 gene expression was significantly higher in the newly diagnosed AS group compared to the control group ($p < 0.001$) and also increased in the anti-TNF group compared to controls ($p < 0.01$). The expression levels of Sestrin2 and NFATc1 in the anti-TNF treatment group were higher than those in both the newly diagnosed and control groups; however, these differences were not statistically significant ($p > 0.05$).
Conclusion: Our results indicate that the expression levels of genes critical for controlling inflammation increased with anti-TNF treatment. This suggests that, in addition to their inhibitory effects on the TNF-α pathway, anti-TNF drugs may also influence the expression of key regulatory genes involved in inflammation.

Keywords: Sestrin, NRF2, NFATc1.

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Abstract: A-10-2271-1

Accelerating Wound Healing with Novel Polylactic Acid (PLA)-Collagen Scaffold Integrating Damaske Rose Nanoparticles

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Background: Nanofibrous polymeric scaffolds, a novel approach in advanced wound care, have garnered significant interest for their ability to expedite wound healing and reduce patient hospitalization. These scaffolds mimic the fibrous structure of the natural extracellular matrix, promoting high cell adhesion and proliferation. In this vein, the innovative combination of polylactic acid (PLA) and collagen with damask rose nanoparticles has surfaced as a hopeful approach for the engineering of wound dressings.
Methods: Our study meticulously crafted nanofibrous scaffolds using electrospinning, incorporating PLA, collagen, and Damask rose nanoparticles in varying ratios. These scaffolds underwent a comprehensive evaluation process, including SEM examination for morphology, tensile tests for mechanical properties, and cell viability and adhesion assessment. This rigorous and thorough testing ensures the reliability and validity of our findings, providing a solid foundation for further research and development in wound healing.
Results: The electrospinning procedure successfully produced nanofibrous scaffolds using an eight wt% PLA solution. SEM examination confirmed the nano-scale diameter of the hollow fibers. Through thermal cross-linking, the PLA and collagen components formed a stable structure. Mechanical testing revealed that the 70:30 weight ratio of the PLA/collagen nanofibrous scaffold exhibited favorable mechanical properties, with fibers in the nano-scale range, further validating the potential of the scaffold.
Conclusion: The nanofibrous scaffold, a unique combination of PLA and collagen with a weight ratio of 70:30, presents a novel and intriguing approach to wound healing. Including damask rose nanoparticles, known for their medicinal properties, further enhances the scaffold's therapeutic capabilities. Additionally, the hollow fibers provide a more three-dimensional structure, increasing the surface area within a given volume and thereby improving the effectiveness of separation operations. This innovative scaffold combines PLA's mechanical strength, collagen's biocompatibility, and the therapeutic qualities of damask rose nanoparticles, making it a promising candidate for advanced wound therapy.

Keywords: Hollow, Fibers, Healing, nanoparticles.

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Abstract: A-10-2287-1

Diagnostic Value of Troponin-T for the Diagnosis of Cardiac Dysfunction in Patients with Major Thalassemia: Evaluation of Sensitivity and Specificity of This Biomarker

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Background: Major thalassemia (MT) is one of the most common hereditary diseases characterized by defects in hemoglobin (Hb) chain synthesis. Patients with MT often require repeated blood transfusions, leading to significantly elevated serum ferritin levels, which increase the risk of cardiac dysfunction. Cardiac biomarkers are essential for diagnosing heart failure in these patients.

Methods: This diagnostic study was conducted on 140 patients with MT, all over ten years of age, each having received more than 100 units of blood transfusions. A 5 ml blood sample was collected from each patient to evaluate serum ferritin levels and determine the sensitivity and specificity of troponin T (TnT). Serum TnT levels were measured using a test kit. Cardiac dysfunction was diagnosed through echocardiography and assessment of ejection fraction (EF). Data were analyzed using SPSS statistical software (v. 22) and Chi-Square tests.

Results: The study found that serum TnT levels exhibited inadequate sensitivity (56.6%) and specificity (75.8%) for detecting cardiac dysfunction in MT patients with abnormal EF. Additionally, no statistically significant differences were observed between TnT levels and serum ferritin (P-value: 0.267, OR: 1.618), hemoglobin levels (P-value: 0.480, OR: 1.328), or gender (P-value: 0.065, OR: 0.504).

Conclusion: Our findings indicate that TnT lacks sufficient sensitivity and specificity for diagnosing heart failure in patients with major thalassemia. Therefore, further research is warranted to explore the use of a combination of laboratory techniques and echocardiography for the early detection of cardiac dysfunction in these patients.

Keywords: Major thalassemia, Cardiac biomarkers, Troponin T, Heart failure, Sensitivity, Specificity.

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Abstract: A-10-2263-2

Nitazoxanide and Cancer Drug Resistance: Targeting Wnt/β-Catenin Signaling Pathway

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Background: Multidrug resistance (MDR) is a significant complication that leads to unsuccessful cancer treatment, particularly in the context of chemotherapy. Therefore, there is a pressing need for novel medications that have low side effects and high efficacy to reverse MDR. The current study aimed to investigate the molecular mechanisms underlying MDR in LS174T and LS174T/Oxaliplatin (OXP) cell lines during treatment with Nitazoxanide (NTZ) in combination with OXP.

Methods: In this in vitro study, we evaluated the effects of NTZ on the cytotoxicity of OXP using the Thiazolyl Blue Tetrazolium Blue (MTT) assay. LS174T and LS174T/OXP cell lines were treated with OXP and NTZ, either alone or in combination, for 24 and 48 hours. Following treatment, we assessed changes in the expression levels of CTNNB1, ABCB1, c-Myc, and cyclin D1 genes across different treatment groups.

Results: Exposure of LS174T/OXP cells to NTZ increased their sensitivity to OXP and induced caspase-3/7 activity, leading to apoptosis. Furthermore, NTZ downregulated the Wnt/β-catenin signaling pathway by significantly decreasing the expression of CTNNB1, c-Myc, ABCB1, and cyclin D1 genes. This downregulation resulted in a reversal of drug resistance and inhibition of cell proliferation.

Conclusion: The findings indicate that the Wnt/β-catenin pathway plays a crucial role in the development of cancer and MDR. In this context, NTZ has the potential to reverse MDR in colorectal cancer (CRC) cells by downregulating the Wnt/β-catenin signaling pathway. These results suggest that NTZ should be further investigated as a promising adjuvant in CRC chemotherapy.

Keywords: Colorectal cancer, Multidrug resistance, Nitazoxanide, Oxaliplatin, Wnt/β-catenin.

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2200-1

Impact of Slc30a8 Rs13266634 Polymorphism on Schizophrenia Risk in Southeast Iranian Population

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Background: Schizophrenia (SCZ) is a complex disorder influenced by both genetic and environmental factors. The SLC30A8 gene, located on chromosome 8q24.11, encodes a novel zinc transporter that plays a crucial role in regulating insulin secretion in response to blood glucose levels. Dysregulation of zinc has been linked to the development of SCZ. This study aimed to investigate the association between a nonsynonymous genetic variation in the SLC30A8 gene (rs13266634), which results in the substitution of arginine for tryptophan at position 325, and SCZ susceptibility in a population from southeastern Iran.

Methods: In this case-control study, we included a total of 300 participants: 150 individuals newly diagnosed with SCZ at Baharan Hospital in Zahedan, Iran, and 150 healthy controls recruited from the community. Diagnosis of SCZ was based on DSM-V criteria, and patients with a history of substance abuse, mood disorders, or intellectual disabilities were excluded. Healthy controls had no family history of neuropsychiatric disorders or drug abuse. The polymorphism was genotyped using the bi-directional amplification refractory mutation system PCR (ARMS-PCR) method.

Results: There were no statistically significant differences in gender ($p = 0.84$) and age ($p = 0.72$) between the groups. A substantial proportion of cases exhibited symptoms of isolation (57.3%) and depression (74.0%). Genotyping data revealed that individuals with the T allele of rs13266634 had a significantly higher risk of schizophrenia under the recessive model (TT vs. CT+CC; Odds Ratio = 1.69, 95% Confidence Interval = 1.02-2.81, $p = 0.041$). However, no significant associations were observed between rs13266634 and SCZ risk under other inheritance models, including codominant, dominant, overdominant, and allelic contrast modes.

Conclusion: These results provide valuable insights into the potential impact of the SLC30A8 polymorphism on susceptibility to SCZ. Further studies with larger sample sizes are needed to validate our findings.

Keywords: SLC30A8, Schizophrenia, Genetic association study, Polymorphism, Zinc Transporter.

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Abstract: A-10-2302-1

Anti-Cancer Effect of Probiotic Bifidobacterium Bifidum on Ovarian Cell Line

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Background: Ovarian cancer affects over 300,000 women annually, causing 200,000 deaths. Recurrence is common with less than 50% survival rate. Vaginal microbiota's regulatory effects have been recognized in health and diseases. A healthy vagina is dominated by lactobacillus, while dysbiosis contributes to diseases. Targeting vaginal microbiota has shown success in treating various diseases, indicating potential for gynecologic disease treatment. This study aims to investigate the toxic effects of probiotic Bifidobacterium bifidum (B. bifidum) on ovarian cell culture conditions.

Methods: B. bifidum was first cultivated in an MRS medium and after 24h, post-fermentation media (PFM) and extraction of bacterial cells (EC) were obtained. For this issue, the culture medium containing the bacteria was centrifuged (10,000 g, 15 minutes). Also, plates were sonicated for extracting EC. Then PFM and EC were gained and the pH was adjusted by NaOH/HCl in the range of 7.0 ± 0.1 (to eliminate the cytotoxic effect of the acid on the cells) and then were filtered using a filter (0.22 micrometer), separately. Next, the MTT assay was performed on CAOV-4 cells in a range of PFM and EC concentrations (%0, %20, %40, %60, %80, %100 v/v).

Results: Cytotoxicity test results showed that only bacterial PFM has cytotoxic effects on CAOV-4 ovarian cancer cells. IC50 was in the concentration of %50 (v/v) of PFM.

Conclusion: PFM extracted-B.bifidum can induce cell death and display an anti-cancer effect in ovarian cancer cells. However, no toxic effect was observed by EC-treated cells.

Keywords: Anti-cancer effect, probiotic, Bifidobacterium bifidum, ovarian cancer cell line.

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2242-1

Inhibitory Effect of Citrullus Colocynthis Compounds on Beta-Glucosidase Using Molecular Docking

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Background: Diabetes is a metabolic disease characterized by the deficiency and dysfunction of insulin, leading to elevated blood sugar levels. The medications used to treat diabetes often have side effects, increasing the interest in medicinal plants as alternative treatments. Citrullus colocynthis is one such medicinal plant known for its beneficial effects on blood sugar regulation.

Methods: This study aimed to identify and investigate the compounds in Citrullus colocynthis that inhibit beta-glucosidase protein (PDB ID: 3VKK), a protein involved in diabetes. We utilized AutoDock Vina software to determine the strongest interactions and lowest binding energies between the compounds of Citrullus colocynthis and the target protein.

Results: Four combinations of herbal compounds demonstrated significantly better results than conventional diabetes medications. The compound dihydrobrassicasterol exhibited the highest binding energy of -11 kcal/mol, followed by other compounds with binding energies of -10.8, -10.8, and -10.6 kcal/mol.

Conclusion: Further investigation into the compounds found in Citrullus colocynthis and their extraction as medicinal agents could help avoid the side effects associated with chemical drugs.

Keywords: Molecular docking, AutoDock Vina, Citrullus colocynthis, beta-glucosidase, Diabetes.

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2305-1

Investigating the Effect of Nanoparticles Magnetic Graphene Oxide on the Level of Intracytoplasmic Expression of Glutathione and Reactive Oxygen Species in NMRI Mouse MII Oocytes

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Background: Nanomaterials based on graphene oxide (GO) and superparamagnetic Fe3O4 have potential as drug carriers due to their high surface area for loading biomolecules. Patients undergoing assisted reproductive techniques (ART) often require high doses of gonadotropins to obtain more oocytes, which can be costly and pose risks to their health. Therefore, the use of substances that enhance the effectiveness of these drugs at appropriate doses is crucial. The objective of this study was to investigate the effect of magnetic graphene oxide (MGO) on the in vivo maturation of mouse oocytes.

Methods: Thirty female NMRI mice (6-8 weeks old, 25 ± 4 g) were treated with intraperitoneal (I.P.) injections of MGO mixed with Pregnant Mare Serum Gonadotropin (PMSG). After 12 hours, Human Chorionic Gonadotropin (HCG) was injected. A control group of female NMRI mice was stimulated without MGO. Oocytes were collected from the left fallopian tubes in each group. Immunocytochemical staining for glutathione and reactive oxygen species (ROS) was performed, along with morphometric analysis of the ovaries.

Results: The results indicated that the simultaneous administration of MGO, PMSG, and HCG significantly increased the expression of glutathione (GSH) compared to the control group receiving hormones alone ($P < 0.01$ for GSH and $P < 0.05$ for PMSG). Additionally, a significant increase in the number of corpus luteum was observed following treatment with the hormone-MGO mixture ($P < 0.01$). However, there was no significant increase in ROS expression.

Conclusion: This study suggests that MGO may enhance the efficacy of ovulation hormones by improving protein and hormone absorption in ovarian tissue. Further research is warranted to explore its potential as an adjuvant in ovulation drugs.

Keywords: Oocyte maturation, Magnetic graphene oxide, Glutathione, ROS.

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2227-1

Acetyl-L-Carnitine Administration Can Reverse Microplastic Hepatotoxicity in Mice

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Background: Microplastics are commonly used in industry and are present in drinking water, food, and various commodities. Plastic pollution is one of the most serious environmental challenges in the 21st century. Acetyl-L-carnitine (ALC) is an antioxidant and anti-inflammatory compound. The present study examines the protective role of ALC in preventing oxidative stress induced by polystyrene microplastics in the liver of mice.

Methods: Mice were randomly divided into five groups: control, another control treated with ALC at a dose of 200 mg/kg, polystyrene, and two groups of polystyrene treated with ALC at doses of 50 or 200 mg/kg. To induce liver damage, polystyrene microplastic was administered orally at a dose of 30 mg/kg for five weeks. For the treatment groups, from one week after the administration of polystyrene, oral ALC was administered daily for four weeks at doses of 50 or 200 mg/kg. The levels of malondialdehyde (MDA), catalase, and superoxide dismutase (SOD) in liver tissue homogenate, as well as ALT and AST, were determined using the specific kits. Statistical analysis was done with one-way ANOVA and Tukey's post hoc tests with a significance level of $p<0.05$.

Results: The polystyrene group showed higher levels of MDA, ALT, and AST, and lower levels of SOD and catalase antioxidant enzymes compared to the control group ($p<0.05$). Moreover, ALC at the dose of 200 mg/kg effectively reduced the amount of MDA, ALT, and AST compared to the polystyrene group ($p<0.05$). Further, this dose of ALC significantly increased the amount of SOD and catalase compared to the polystyrene group ($p<0.05$).

Conclusion: Administration of ALC can prevent oxidative stress and hepatotoxicity induced by polystyrene microplastics in mice.

Keywords: Acetyl-L-carnitine, Polystyrene microplastic, Oxidative stress, Liver.

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Abstract: A-10-2308-1

Evaluation of Two Common Mutations (ivs-Ii-I (g-A) and Fsc 8/9 Insg) in B -Thalassemia Major Patients of Soodeh Medical Center, Using Tetra Arms PCR Method

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Background: The β-thalassemia, is the most common monogenic autosomal recessive disorder worldwide (Approximately 1.5% of the world population are carriers of beta-thalassemia). It is related to abnormal hemoglobin synthesis, resulting from over 200 different mutations of globin genes. The aim of this study was to evaluate two common mutations (IVS-II-I (G-A) and FSC 8/9 InsG) in β-thalassemia major patients using Tetra ARMS PCR method.
Methods: In the present study, 50 unrelated β-thalassemia major patients were selected from Soodeh Medical Center in Tehran Province. 5ml of whole peripheral blood samples were collected from each individual and the Blood genomic DNA Extraction Mini Kit (Favorgen, Taiwan) was used to extract the genomic DNA. By designing tetra primers for two prevalent mutations of IVSII-I (G-A) and FSC-8/9 insG, samples were genotyped using tetra-primers ARMS PCR method. The results were interpreted using DNA electrophoresis.
Results: We have determined homozygous and heterozygous forms of IVSII-I (G-A) and FSC-8/9 insG mutations. The frequency of IVSII-1 (G-A) mutation from 50 patients was 2% heterozygote, and 40% mutant homozygote (A allele) and for FS8-9 insG mutation was 2% heterozygote, and 6% mutant homozygote (+G allele).
Conclusion: Tetra-primers ARMS PCR is a reliable, simple and accurate method to genotype different mutations. This method could be beneficial to evaluate patients with β-thalassemia at diagnosis of laboratory centers without sequencing facilities. Moreover, our data showed that the highest rate of patients had IVSII-1 (G-A) mutation.

Keywords: β-thalassemia, IVSII-I mutation, FSC-8/9 mutation, Tetra primers ARMS.

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Abstract: A-10-2306-1

Il-18 and Cd14 Variants in Chronic Hbv Predisposition: A Case-Control Study with in Silico Analyses Focused on Transcription and Splicing

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Background: Hepatitis B virus (HBV) is a vaccine-preventable infection that poses significant global health challenges, leading to liver disorders such as acute self-limiting hepatitis, chronic hepatitis, liver failure, hepatic cirrhosis, and hepatocellular carcinoma if left untreated. Variations in the pro- and anti-inflammatory cytokines, referred to as 'immunogenetic profiling,' can lead to individual differences in immune response and disease manifestation. This study aimed to investigate the association of promoter variants IL-18–rs187238 C>G and IL-18–rs1946518 T>G, as well as the intronic variant CD14–rs2569190 A>G, with chronic HBV.

Methods: A total of 400 participants, including 200 cases and 200 controls, were genotyped using the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique. Bioinformatics analyses were performed to assess conservation, genomic transcription, splicing, and protein interactions.

Results: Our findings indicated that IL-18–rs187238 C>G is associated with a protective effect against chronic HBV (odds ratio [OR] = 0.62; 95% confidence interval [CI]: 0.46–0.83; p = 0.002), unlike IL-18–rs1946518 T>G and CD14–rs2569190 A>G. The combined genotypes TG/CC/AA, TG/CC/AG, TT/CC/AG, and GG/CC/AA significantly increased the risk of chronic HBV ($p < 0.05$), while the IL-18 G/T and G/G haplotypes were associated with a reduced risk ($p < 0.05$). Additionally, IL-18–rs1946518 T>G is located in genomic regions that are conserved across mammalian species.

Conclusion: Unlike IL-18–rs1946518 T>G, the IL-18–rs187238 C>G variant may create novel binding sites for transcription factors, while CD14–rs2569190 A>G may alter RNA splicing patterns. Further research involving larger populations and diverse ethnic groups is needed to validate these findings.

Keywords: Hepatitis B, Interleukin-18, CD14, Transcription factors, RNA splicing factors, In silico.

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Abstract: A-10-2408-1

TNF-α /NF-κB Signaling Pathway in the MCF-7-Derived Organoid Model Leads to Tamoxifen Resistance

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Background: Drug resistance poses a significant challenge in breast cancer therapy. Tamoxifen, a commonly used selective estrogen receptor modulator in endocrine therapy, is often met with resistance. Understanding the mechanisms behind this resistance is crucial. While 2D cell culture models are frequently used to study drug resistance, they fail to accurately represent tumor tissue characteristics. In contrast, cell line-derived organoids mimic tumor properties, including cellular heterogeneity and acinar structures, and have been shown to exhibit resistance to Tamoxifen. The TNF-α/NF-κB pathway is an inflammatory pathway that may contribute to tumor drug resistance. Inhibiting NF-κB in Tamoxifen-resistant MCF-7 cells has been found to resensitize them to endocrine therapy, and clinical evidence indicates that NF-κB is upregulated in endocrine-resistant patients. However, the specific role of the TNF-α pathway in Tamoxifen resistance remains unclear.

Methods: To investigate the role of the TNF-α/NF-κB pathway in Tamoxifen resistance, we first developed and characterized an MCF-7-derived organoid model. We then assessed the expression of TNF-α pathway components in both organoid and monolayer cell cultures. Additionally, we measured NF-κB activation in response to Tamoxifen, Infliximab (an anti-TNF-α antibody), and the combination of Tamoxifen and Infliximab using Western blotting.

Results: Our results indicate that TNFR1, TNFR2, and TRAF2 showed no significant changes in expression between organoid and monolayer cultures. However, NF-κB activation was elevated in organoids due to increased TNF-α levels.

Conclusion: The combination of Infliximab and Tamoxifen effectively decreased active NF-κB levels, demonstrating the potential of targeting TNF-α signaling to enhance Tamoxifen therapy outcomes.

Keywords: Breast cancer, Organoid model, Inflammation, TNF-α Signaling pathway, Tamoxifen resistance.

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Abstract: A-10-2316-1

Investigating the Effect of Combined Treatment of Inulin and Resveratrol on Apoptosis in Pancreatic Tissue of Diabetic Animal Model

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Background: Type 1 diabetes is characterized by insulin deficiency and hyperglycemia, with apoptosis playing a crucial role in the destruction of pancreatic β-cells. Resveratrol and inulin are effective in managing blood sugar levels and improving insulin resistance in diabetes. This study investigates the combined effects of inulin and resveratrol on apoptosis in the pancreatic tissue of diabetic animal models.

Methods: Forty-eight male Wistar rats were divided into six groups: control, diabetic, inulin treatment (100 mg/kg), resveratrol treatment (20 mg/kg), combined treatment of inulin and resveratrol, and insulin treatment. Diabetes was induced in groups 2-6 through intraperitoneal injection of streptozotocin (65 mg/kg). At the end of the study, serum glucose levels were measured, and pancreatic tissue was collected for pathological examination and assessment of caspase activity.

Results: The diabetic model group exhibited significantly elevated glucose levels and caspase 7.3 activity compared to the control group. Treatment with inulin, resveratrol, and their combination significantly reduced glucose levels relative to the diabetic group. Additionally, resveratrol alone and its combination with inulin significantly lowered caspase 7.3 activity compared to the diabetic group. Hematoxylin and eosin (H&E) staining revealed degenerative and apoptotic changes in the islets of Langerhans in the diabetic group, while treatment with inulin, resveratrol, and their combination improved these conditions.

Conclusion: The findings suggest that the combination of resveratrol and inulin can enhance pancreatic β-cell integrity and effectively reduce apoptosis in the pancreatic tissue of diabetic rats.

Keywords: Apoptosis, Streptozotocin, Diabetes, Inulin, Resveratrol.

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Abstract: A-10-2316-2

Combinational Effect of Inulin and Resveratrol on Inflammation in the Pancreatic Tissue of Diabetic Rats

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Background: Type 1 diabetes (T1D) is an autoimmune disease characterized by chronic inflammation of the pancreatic islets of Langerhans. Resveratrol and inulin are known for their anti-inflammatory properties. This study aimed to investigate the combined effects of inulin and resveratrol on inflammation in the pancreatic tissue of a diabetic animal model.

Methods: This study involved 48 male Wistar rats, divided into six groups: control, diabetic, diabetic + inulin (100 mg/kg), diabetic + resveratrol (20 mg/kg), diabetic + combined inulin and resveratrol, and diabetic + insulin. Diabetes was induced via intraperitoneal injection of streptozotocin (STZ; 65 mg/kg). At the conclusion of the study, serum glucose levels were measured, and the mRNA expression of target genes (TNF-α, IL-6, IL-1β) in pancreatic tissue was evaluated using real-time PCR.

Results: The diabetic group exhibited significantly higher glucose levels compared to the control group ($p < 0.001$). Inulin ($p < 0.05$), resveratrol ($p < 0.05$), and their combination ($p < 0.01$) significantly decreased glucose levels compared to the diabetic group. The expression levels of IL-6, IL-1β, and TNF-α were significantly elevated in the diabetic group relative to the control group. Treatment with resveratrol ($p < 0.0001$), inulin ($p < 0.0001$), and the combination of both ($p < 0.0001$) significantly reduced the expression of IL-6, IL-1β, and TNF-α genes.

Conclusion: The findings of this study indicate that inulin and resveratrol, both individually and in combination, effectively mitigate inflammation in the pancreatic tissue of diabetic rats.

Keywords: Inflammation, Streptozotocin, Diabetes, Inulin, Resveratrol.

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Abstract: A-10-2329-1

Comparing and Investigating the Antidiabetic Effects of Hesperidin and Piperine in Rats with Diabetes

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Background: Herbal medicines are increasingly recognized as effective alternatives to synthetic drugs for diabetes treatment. This study aimed to compare the antidiabetic effects of hesperidin and piperine in diabetic rats.
Methods: Type 2 diabetes was induced in male rats via intraperitoneal administration of streptozotocin (60 mg/kg). Following diabetes induction, the experimental groups included a normal control group receiving distilled water, a positive control group treated with metformin (500 mg/kg), and groups receiving oral treatments of hesperidin (0.25 and 0.50 mg/kg) and piperine (0.25 and 0.50 mg/kg) for 30 days.
Results: The findings indicated that both hesperidin and piperine, at all administered doses, significantly reduced serum glucose, total cholesterol, and triglyceride levels in diabetic rats compared to the diabetic control group.
Conclusion: This study demonstrates the potential of hesperidin and piperine as therapeutic agents for the management of diabetes and its associated complications.

Keywords: Diabetic rat, Metformin, Hesperidin, Piperine, Streptozotocin.

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Abstract: A-10-2310-1

Evaluating the Efficacy of Sacubitril/valsartan in Heart Failure Management: A Systematic Review

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Background: Heart failure is a complex clinical syndrome involving multiple neurohormonal pathways, with the renin-angiotensin-aldosterone system serving as an initial compensatory mechanism that plays a significant role in the development of heart failure with reduced ejection fraction (HFrEF). Biomarkers such as natriuretic peptides and neprilysin indicate the activation of these pathways. Inhibiting neurohormonal pathways, particularly the renin-angiotensin-aldosterone system, is crucial for effective heart failure treatment. Neprilysin, an enzyme that degrades vasoactive peptides like natriuretic peptides, represents a novel therapeutic approach in heart failure management. The new class of drugs known as angiotensin receptor-neprilysin inhibitors (ARNi), which combines sacubitril and valsartan, counteracts the effects of angiotensin II while enhancing natriuretic peptide activity.

Methods: A systematic literature search was conducted to identify studies investigating ARNi therapy for heart failure in the PubMed database.

Results: A total of 8 studies involving 9,000 participants reported the efficacy of sacubitril–valsartan on hospitalization rates among heart failure patients. The pooled relative risk (RR) was 0.76 (93% CI: 0.70 to 0.87; I^2 = 23%), indicating that patients treated with sacubitril–valsartan experienced significantly fewer hospital admissions compared to those receiving alternative treatments ($p < 0.001$). Additionally, 10 studies with 1,400 participants assessed the impact of sacubitril–valsartan on left ventricular ejection fraction (LVEF). The pooled mean difference (MD) was 3.74 (96% CI: 1.93 to 5.55; I^2 = 88.4%), demonstrating that patients receiving sacubitril–valsartan had significantly higher LVEF compared to those on standard medications ($p < 0.001$).

Conclusion: Sacubitril/valsartan has proven effective in managing heart failure with reduced ejection fraction, significantly reducing mortality and morbidity in affected patients.

Keywords: Heart failure, Neurohormone, Neprilysin inhibitor, sacubitril/valsartan, ARNi.

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Abstract: A-10-2319-1

Comparison of Sesn2, Nfatc1 and Nrf2 in Pbmcs of Patients with the Newly Diagnosed Rheumatoid Arthritis with Under Treatment Patients

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Background: Rheumatoid arthritis (RA) is an autoimmune disease in which the immune system attacks to the internal tissues and forming antigen-antibody complexes that cause inflammation by settling in different organs of the patient's body. Genetic and environmental factors can affect this disease. NFATC1 is a transcription factor that is activated by the binding of RANKL to the receptor and induces osteoclastogenesis. Considering the importance of the activity of these genes in the inflammation, it is possible to find out their role in inflammation, especially in inflammation caused by autoimmune diseases, by carefully evaluating of these genes.
Methods: Investigation of SESN2, NRF2 and NFATC1 genes by Real time-PCR method on cDNA samples synthesized from peripheral blood mononuclear cells (PBMCs) of 60 samples including 20 newly diagnosed patients with rheumatoid arthritis as well as 20 chronic patients with the same disease compared to the control group.
Results: NRF2 and SESN2 gene expression increased in the newly diagnosed-RA patients compared to the control group and chronic patients and also increased in the chronic patients compared to the control group. Also, NFATC1 was lower in the newly diagnosed patients and chronic patients compared to the control group.
Conclusion: This study revealed that the expression levels of these genes have changed in the treatment conditions compared to the newly diagnosed patients, which indicates the necessity of evaluating the effect of the treatment on the precise downstream pathways in future studies.

Keywords: Inflammation, Rheumatoid arthritis, SESN2, NFATC1, NRF2.

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Abstract: A-10-2322-1

Construction of An Expression Vector Encoding Hiv-1 Nef-Tat Antigen Linked to An Antimicrobial Peptide

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Background: Therapeutic vaccination against HIV-1 has the potential to eradicate HIV infection and enhance HIV-specific immunity. Defensins play a critical role in modulating various cellular activities, including cytokine secretion, and exhibit a broad range of antimicrobial activity against bacteria, fungi, and viruses. This study aimed to construct an expression vector encoding the HIV-1 Nef-Tat antigen linked to β-defensin as a novel formulation for vaccine development.

Methods: Initially, the β-defensin-Nef-Tat fusion construct was designed using SnapGene software and synthesized in a cloning vector (pUC57). This fusion was then subcloned into a prokaryotic expression vector (pET-24a(+)). The subcloning process involved digestion with NheI and SalI enzymes, gel extraction, ligation with T4 DNA ligase, transformation into DH5α competent cells, and subsequent extraction and confirmation of the recombinant plasmid. The concentration (ng/µL) and purity (OD260/OD280) of the pET24a-β-defensin-Nef-Tat plasmid were determined using NanoDrop spectrophotometry.

Results: Our data demonstrated that the β-defensin-Nef-Tat fusion was successfully subcloned into the pET24a(+) vector. The success of this process was validated through enzymatic digestion and Sanger sequencing. Digestion of pET24a-β-defensin-Nef-Tat revealed a clear band of approximately 1100 bp after electrophoresis on agarose gel, corresponding to the β-defensin-Nef-Tat fusion gene. The concentration and purity of the plasmid, determined using a plasmid DNA extraction Mini-kit, were found to be 171 ng/mL.

Conclusion: Our findings indicate the successful construction of a prokaryotic expression vector encoding the HIV-1 Nef-Tat antigen linked to an antimicrobial peptide. This vector can be utilized for future studies in the field of HIV-1 vaccination.

Keywords: HIV-1, Nef, Tat, antimicrobial peptide, prokaryotic expression vector.

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Abstract: A-10-2321-1

Investigating the Effect of Resveratrol and Black Grape Extract on Nmdar Gene Expression Related to Alzheimer's Disease in Pc12 Model Cells

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Background: Alzheimer's disease (AD) is a neurodegenerative disorder characterized by both genetic and sporadic factors, leading to the loss of synaptic homeostasis and brain dysfunction. Resveratrol, a nutraceutical abundant in grapes, has several therapeutic effects. This study aims to analyze the potential effects of resveratrol on N-methyl-d-aspartate receptor (NMDAR) gene expression in PC12 cells exposed to formaldehyde.
Methods: The MTT assay and reverse transcription polymerase chain reaction (RT-PCR) were employed to investigate cell toxicity and NMDAR gene expression levels.
Results: The results indicated that both resveratrol and black grape extract increased cell survival. Additionally, grape extract significantly decreased NMDAR gene expression by 47% compared to the modeled group ($P \leq 0.05$; sig = 0.044). Resveratrol also reduced gene expression by 36%, with a significant difference between the two groups ($P \leq 0.05$; sig = 0.02).
Conclusion: The search for new therapeutic agents remains a challenge for researchers. Based on our findings, resveratrol and black grape extract show promise for development into new drugs that may offer greater safety than current treatments. They may also be beneficial as dietary supplements for individuals at risk of or suffering from Alzheimer's disease.

Keywords: Alzheimer's disease, resveratrol, black grape, NMDAR, gene expression.

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Abstract: A-10-2199-1

Complete Inhibition of Phosphatase and Tensin Homolog Promotes the Normal and Oxygen-Glucose Deprivation/reperfusion-Injured Pc12 Cells to Cell Death

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Background: The lipid phosphatase and tensin homolog deleted from chromosome 10 (PTEN) acts as a negative regulator of the phosphoinositide 3-kinase (PI3K)/AKT cell survival pathway. However, the impact of PTEN inhibitors on cell survival following reperfusion injury has been minimally explored. This study aimed to investigate the neuroprotective properties of SF1670, a novel PTEN inhibitor, in an in vitro stroke-like model.

Methods: PC12 cells were subjected to oxygen-glucose deprivation/reperfusion (OGD/R). Five experimental conditions were established: normoxic normoglycemic (NO/NG), 60 minutes of oxygen-glucose deprivation (OGD), 60 minutes of OGD followed by 6 hours of reperfusion (OGD/R), OGD/R treated with 10 µM SF1670 (OGD/RSF), and NO/NG treated with 10 µM SF1670 (NO/NG-SF). The phosphorylation levels of AKT and P38 in PC12 cells were quantified using immunoblotting, and cell viability was assessed through a colorimetric assay.

Results: Immunoblotting revealed a significant decrease in phosphoAKT (p-AKT) levels following OGD/R compared to NO/NG cells ($P < 0.05$). However, the p-AKT/total AKT ratio increased significantly in the OGD/R-SF group treated with SF1670, compared to the OGD/R condition. Conversely, SF1670 markedly reduced the levels of p-P38 MAPK and p-JNK in OGD/R cells. Cell viability significantly decreased in both the OGD and OGD/R conditions compared to the NO/NG group. Notably, cells treated with SF (OGD/R-SF and NO/NG-SF groups) exhibited significantly lower cell viability than the NO/NG condition.

Conclusion: Our findings indicate that complete inhibition of PTEN phosphatase activity not only fails to provide neuroprotection but also induces cell death in PC12 cells subjected to deprivation.

Keywords: OGD, Reperfusion Injury, AKT, p38, MAPK, PC12 Cells.

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Abstract: A-10-2347-1

Attenuation of the Non-Alcoholic Fatty Liver Disease in C57/bl6 Mice by Targeting Sirt1/AMPK/Smad3/TGF-β Genes and Mirna-141 By Resveratrol

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Background: This study investigates the impact of resveratrol on the miR-141/SIRT1/AMPK/ TGF-β/Smad3 pathway in the fatty liver of male C57/BL6 mice.
Methods: The mice were induced with a high-fat diet and resveratrol treatment, and the gene expressions of TGF-β, Smad3, SIRT1, and miR-141 were assessed using real-time PCR and The levels of SIRT1 and AMPK proteins were evaluated by Western blot assay.
Results: According to the pathology studies, resveratrol reduced fat accumulation in the liver of mice with fatty liver. The study found that intracellular lipid accumulation in hepatocytes increased miR-141 levels, leading to downregulation of endogenous SIRT1 expressions in the liver. SIRT1 mRNA and protein levels were reduced, while Smad3 and TGF-β mRNA levels increased. Also, the level of P-AMPK decreased and resveratrol significantly affected the level of P-AMPK.
Conclusion: In conclusion, Resveratrol significantly impacted the miR-141/SIRT1/AMPK/Smad3/TGF-β pathway in C57/BL6 mice, suggesting it could be a potential therapeutic target for NAFLD.

Keywords: Fatty liver, Oxidative stress, Lipid metabolism, Polyphenols, SIRT1, miRNA-141.

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Abstract: A-10-2349-1

Nephroprotective Effects of Linalool Against Gentamicin-Mediated Nephrotoxicity Through Its Antioxidant and Anti-Apoptotic Activities

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Background: Gentamicin (GM) is an aminoglycoside antibiotic effective against Gram-negative bacterial infections, but its nephrotoxic effects limit its clinical use. Linalool (Lin) is a linear monoterpene known for its potent antioxidant properties. This study aimed to evaluate the effects of linalool on GM-induced nephrotoxicity in Wistar rats.

Methods: Thirty-two rats were divided into four groups (n = 8 each). The control group received normal saline intraperitoneally, the Lin group received Lin, the GM group was administered GM (100 mg/kg), and the GM + Lin group received both GM (100 mg/kg) and Lin (100 mg/kg) for 12 days. After treatment, the kidneys were carefully removed; the left kidney was frozen for biochemical analysis, while the right kidney was stored in neutral buffered formalin for immunohistochemical analysis. Renal catalase (CAT) activity and malondialdehyde (MDA) concentrations were measured spectrophotometrically in kidney tissues, and caspase-3 expression was assessed using immunohistochemistry.

Results: Rats in the GM group exhibited significantly increased renal MDA concentrations and caspase-3 expression compared to the control group. In contrast, CAT activity was significantly decreased in GM-intoxicated rats. Notably, treatment with Lin significantly reduced renal MDA levels and caspase-3 expression compared to the GM group. However, Lin treatment in the GM + Lin group resulted in a significant increase in these parameters compared to the GM group.

Conclusion: Our findings suggest that linalool administration partially mitigates GM-induced nephrotoxicity in rats, likely through its antioxidant and anti-apoptotic properties.

Keywords: Gentamicin, Linalool, Nephrotoxicity, Rat.

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Abstract: A-10-2350-1

Investigating the Association Between Ace I/d Polymorphism and Type 2 Diabetes Mellitus Risk in the Iranian Population

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Background: The relationship between Type 2 Diabetes Mellitus (T2DM) and polymorphisms in the renin-angiotensin system (RAS) genes has garnered significant research interest. The RAS is essential for regulating blood pressure, fluid, and electrolyte balance. Genetic variations in RAS genes, particularly the angiotensin-converting enzyme (ACE) gene, have been implicated in various diseases, including T2DM. This study aims to investigate the potential association between T2DM and RAS gene polymorphisms in the Iranian population of Gonabad.
Methods: A total of 100 Iranians participated in the study, comprising 50 patients with T2DM and 50 age-matched healthy controls. DNA was extracted using the salting-out method, and polymerase chain reaction (PCR) was employed to amplify the ACE gene. Genotyping was performed using electrophoresis techniques.
Results: The frequency of the I/D genotype was significantly different between patients and controls. Individuals with the I/D genotype had a tenfold increased risk of developing T2DM (OR, 10 [95% CI, 3.7 to 27]; $P < 0.0001$). Furthermore, the risk was 2.88 times higher in those carrying the D allele (OR, 2.88 [95% CI, 1.55 to 5.24]).
Conclusion: The presence of the D allele and the I/D genotype of the ACE polymorphism may increase the likelihood of developing T2DM. Understanding the relationship between T2DM and RAS gene polymorphisms is vital for identifying individuals at higher risk and for developing personalized prevention and treatment strategies. Further research in this area could provide valuable insights into the mechanisms linking RAS gene polymorphism with the pathogenesis of T2DM.

Keywords: Polymorphism, Type 2 Diabetes Mellitus, Insertion-Deletion.

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Abstract: A-10-2354-1

Increased Serum Level of S100a12 and Gene Expression of S100a12 in Peripheral Blood Mononuclear Cells of Subjects with Significant Coronary Artery Stenosis, As A Good Diagnostic Biomarker

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Background: Inflammation plays a significant role in atherosclerosis. S100A12, released by white blood cells, is implicated in inflammatory cardiovascular events. This study aimed to assess the serum level of S100A12 and its gene expression in peripheral blood mononuclear cells (PBMCs) of individuals with coronary artery stenosis, examining its correlation with the severity of stenosis.

Methods: A total of 120 Iranian individuals were enrolled, comprising 70 patients with coronary artery stenosis greater than 50% (CAD group) and 50 individuals with stenosis less than 30% (control group). Participants underwent coronary angiography at Hajar Hospital. Angiographic data were recorded, serum samples were collected for biochemical analysis, and PBMCs were isolated using Ficoll solution. S100A12 gene expression was assessed using quantitative real-time polymerase chain reaction (qRT-PCR), while serum levels of S100A12 were measured by enzyme-linked immunosorbent assay (ELISA). Receiver operating characteristic (ROC) curve analysis was conducted to evaluate the diagnostic value of these molecular alterations.

Results: CAD patients exhibited higher total cholesterol levels compared to controls, although other lipid profile parameters did not show significant differences. Both gene expression and serum levels of S100A12 were significantly elevated in the CAD group compared to controls. The diagnostic accuracy was indicated by the area under the curve (AUC).

Conclusion: The alterations in S100A12 gene expression in PBMCs, alongside elevated serum levels of S100A12, may serve as promising diagnostic biomarkers for coronary artery disease, either alone or in conjunction with conventional risk factors. Further studies with larger sample sizes are warranted to validate these findings.

Keywords: S100A12, Coronary Artery Disease, Diagnostic Value.

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Abstract: A-10-2354-2

Increased Serum Level of Ox-Ldl and Expression of McP1 in the Peripheral Blood Mononuclear Cells, As Key Players Through Pathogenesis of Coronary Slow Flow Phenomenon

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Background: The coronary slow flow phenomenon (CSFP) is characterized by delayed filling of terminal vessels in the coronary arteries, occurring without significant coronary stenosis. It is a leading cause of chest pain in affected patients. However, the etiology and pathogenesis of CSFP are not well understood. This study aimed to investigate serum levels of oxidized low-density lipoprotein (Ox-LDL) and the expression of monocyte chemoattractant protein-1 (MCP-1) in peripheral blood mononuclear cells (PBMCs) from CSFP patients, comparing them to control subjects without CSFP or coronary stenosis.

Methods: We enrolled 120 participants, dividing them into two groups: CSFP and control, based on angiography reports from Hajar Hospital. Blood samples were collected, and PBMCs were isolated using Ficoll solution. We measured anthropometric data and serum biochemical parameters. MCP-1 gene expression in PBMCs was analyzed using quantitative real-time polymerase chain reaction (qRT-PCR), and serum Ox-LDL levels were quantified using enzyme-linked immunosorbent assay (ELISA). Correlations between the data were also explored.

Results: Demographic analysis revealed that systolic and diastolic blood pressure were significantly higher in the control group compared to CSFP patients ($P < 0.05$). While no significant changes were detected in other biochemical parameters, serum Ox-LDL levels were significantly elevated in the CSFP group compared to controls ($P < 0.05$). Furthermore, MCP-1 gene expression showed a marked increase in the CSFP group relative to the control group ($P < 0.05$). A significant correlation was found between elevated Ox-LDL levels and increased MCP-1 expression, linking these factors to the incidence of CSFP.

Conclusion: We hypothesize that the pathogenesis of CSFP may involve MCP-1 as a chemotactic agent and Ox-LDL as a trigger for foam cell formation. Further in-depth research with a larger sample size is needed to validate this hypothesis.

Keywords: Coronary Slow Flow Phenomenon, Ox-LDL, MCP-1, PBMCs.

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Abstract: A-10-2282-1

Synthesis of Magnetic Nanotaurine and Its Effect in Inhibiting Gastric Cancer Cells and Immunogenetic Gene Expression

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Background: Stomach cancer is a significant health issue in Iran, particularly in Ardabil province. Alongside aggressive treatments such as radiation therapy and chemotherapy, compounds like oleuropein, resveratrol, and taurine have been reported to inhibit gastric cancer cells. However, effectively targeting these compounds to tumor cells remains a critical challenge. Taurine, a sulfur-containing amino acid, not only serves structural roles in the body but also has potential anticancer properties. This study aims to synthesize magnetic nanotaurine and evaluate its effects on inhibiting cancer cells by enhancing immune-related gene expression.

Methods: To achieve targeted delivery of taurine to cancer cells, magnetic nanotaurine was synthesized using a hydrothermal method. The inhibitory effects on AGS cells were assessed by applying various doses of magnetic nanotaurine. The lethal dose required to inhibit 50% of cell viability (LD50) was determined using the MTT assay. Subsequently, the expression levels of immune-related genes (IL6, IL12, and CD8) were quantified using real-time PCR.

Results: The results indicated that magnetic nanotaurine significantly inhibited AGS cancer cells, confirmed by the increased expression of immune-related genes (CD8, IL6, and IL12) at the molecular level. In vitro studies demonstrated that AGS cancer cells were effectively inhibited by a dose of 780 µg/mL of magnetic nanotaurine and 1250 µg/mL of taurine.

Conclusion: These findings suggest that magnetized nanotaurine may serve as a targeted approach for controlling cancer cells, pending further validation through in vivo studies.

Keywords: Nanotaurine, AGS, CD8, IL6, IL12.

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Acta Biochimica Iranica

Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2282-2

The Effect of Nanosilver @ Taurine in Inhibiting Acinetobacter and Inducing Anti-Inflammatory Properties in Skin Cells

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Background: Acinetobacter is a significant soil bacterium known for its resistance to many antibiotics, including penicillin. One promising approach to combat this resistance involves the use of silver core nanomaterials. Taurine, a naturally occurring sulfur-containing amino acid, possesses strong antioxidant and anti-inflammatory properties, making it a potential natural antibiotic. This study aims to investigate the synergistic effects of nanosilver combined with taurine in promoting tissue regeneration, reducing inflammation, and inhibiting Acinetobacter.

Methods: Nanosilver was synthesized through the reduction of silver oxide using taurine extract, followed by the reattachment of taurine via a hydrothermal method. The properties of the nanosilver-taurine complex were confirmed using scanning electron microscopy (SEM), dynamic light scattering (DLS), and Fourier-transform infrared spectroscopy (FTIR). The antimicrobial activity was assessed through minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) tests. The anti-inflammatory effects were evaluated at the cellular level, and the expression of immune-related genes (CD8, IL6, IL12) was analyzed using real-time PCR.

Results: The results indicated that nanosilver-taurine treatment significantly inhibited Acinetobacter compared to taurine alone across all evaluation methods. Additionally, the expression levels of CD8, IL6, and IL12 genes showed significant changes in the HFF2 skin cell line following treatment.

Conclusion: Nanosilver-taurine demonstrates a restorative effect, not only inhibiting the pathogenic agent Acinetobacter but also reducing inflammation on the skin surface, highlighting its potential as a novel therapeutic agent.

Keywords: Nanosilver, Taurine, Skin Cells, Acinetobacter, CD8, IL6, IL12.

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Abstract: A-10-2359-1

Alpha-7 Subunit of Nicotinic Acetylcholine Receptor Regulates Pd-L1 and Ctla-4 Expression in Hepg2 Cells

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Background: The liver, the largest solid organ in the body, plays a crucial role in immunoregulation. The alpha7 subtype of the nicotinic acetylcholine receptor (α7nAChR) is expressed in the liver and has diverse immunomodulatory effects. Programmed death ligand 1 (PD-L1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) are critical immune checkpoints that negatively regulate immune responses. This study investigates the impact of α7nAChR activation (via nicotine) and inhibition (via specific siRNA) on the gene expression of PD-L1 and CTLA-4.

Methods: Human hepatocellular carcinoma (HepG2) cells were treated with low (1 µM) and high (10 µM) doses of nicotine to assess its effects on PD-L1 and CTLA-4 expression. Additionally, the effects of α7nAChR-specific siRNA (α7-siRNA) at a concentration of 100 nM were examined using quantitative real-time PCR (qRT-PCR).

Results: Nicotine treatment resulted in a significant dose-dependent decrease in PD-L1 expression compared to untreated cells. Nicotine exhibited a biphasic effect on CTLA-4 expression, reducing its levels at a 10 µM concentration. qRT-PCR results indicated that α7-siRNA significantly reduced α7nAChR mRNA levels ($P < 0.01$). Furthermore, α7-siRNA treatment led to a significant increase in both PD-L1 and CTLA-4 expression compared to control cells.

Conclusion: These findings demonstrate that nicotine decreases PD-L1 and CTLA-4 expression, an effect that is reversed by α7-siRNA treatment. This suggests that α7nAChR-mediated mechanisms play a crucial role in regulating these immune checkpoints.

Keywords: PD-L1, CTLA-4, α7nAChR, Nicotine, siRNA.

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2357-1

Examining the Expression of Nidogen Gene in the Liver Tissue of Patients with Cirrhosis Caused by Nash, Viral Hepatitis, Autoimmune Hepatitis and Primary Sclerosing Cholangitis, Patients with Simple Non-Alcoholic Steatosis and Control Subjects

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Background: Liver inflammation can arise from various causes, leading to fibrosis and ultimately resulting in cirrhosis and liver failure. Nidogen is an extracellular matrix glycoprotein that promotes the formation and stability of the basement membrane, and several studies have indicated its potential anti-fibrotic effects. This study aims to investigate the expression of the Nidogen gene in liver tissue from cirrhotic patients and its relationship with different etiologies of the disease, including cirrhosis caused by NASH, viral hepatitis, autoimmune diseases, and primary sclerosing cholangitis (PSC).

Methods: The study analyzed liver tissue samples from 24 cirrhotic patients with varying etiologies, alongside 8 normal tissue samples as a control group. RNA was extracted from the tissues, cDNA was synthesized, and the expression of the Nidogen gene was measured using quantitative real-time PCR (qRT-PCR). Statistical analyses were performed using SPSS software version 16.0.

Results: The results revealed a significant decrease in Nidogen gene expression in cirrhotic patients compared to healthy individuals ($P = 0.001$). This decrease was observed across all cirrhosis groups compared to healthy controls; however, it was only statistically significant in patients with cirrhosis due to biliary tract disorders ($P = 0.003$) and autoimmune diseases ($P = 0.003$). Among the cirrhosis groups, the highest expression was observed in patients with fatty liver-related cirrhosis, while the lowest was found in those with biliary tract disorders.

Conclusion: The reduction in Nidogen gene expression in liver cirrhosis patients may be associated with the underlying causes of the disease and could play a significant role in its progression.

Keywords: Liver, Cirrhosis, Nidogen.

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Abstract: A-10-2363-1

The Effect of Bifidobacterium Bifidum Bacteria on the Expression of Cyclooxygenase-2 Enzyme in Peripheral Blood Mononuclear Cells

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Background: Cyclooxygenase exists in two isoforms: COX-1 and COX-2. The expression of the COX-2 gene is induced by inflammatory stimuli. For instance, TNF-α triggers the release of pro-inflammatory factors, leading to increased expression of cyclooxygenase enzymes and intensifying the inflammatory process. Inhibiting COX-2 can alleviate the symptoms of allergic reactions and pain. Given the critical role of COX-2 in inflammation, this study aimed to determine the effect of Bifidobacterium bifidum on COX-2 gene expression.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from heparinized blood of healthy individuals aged 20-40 years. A standard strain of Bifidobacterium bifidum was obtained from the Tehran Genetic Resource Center's Microbial Collection, and bacterial cytoplasmic and cell wall extracts were prepared. PBMCs were treated in 96-well plates in two groups: a control group (normal saline) and an intervention group (with Bifidobacterium bifidum). After 72 hours, the precipitate from each well was collected for RNA extraction and cDNA synthesis. Real-Time PCR was performed, and data were analyzed using Qount3 and SPSS version 26, employing a one-way analysis of variance.

Results: Expression analysis revealed a significant decrease in COX-2 gene expression in the intervention group treated with Bifidobacterium bifidum compared to the control group ($P < 0.05$). The COX-2 gene expression in the control group was notably low.

Conclusion: The findings indicate a significant correlation between the reduction in COX-2 gene expression and the effect of Bifidobacterium bifidum. Therefore, Bifidobacterium bifidum may represent a novel treatment approach with high efficacy, low side effects, and biological safety. Further investigations are recommended to explore its potential for treating and preventing inflammation.

Keywords: Bifidobacterium bifidum, cyclooxygenase-2, peripheral blood mononuclear cells, Real-Time PCR.

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Abstract: A-10-2364-1

Synthesis of Nanosilver Taurine and Its Effect in Inhibiting Staphylococcus Aureus in Diabetic Foot Ulcers

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Background: Staphylococcus aureus is one of the most successful pathogenic bacteria and ranks among the top five causes of hospital infections, particularly wound infections following surgery. This bacterium is frequently found in diabetic foot ulcers, which affect approximately 15% of individuals with diabetes, often due to infection and insulin insensitivity. Taurine, one of the most abundant sulfur-containing amino acids in the body, possesses antioxidant and anti-inflammatory properties that can enhance insulin sensitivity. This study aims to investigate the synergistic effects of nanosilver combined with taurine on Staphylococcus aureus infections in diabetic foot ulcers.

Methods: Nanosilver was synthesized through the reduction of silver oxide using taurine extract, followed by the reattachment of taurine via a hydrothermal method. The synthesis was confirmed using spectroscopic methods and scanning electron microscopy (SEM). The inhibitory effects of the nanosilver-taurine composite were evaluated using well tests, halo tests, minimum inhibitory concentration (MIC), and minimum bactericidal concentration (MBC) assays.

Results: The results demonstrated that treatment with nanosilver-taurine significantly inhibited Staphylococcus aureus compared to taurine alone across all four evaluation methods.

Conclusion: The synthesis of nanosilver represents a novel material that not only inhibits the pathogenic effects of Staphylococcus aureus but also may improve insulin sensitivity and reduce inflammation. This dual action suggests its potential application in the treatment of diabetic foot ulcers.

Keywords: nanosilver, taurine, Staphylococcus aureus, diabetes, foot ulcers.

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Abstract: A-10-2366-1

Copper-Cysteamine Nanodrugs Boost Chemo-Radiotherapy in Cervical Cancer

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Background: Copper-Cysteamine nanoparticles (Cu-Cy NPs) have emerged as promising radiosensitizers in cancer treatment. This study aims to investigate the combined therapeutic effect of these nanoparticles and cisplatin using a clinical linear accelerator to enhance the efficacy of chemoradiation therapy for cervical cancer.

Methods: Following successful synthesis and characterization of Cu-Cy NPs, the cytotoxicity effect of these nanoparticles and cisplatin in various concentrations was evaluated on HeLa cancer cells, individually and in combination. Additionally, the radiobiological effects of these agents were investigated under a 6MV linear accelerator.

Results: At a concentration of 25 mg/L, Cu-Cy NPs displayed no significant cytotoxicity toward HeLa cancer cells. However, when combined with 2Gy X-ray irradiation at this concentration, the nanoparticles demonstrated a potent radiosensitizing effect. Notably, cell viability and migration rate in the combination group (Cu-Cy NPs + cisplatin + radiation) were significantly reduced compared to the radiation-alone group. Additionally, the combination treatment induced a significantly higher rate of apoptosis compared to the radiation-alone group.

Conclusion: Overall, Cu-Cy NPs exhibited a significant dose-dependent synergistic enhancement of radiation efficacy when combined with cisplatin under X-ray exposure, and may provide a promising approach to improve the therapeutic effect of conventional radiation therapy.

Keywords: Copper-Cysteamine nanoparticles, Cisplatin, Cervical cancer, Radiosensitizer, Chemoradiation therapy.

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Abstract: A-10-2367-1

Pnu-74654 Enhanced the Antiproliferative Activity of Gemcitabine Via Targeting Wnt/β-Catenin Pathway in Pancreatic Cancer

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Background: The Wnt/beta-catenin pathway is frequently deregulated in pancreatic cancer and is associated with poor prognosis. This highlights the need for novel agents to enhance the efficacy of current therapies. In this study, we explored the anticancer activity of PNU-74654, both alone and in combination with gemcitabine, in two- and three-dimensional cell culture models of pancreatic cancer.

Methods: The MTT assay was utilized to assess the viability of pancreatic cancer cells (PCC). The cytotoxicity of PNU-74654 was evaluated in a 3D cell culture model (spheroid). Additionally, the effects of PNU-74654 were investigated in established cell migration and invasion assays.

Results: We evaluated the expression of candidate genes involved in the cell cycle, migration, and the Wnt/beta-catenin pathway using RT-PCR and Western blotting. PNU-74654 inhibited cell growth with an IC50 of 122±0.4 µmol/L and exhibited a synergistic effect with gemcitabine, modulating the Wnt pathway. The combination of PNU-74654 and gemcitabine significantly reduced the migration and invasiveness of pancreatic cancer cells compared to control cells, primarily through the modulation of E-cadherin expression.

Conclusion: Our findings demonstrate the potent antitumor properties of PNU-74654 in in vitro models of pancreatic cancer, warranting further in vivo studies to evaluate the therapeutic potential of this novel agent in targeting the Wnt pathway for pancreatic cancer treatment.

Keywords: pancreatic cancer, PNU-74654, Wnt pathway, gemcitabine.

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Abstract: A-10-2367-2

The Predictive Potential Value of Collagen Type IX Alpha 1 Chain in Colorectal Cancer: Integrative Analysis Using Rna/dna Sequencing and Pan-Cancer Studies

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Background: Colorectal cancer (CRC) is the second most common cause of cancer-related deaths globally. Metastatic spread and multifactorial chemoresistance have limited the benefits of existing therapies. Hence there is an imperative for the identification of biomarkers and novel therapeutic targets to increase the efficacy of current therapy. This study aimed to provide a comprehensive analysis of the Collagen type IX alpha 1 chain (COL9A1) from a pan-cancer perspective employing multiomics data followed by validation in an additional cohort of CRC.
Methods: The expression profile and function of COL9A1 across different tumors were investigated to investigate the expression profile, genomic alterations, survival analysis, protein-protein interaction, correlation with immune cell subtypes, tumor immune microenvironment, and enrichment analysis.
Results: Among the high top-score genes and dysregulated pathways associated with CRC, COL9A1 was detected and further validated in 120 CRC patients. Collagen family members were identified as core upregulated genes through protein-protein interaction (PPI) network analysis. The pan-cancer analysis demonstrated a consistent upregulation of COL9A1 expression in various cancers, including CRC. Moreover, the correlations between COL9A1 and immune infiltration were assessed to evaluate its potential as a therapeutic target. The findings suggest that increased COL9A1 expression was associated with poorer overall and disease-free survival outcomes across multiple cancer types. Functional enrichment analysis highlighted the role of COL9A1 in extracellular matrix and tumor microenvironment-associated pathways.
Conclusion: In conclusion, the overall comprehensive pan-cancer analysis affirms that COL9A1 could be a promising diagnostic and therapeutic target, and offer insightful strategies to guide the therapeutic direction in colorectal cancer.

Keywords: COL9A1, Colorectal cancer, Pan-cancer, EMT.

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2164-1

Effect of Histamine Treatment on the Proliferation of Oral Squamous Cell Carcinoma (OSCC) and Downstream Genes

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Background: Oral squamous cell carcinoma (OSCC) is a type of head and neck cancer characterized by the uncontrolled growth of malignant cells in the oral cavity. Histamine, a biogenic amine, has been implicated in the proliferation of OSCC cell lines. This review examines the effects of histamine treatment on OSCC cell proliferation and its influence on downstream genes, particularly those related to apoptosis.

Methods: A comprehensive literature search was conducted using electronic databases to identify studies investigating the impact of histamine treatment on OSCC cells. In vitro experiments utilizing OSCC cell lines and animal models were included. Data on cell proliferation assays, gene expression analyses, and signaling pathway investigations were extracted and analyzed.

Results: Histamine treatment consistently exhibited a pro-proliferative effect on OSCC cells, stimulating cell growth through the activation of histamine receptors, predominantly H1R and H2R. Mechanistic insights revealed the involvement of key signaling pathways, including MAPK and PI3K/Akt. Furthermore, histamine treatment resulted in the upregulation of several genes associated with cell proliferation, such as cyclin D1, cyclin E1, and c-Myc, while downregulating genes involved in apoptosis, including Bax and caspase-3.

Conclusion: The evidence presented in this review suggests that histamine treatment may promote OSCC cell proliferation by upregulating genes involved in cell cycle progression and downregulating those related to apoptosis. Further studies are needed to elucidate the molecular mechanisms underlying these effects and to explore the potential clinical applications of histamine in OSCC treatment.

Keywords: Oral squamous cell carcinoma, histamine, apoptosis.

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Abstract: A-10-2375-1

Protective Effects of Herbal Drug in Rat Model of Post-Surgical Uterine Adhesion

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Background: One of the most prevalent complications after gynecological surgeries is the formation of uterine adhesion, which can compromise the proper functioning of the targeted organ. It is commonly observed after curettage or caesarean section, which may result in the formation of fibrotic tissue within the uterine cavity and potentially contribute to reproductive disorders such as infertility. Considering the relatively high prevalence of this disorder, the adverse effects of biochemical drugs and the invasiveness of current treatment modalities, it seems necessary to use alternative herbal treatment options with less side effects and more cost-effectiveness. Due to the pharmacological attributes of evening primrose oil (EPO), the aim of this study was to examine the protective effects of EPO in managing this condition.

Methods: The experimental rats were divided into three groups; sham, positive control, and treatment groups. Adhesion was induced through a fine scratch in uterine wall in the positive control and treatment groups, followed by the administration of a specific dosage of EPO via oral gavage to the treatment group over 10-days. To assess the therapeutic impact of the drug following the treatment, histological, molecular, and physiological assessments was employed.

Results: Histological examinations, including H&E and Masson's trichrome staining, and immunohistochemical staining revealed that the treatment effectively restored uterine tissue near to normal conditions and molecular technics demonstrated its anti-inflammatory, antioxidant, and anti-fibrotic attributes. Moreover, the treated rats group exhibited higher fertility rates and improved delivery outcomes in contrast to the positive control group.

Conclusion: Our study demonstrated that EPO could be beneficial in treating uterine adhesion as well as reducing infertility.

Keywords: Gynecological disorder, Infertility, Cesarean operation, Curettage, Herbal medicine

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Abstract: A-10-2388-1

Down-Regulation of Steroid 5-alpha-Reductase 1 (SRD5A1) and Progesterone Receptor-B (PGR-B) Impairs Vascular Remodeling and Endometrial Decidualization in Women with Recurrent Implantation Failure

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Background: The endometrium is a multifaceted, steroid-dependent tissue that undergoes dynamic cyclical remodeling. The recent elucidation of the local pro-androgenic microenvironment that arises during the decidualization of ESC indicates that intracrine androgens may serve as crucial physiological regulators of decidualization. Androgens and progesterone are crucial for promoting stromal fibroblast differentiation and signaling for endometrial remodeling.

Methods: In present study, women with recurrent implantation failure (RIF) (n=50) and fertile women (n=50) were recruited. The endometrial expression of steroid 5α-reductase type 1 (SRD5A1) and VEGF-A and progesterone Receptor-B (PGR-B) was measured. Serum levels of VEGF, progesterone (P4) and estrogen (E2) and testosterone (T) was measured by ELISA method.

Results: Our research findings suggest that women with RIF have lower expression levels of SRD5A1 and VEGF-A compared to fertile women. Interestingly, despite similar serum levels of progesterone (P4), estrogen (E2), and testosterone (T) in both groups, VEGF levels were lower in RIF women. In RIF women, there was a significant positive correlation between VEGF-A gene with serum VEGF and P4, whereas endometrial SRD5A1 expression negatively correlated with LH levels in RIF. However, in healthy fertile women endometrial expression of SRD5A1 significantly correlated with VEGF-A and PGR-B expression (r=0.655 and r=0.499, all P=0.001). linear regression analysis revealed that VEGF-A gene expression was correlated with SRD5A1 gene expression. Binary logistic regression revealed that down regulation of LH levels, SRD5A1 and VEGF-A gene expression enhanced the risk of RIF in women (OR= 1.5, OR=8.2, OR=250, all P-value <0.05).

Conclusion: These findings demonstrate the necessity of intracrine androgen signaling for optimal decidualization. Additionally, the regulation of the VEGF pathway confirms the significant role of androgens and P4-PGR-B interaction in vasculature development during decidualization.

Keywords: RIF, SRD5A1, Progesterone Receptor-B, VEGF, decidualization

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Abstract: A-10-2396-1

Investigating the association between the rs4588 polymorphism and polycystic ovarian syndrome in Iranian women

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Background: Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder affecting women of reproductive age. Women with PCOS often exhibit irregular menstrual cycles, hirsutism, and acne, along with polycystic ovarian morphology. Vitamin D deficiency and genetic variations in the vitamin D binding protein (VDBP) gene may contribute to PCOS. This study investigates the potential association between the rs4588 polymorphism in the VDBP gene and PCOS, as well as its potential impact on infertility and recurrent pregnancy loss (RPL) in Iranian women with PCOS.

Methods: The study involved 297 women including 100 healthy individuals, 96 infertile-PCOS women, and 101 PCOS women experiencing RPL. Blood samples were taken from all participants to measure biochemical and hormonal parameters. Genotyping for the rs4588 polymorphism was performed using the PCR-RFLP assay.

Results: There were significant differences in the distributions of genotypes and alleles of the rs4588 polymorphism among the three groups. The study revealed that women with the AC genotype and A allele were more likely to have PCOS and infertility, while no association was found between these genetic variations and RPL.

Conclusion: The study indicates that genetic variations in the rs4588 region of the VDBP gene may increase the risk of PCOS and infertility.

Keywords: Vitamin D binding protein, Polycystic ovary syndrome, Polymorphism, Infertility, Recurrent pregnancy loss

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Abstract: A-10-2231-1

Drug Repositioning in Colorectal Cancer: A Promising Strategy for Enhanced Therapeutics

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Background: Colorectal cancer (CRC) remains a leading cause of cancer-related morbidity and mortality worldwide. Traditional treatments, including surgery, chemotherapy, and radiation, often suffer from limitations such as resistance, toxicity, and suboptimal efficacy. Drug repositioning, the process of identifying new therapeutic uses for existing drugs, offers a promising avenue to enhance CRC treatment, leveraging the established safety profiles and mechanisms of existing pharmaceuticals.

Methods: We analyzed peer-reviewed literature, databases, and clinical trial repositories up to February 2024, focusing on FDA-approved drugs for CRC treatment. Included were preclinical studies, clinical trials, and retrospective analyses showing efficacy, mechanisms, and outcomes. Data were extracted and analyzed per PRISMA guidelines, ensuring a thorough and unbiased summary of current evidence.

Results: Our review identified 35 studies that met the inclusion criteria. Key repositioned drugs showing promise included metformin, statins, non-steroidal anti-inflammatory drugs (NSAIDs), and anti-psychotics. Metformin demonstrated significant anti-proliferative effects on CRC cells through AMPK activation and inhibition of mTOR pathways. Statins were associated with reduced CRC incidence and enhanced chemotherapeutic efficacy via cholesterol-lowering independent mechanisms. NSAIDs, particularly aspirin, showed preventive benefits and were linked to COX-2 inhibition and apoptosis induction. Antipsychotics, such as clozapine, exhibited tumor-suppressive properties by modulating the dopamine receptor pathways and inducing autophagy. Several of these drugs are currently undergoing phase II and III clinical trials, underscoring their translational potential.

Conclusion: Drug repositioning offers a viable and innovative strategy to improve CRC therapeutics. The repositioned drugs highlighted in this review demonstrate significant potential in enhancing treatment efficacy, reducing resistance, and offering new hope for patients. Further clinical investigations are warranted to confirm these findings and facilitate the integration of these agents into standard CRC treatment regimens, ultimately improving patient outcomes and broadening therapeutic options.

Keywords: Colorectal cancer, Drug reposition, CRC treatment

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Abstract: A-10-2419-1

Synthesis of Zinc Oxide Nanoparticle by Green Method Using Calotropis Procera Plant Extract

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Background: Today, plants and agricultural products have received special attention as renewable and cheap sources for the preparation of various biological nanomaterials. Synthesis of zinc oxide nanoparticles is very valuable due to its many applications in cancer treatment, identification of pathogenic agents, and unique optical and thermal electronic properties. In this study, the synthesis of zinc oxide nanoparticles was carried out using the extract of Calotropis procera plant in a green method, and natural solvents were used, which are both low cost and do not pose a risk to the environment.

Methods: In this study, the extract of the Calotropis procera plant was used as a reducing and stabilizing agent for the biological production of zinc oxide nanoparticles. The reaction was carried out by adding the extract to zinc nitrate salt with a concentration of 0.1 molar and increasing the temperature to 80°C for 2 hours. The color change of the extract from green to yellow indicated the production of zinc oxide nanoparticles.

Results: The formation of zinc oxide nanoparticles was shown by the formation of an absorption peak at a wavelength of about 275 nm using a spectrophotometric device as well as an X-ray diffraction pattern. The size and morphology of synthesized nanoparticles were determined by a TEM electron microscope. It was found that the shape of the particles is multifaceted and round and their average size is around 60 nm. The range of size changes of nanoparticles was obtained by a dynamic light scattering device between 16 and 70 nm.

Conclusion: In this research, zinc oxide nanoparticles were produced with a method compatible with nature and without harmful chemicals. Due to having secondary metabolites and antioxidant properties, plants play the role of stabilizing and regenerating nanoparticles.

Keywords: Key words: Calotropis procera, zinc oxide nanoparticle, plant, green method

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Abstract: A-10-2388-2

Low Serum Cxcl12 as Anti-Inflammatory Cytokine Enhances Implantation Defect and Reduces Endometrial Receptivity in Women with Recurrent Implantation Failure

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Background: The successful implantation of an embryo hinges on the receptiveness of the endometrium and the process of decidualization. Although various cytokines have been proposed to improve implantation rates by enhancing endometrial receptivity, there are currently no evidence-based treatments available for this issue. It has been observed that stromal cell-derived factor 1 (CXCL12) plays a crucial role in regulating trophoblast cell proliferation, migration, survival, and the maternal immune response in humans.

Methods: This case-control study took place between June 2022 and July 2023 and involved 50 patients with RIF and 50 control subjects who had previously experienced a spontaneous full-term pregnancy with a live birth. The study was conducted at the Medical Center of Arash Hospital in Tehran, Iran. Serum levels of P4, E2, Vit-D3, IL-6, IL-1b, IL-10, and CXCL-12 were measured using the ELISA method. Statistical analysis was performed using SPSS and GraphPad.

Results: In the recent study, it was found that women with RIF had lower serum concentrations of IL-10, CXCL-12, and Vit-D3 compared to the fertile women, while showing significantly higher levels of IL-6 and IL-1b than fertile women. No significant differences were observed in the serum levels of E2 and P4 between the two groups. Spearman rank analysis revealed a positive correlation between serum levels of CXCL-12 and IL-10 ($r= 0.650$, $P<0.05$), as well as a significant negative association between CXCL-12 and IL-1b, IL-6, and E2 ($r= – 0.417$, $r= – 0.252$, $r= – 0.305$, $P<0.05$). However, in fertile women, serum levels of IL-4 were significantly associated with serum IL-10 ($r=0.654$, $P<0.05$).

Conclusion: The study suggests that women with RIF experience an imbalance of pro-inflammatory and anti-inflammatory cytokines. Elevated levels of E2 in women with RIF may impair CXCL12's function, which is crucial for trophoblast migration and T-cell recruitment, essential processes for successful implantation and pregnancy.

Keywords: Recurrent implantation failure CXCL-12, Progesterone, Estrogen, pro-inflammatory cytokines

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2423-1

Hepatoprotective Effects of Cerium Oxide Nanoparticles in Carbon Tetrachloride-Induced Liver Injury

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Background: Numerous agents and drugs are accountable for various types of liver disorders. Carbon tetrachloride (CCl4) is used to induce liver injury in animal models. CCl_4 induces oxidative stress, inflammation, fibrosis, and liver necrosis. Previous experiments showed the antioxidant effects of Cerium oxide nanoparticles (CeO_2 NPs). Hence, this experiment aimed to evaluate the effects of the CeO_2 NPs in carbon tetrachloride (CCl_4)-induced liver damage in rats.

Methods: male Wistar rats were randomly divided into 3 groups, including; group 1: Normal rats, 2: CCl_4 group, 3: CCl_4 + CeO_2 NPs. Nanoparticles were administered orally for 14 weeks (0.1 mg/kg). Two hours after the last dosage, liver damage was induced by CCl4 (1 ml/kg of 50% CCl_4). After overnight, animals were euthanized and blood was collected. Antioxidant markers such as glutathione (GSH), total antioxidant capacity (TAC), total oxidant status (TOS), and malondialdehyde (MDA) were measured. Tumor necrosis factor-α (TNF-α) levels were determined by ELISA. Liver morphological alterations were evaluated.

Results: Our result showed that administration of CCl_4 significantly increased MDA ($P<0.05$) and total oxidant status (TOS) levels ($P<0.05$), while reducing total antioxidant capacity (TAC) ($P<0.05$) and glutathione (GSH) levels ($P<0.05$). Treatment with nanoparticles normalized MDA, TOS, TAC, and GSH levels in animal models ($P<0.05$). CeO_2 NPs also reduce TNF-α levels in rats ($P<0.05$). These nanoparticles also alleviated the liver histological changes.

Conclusion: These results showed CeO_2 NPs have hepatoprotective against CCl_4-induced liver damage.

Keywords: Cerium oxide nanoparticles, rats, oxidative stress, nanoparticle

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Abstract: A-10-2372-2

Novel Strategies for Improving Cancer Immunotherapy Using Zif8 Nanoparticles

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Background: ZIF-8 nanoparticles are a potentially effective Target drug delivery system. The nanoparticles unequivocally induce pyroptosis, necrosis, and immunogenic cell death, activating antitumor immunity and reshaping the tumor microenvironment for highly effective immunotherapy and prevention of tumor growth. Cancer immunotherapy offers significant advantages over traditional antitumor therapy, prolonging progression-free survival and overall survival. Cancer immunotherapy uses the body's immune system to target and eradicate cancer cells, a promising treatment method despite challenges like tumor heterogeneity and immune evasion mechanisms.
Methods: This review paper was conducted using articles available on PubMed, Science Direct, and Google Scholar up until May 2024.The Keywords were ZIF8, Cancer Immunotherapy, Nanoparticles and Delivery system. 28 articles were identified by searching this database; however, after reviewing the titles and abstracts, 17 of them were eliminated. Eleven articles met the inclusion criteria and were chosen.
Results: One novel strategy involves using ZIF8 nanoparticles as a delivery system for cancer immunotherapy agents. ZIF8 nanoparticles are an excellent option for drug administration because of their unique qualities, which include high surface area, biocompatibility, and variable pore size. Researchers can increase immunotherapy drugs' stability, bioavailability, and targeted specificity by encasing them in ZIF8 nanoparticles. For instance, in preclinical settings, ZIF8 nanoparticles containing immune checkpoint inhibitors have demonstrated enhanced antitumor effectiveness. ZIF8 nanoparticles can also be functionalized with targeted ligands to decrease off-target effects and improve accumulation in tumor tissues. Modifying ZIF8 nanoparticles to release their payload in response to specific stimuli, such as acidic pH or enzyme activity, can enhance the therapeutic index of immunotherapy drugs.
Conclusion: In summary, ZIF8 nanoparticles offer a promising way to get around present obstacles and enhance treatment results in cancer immunotherapy. Further research is needed to optimize ZIF8 nanoparticle design, safety profile, and clinical applications for effective cancer immunotherapy strategies, improving patient outcomes.

Keywords: ZIF8, Cancer Immunotherapy, Nanoparticles, Delivery system

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Abstract: A-10-2372-3

Exploring the Interaction Between Flavonoids and Beta-Lactoglobulin: A Comprehensive MD Simulation Study

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Background: This study investigated the interaction between flavonoids and beta-lactoglobulin (β-LG) using molecular dynamics simulations (MDS) to analyze structural changes in β-LG in the presence of two flavonoids, luteolin and quercetin. Our aim was to analyze the binding of β-LG with these compounds and the conformational changes in the protein upon their presence.

Methods: This study employed comprehensive MDS to elucidate the binding mechanisms and structural impacts of flavonoids on β-LG. By simulating various flavonoid-β-LG complexes over extended time scales, we assessed binding affinities, conformational changes, and potential functional implications. Our results revealed distinct binding sites on β-LG, with flavonoids inducing specific conformational adjustments that may affect protein stability and functionality. By combining MDS with GROMACS software and molecular docking using AutoDock and Discovery Studio, along with visual analysis in VMD, we established a comprehensive framework for studying the interactions of flavonoids with proteins.

Results: The results indicated that the ligands bound to β-LG significantly enhance the protein's stability, forming a stable complex between them. Simulation parameters showed that both ligands led to decreased compactness and increased radius of gyration (RG). Additionally, RMSD and RMSF analyses revealed that the presence of luteolin and quercetin notably altered the structural stability of β-LG compared to its unbound form. Solvent-accessible surface area (SASA) calculations also demonstrated that ligand binding exposed some hydrophobic regions, which may influence protein interactions.

Conclusion: The findings suggest that luteolin and quercetin can induce significant structural changes in β-LG that may affect its functional properties.

Keywords: beta-lactoglobulin (β-LG), flavonoid, luteolin, quercetin, MD simulation

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Abstract: A-10-2432-1

The Effects of Quercetin on MicroRNAs Expression in the Breast Cancer Cell Lines: A Systematic Review

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Background: Although standard therapeutic modalities have significantly improved the treatment of patients with breast cancer (BC), it is the most common leading cause of cancer mortality worldwide. Evidence indicates quercetin could inhibit signal transduction, inducing cancer cell apoptosis, and suppressing proliferation, invasion, and metastases of tumor cells via regulation of microRNA (miRNA) expression in different cancer types. Hence, this study was conducted to systematically assess the effect of quercetin on miRNA expressions in BC cell lines.
Methods: A comprehensive search of electronic databases including Scopus, Cochrane Library, PubMed, and Web of Science was conducted with keywords (i.e., “MicroRNA”,” Quercetin”, “Normal tissue”, “Breast cancer”, “Cell line”, “Apoptosis”, “Survival”, “Prognosis”, “Up-regulation”, “Down-regulation”, “Proliferation”, “Overexpression”, and “Lower expression”) to identify relative articles published until August 2023. Studies that investigated the effects of quercetin on BC cell lines were included. Data regarding miRNA expression and cell survival were extracted.
Results: Initially, 6753 studies were retrieved, of which 14 studies met inclusion criteria. Accordingly, two studies were included in the final assessments. The findings of two studies about miRNA expression revealed that quercetin through up-regulation of the miR-146a in MCF-7 and MDA-MB-231 cell lines, and down-regulation of miR-21 in MCF-7 cells cloud inhibit the progression of BC cell lines.
Conclusion: Our study showed the inhibition role of quercetin on the BC cell line could provide via miRNA expression.

Keywords: Breast cancer, Quercetin, miR-21, miR-146a, MCF-7 cell line, MDA-MB-231 cell line

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Abstract: A-10-2370-1

Iranian Phytotherapy Against Uterine Adhesion Bands Formation

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Background: Asherman Syndrome, also referred to as intrauterine adhesions (IUA), is a medical condition that impacts women within the reproductive age range. The potency of oral administration of Ziziphus jujube (Z. jujube) was evaluated in reducing the formation of intra- and extra-uterine adhesion bands.
Methods: A total of 72 female rats were allocated into three cohorts (n=6 in each cohort): control, IUA positive control, and Z.jujube-treated (10 days of 400 mg/kg/day). This research comprised three phases subsequent to the induction of the model through mechanical injury to the uterus during the estrous cycle. In phase 1, an analysis of uterine tissues at the molecular and histological levels was conducted to assess inflammatory and fibrotic indicators at both mRNA and protein tiers. Moving on to phase 2, female rats were paired with male rats. Subsequently, on the 15th gestational day, the pregnant rats were euthanized, and factors such as the number, weight, implantation of embryos, and placental weight were juxtaposed among the cohorts. In phase 3, the phenotypic and neonatal consequences of the pregnancy were scrutinized.
Results: Z. jujube significantly decreased uterine adhesion bands resulting from injury, leading to uterine shortening, while simultaneously promoting endometrial regeneration. Furthermore, the anti-inflammatory properties of Z. jujube were validated through the enhancement of antioxidant enzyme activity and reduction in the expression of various inflammatory cytokines. Treatment with Z. jujube resulted in a decrease in fibrosis within uterine tissue, as indicated by histological trichrome staining and reduced expression of profibrotic factors in uterine tissue samples. Moreover, Z. jujube exhibited enhancements in fetal growth and pregnancy outcomes.
Conclusion: The results demonstrate that Z. jujube possesses inherent qualities that are both anti-inflammatory and anti-fibrotic. This fact renders it a crucial candidate for incorporation in clinical trials aimed at mitigating the formation of uterine adhesions in eligible subjects.

Keywords: uterine adhesion, Z. jujube, fibrosis, inflammation, pregnancy

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Abstract: A-10-2339-1

The Prevalence of Cancer in Patients with Multiple Sclerosis (MS) Who Received Rituximab: A Systematic Review and Meta-Analysis

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Background: To estimate the pooled prevalence of cancer in patients with multiple sclerosis (MS) who were under treatment with rituximab.

Methods: We searched PubMed, Scopus, EMBASE, Web of Science, and google scholar along with gray literature up to April 2021. The search strategy included the MeSH and text words as ("CD20 Antibody" AND Rituximab) OR "Rituximab CD20 Antibody" OR Mabthera OR "IDEC-C2B8 Antibody" OR "IDEC C2B8 Antibody" OR IDEC-C2B8 OR "IDEC C2B8" OR GP2013 OR Rituxan OR rituximab) AND ((Sclerosis AND multiple) OR (sclerosis AND disseminated) OR "disseminated sclerosis" OR "multiple sclerosis" OR "acute fulminating"). Two independent researchers screened, Inclusion criteria Included Cross sectional studies, cohort studies, any related articles published in the English language and any associated conference abstracts which was related to the subject. However, exclusion criteria were case-reports, RCT studies. We collected data regarding first author, country of origin, number of enrolled patients, number of possible/confirmed cases, mean age, F/M ratio, mean Expanded Disability Status Scale (EDSS), mean duration of the disease, and number of patients with cancer. We evaluated the risk of potential bias by the NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE (NOS; adapted for cohort studies). The value ≥ 4 was considered acceptable for us. All statistical analyses were performed using STATA V.14 and I2 was calculated to determine heterogeneity. We estimated the prevalence in 100,000 cases.

Results: The literature search revealed 3577 articles, after deleting duplicates 2066 remained. For the meta-analysis, 22 studies were included. Totally, 15599 patients were enrolled while 133 cancers were detected. The pooled prevalence of cancer in MS patients under treatment with rituximab was 1 in 100,000 ($I^2 = 99.9\%$, $p < 0.001$).

Conclusion: The results of this systematic review and meta-analysis show that the pooled prevalence of cancer in MS patients who received rituximab is 1 in 100,000 cases.

Keywords: Multiple sclerosis, Neoplasm, Rituximab, systematic review

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Abstract: A-10-2435-1

Elongation of Very Long Chain Fatty Acids Protein 6 (ELOVL6) Activity in Human Breast Cancer

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Background: The metabolic disorders including lipid metabolism is a hallmark and a common feature of cancer cells metabolism. Changes in the length and degree of desaturation of fatty acid (FA) chains are one of the most important biological changes. Among the rate-limiting enzymes catalyzing long-chain FA elongation [elongation of very long-chain fatty acid proteins (ELOVL1–7)], ELOVL6 converts C16 saturated and monounsaturated FAs to C18 species, the most important step for the de novo synthesis of endogenous long-chain FAs. The objective of this study was to estimate the activity of ELOVL6 enzyme to predict the outcome of breast cancer (BC) tissue.
Methods: Fifty-five pairs of fresh-frozen samples of BC and adjacent normal tissue were used to analyze for FAs composition of tissue using gas chromatography, and stearic acid/palmitic acid concentration ratios were used to estimate ELOVL6 activity.
Results: Our results show that the relative activity of ELOVL6 was significantly higher in BC tissues compared to the adjacent normal tissue, and furthermore, high ELOVL6 activity was positively correlated with tumor size ($P<0.007$).
Conclusion: Overall, these results indicated that ELOVL6 may be considered as an appropriate therapeutic target in BC. However, further studies are needed to confirm the significance of these findings.

Keywords: breast cancer (BC), ELOVL6, metabolic disorders

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Abstract: A-10-2298-1

Colorimetric Detection and Determination of Glutathione in Human Serum Based on Peroxidase-Like Activity of MOF-808-FA Frameworks

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Background: Cancer is one of the most common chronic diseases today. With the development of cancer diagnosis in its early stages, many costs and problems can be prevented. Abnormal expression of GSH is closely related to a variety of diseases such as cancer, liver damage, loss of leukocytes, damage to the immune system, and other diseases. Therefore, the measurement of GSH as a globally recognized biomarker in the diagnosis and monitoring of cancer treatment has a significant impact on timely diagnosis, treatment, and ultimately human health.
Methods: A calorimetric method has been used to measure glutathione. First of all, MOF-808-FA was synthesized by hydrothermal method and characterized by SEM, XRD, and FT-IR. Then peroxidase activity of MOF was evaluated. The measurement performance was done at the optimized conditions of MOF-808FA= 20 mg, pH=7.92, and TMB concentration of 0.77 mM, and time =25 min, 1.18 mM H_2O_2. After drawing the calibration curve and calculating analytical information according to USP, the recoveries were calculated by using real samples of human serum.
Results: The linear range of the method was found to be 0-164.01 µM for the plain line, and the logarithmic linear range was calculated 2.17-164.01 µM, and the limit of detection was 0.23 and 0.716 µM respectively. Results of glutathione determination on real samples of human serum showed recoveries values of 102.54-117.94% and RSD of 0.1-1.11%. Moreover, selectivity analysis illustrated that MOF-808-FA showed selective sensitivity to measure glutathione compared to interfering materials.
Conclusion: In conclusion, MOF-808-FA as a peroxidase-like enzyme showed good peroxidase activity and developed a sensitive and selective colorimetric method to determine glutathione.

Keywords: Glutathione, MOF-808FA, Colorimetric, Cancer, peroxidase. Enzyme mimic

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Abstract: A-10-2443-1

Treatment of Recombinant and Active Caspase 9 Protein Bound to the Cluc Domain of Split Luciferase with Anticancer Drugs

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Background: Monitoring cell apoptosis can provide valuable insights into early diagnosis and treatment efficacy in disease progression. Caspase 9, plays a central role in the intrinsic or mitochondrial apoptosis pathway. It is activated in response to various cellular stress signals, including DNA damage or perturbations in cellular homeostasis. We aimed in this study to construct a mutated form of caspase 9 fused to domain C luciferase (Cluc) establishing a system to evaluate caspase 9 dimerization, activity and treatment with some anticancer drugs.
Methods: The mutant form of caspase 9(D315A-D330A) was sub-cloned from pcDNA plasmid into the pET-28a+ vector containing domain C luciferase (Cluc) as a fusion gene with a (G4S)3 linker in between. The recombinant construct was confirmed using DNA sequencing, and expressed in E. coli BL21(DE3) as a protein expression host. After recombinant protein expression, the protein was purified with affinity chromatography Ni-NTA Sepharose column. After dialysis, activity of caspase 9-(G4S)3-CLuc was assessed using caspase 9 activity assay and protein-protein interaction was assessed by luciferase assay.
Results: The accuracy of caspase 9-(G4S)3-Cluc sequence produced in pET28a+ was confirmed through restriction endonuclease digestion and DNA sequencing. The molecular weight (65 kDa) was confirmed using SDS-PAGE in comparison with caspase 9 wild type. Enzymatic activity of the mutant caspase 9-(Ga4S)3-Cluc was measured using luminometry. The amount of enzyme activity was measured nearly 50000 RLU/Sec in different repeats compared to control (10000 RLU/Sec). Protein-protein interaction was increased after treatment by sulfadimidin and carboplatin.
Conclusion: We constructed a new chimeric protein consisting of mutant caspase 9-(G4S)3-Cluc with an acceptable caspase activity. This construct can be used to explore the impact of different anti-cancer agent on in vitro caspase activity and pave the road to analyze apoptotic effect of different small molecules and anti-cancer drugs.

Keywords: apoptosis, caspase 9, recombinant protein, anticancer drugs

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Abstract: A-10-2193-2

MicroRNAs As Therapeutic Targets in Breast Cancer Metastasis

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Background: Breast cancer is a complex disease with multiple risk factors. Among these factors, microRNAs are considered for playing a fundamental role in the development and progression of malignant tumors. The studies have demonstrated that several microRNAs exhibit increased or decreased expression, acting as indicators of metastatic potential in body fluids and tissue samples. The identification of these microRNA expression patterns could prove instrumental for the development of novel therapeutic molecules that either mimic or inhibit microRNA action. Additionally, an efficient delivery system mediated by viral vectors, nonviral carriers, or scaffold biomaterials is a prerequisite for implementing microRNA-based therapies; therefore, this review attempts to highlight essential microRNA molecules involved in the metastatic process of breast cancer and discuss recent advances in microRNA-based therapeutic approaches with potential future applications to the treatment sequence of breast cancer.
Methods: We searched “MicroRNAs ", “Breast cancer " and " Vector " as primary terms in three popular search engines in medical sciences including PubMed, Science Direct and Google scholar databases.
Results: It is possible to adjust the expression of dysregulation microRNAs using techniques such as microRNA inhibition or microRNA mimic. Such microRNAs can be transmitted to the target tissue using viral and non-viral vectors. But viral vectors have not yet been able to be used safely to treat the disease due to stimulation of the immune system, toxicity, and extra-target effects. Studies show that using nonviral vectors has an advantage over viral vectors because of higher biocompatibility, lower production costs, and lower immunosuppression, but non-viral vectors are less effective.
Conclusion: Therefore, a suitable vector system for microRNAs has not been defined yet, and it is necessary to design optimized models of these vectors or other models to perform a more effective treatment of the disease.

Keywords: Breast cancer, MicroRNA, Vector

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Abstract: A-10-2445-1

Investigation of Reporting the Present or Unknown Nasal Bone in Down Syndrome Prognosis: A Prospective Study in North East of Iran

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Background: There are several tests for screening of trisomy 21 fetuses in first trimester of gestation. At 11–14 weeks of pregnancy, nasal bone is not visible in sonographic examination in about <1% of chromosomally normal fetuses. So, many sonographers report an absent or unknown Nasal Bone (NB) in their reports. Since NB report is used in prenatal prognosis software tools, the failed NB examination could influence congenital anomalies outcomes and lead to false-positive results. Herein, we investigate the effect of presence or unknown NB reports on congenital anomalies outcomes.

Methods: This study was performed on women who underwent contingent prenatal screening in first trimester of gestation. To investigate the reporting of present or unknown NB in Down syndrome prognosis, all women with present NB reports were considered as unknown NB. Conversely, women with unknown NB reports were considered as present NB. Down syndrome prognosis was predicted through Benetech-PRA software. All cases with Down syndrome risk prognosis were followed up to postpartum.

Results: The reported NB significantly affects Benetech-PRA software outcomes in women with reported unknown NB despite in the women with reported present NB. At the end of the follow-up, it was found that only 5% fetuses had Down syndrome. The sonographers reported about 7.3% unknown NB reports which resulted in 16±1% false-positive Down syndrome screening.

Conclusion: Correct NB examination exerts a significant effect on Down syndrome prognosis in fetus with unknown NB reports. The failed NB examination could influence congenital anomalies outcomes and led to false-positive results.

Keywords: Nasal bone, Down syndrome, Contingent prenatal screening test, Trisomy 21

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Abstract: A-10-2376-3

A Quantum Mechanical Investigation on Elafibranor

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Background: In June 2024, the FDA granted accelerated approval for Elafibranor for the treatment of primary biliary cholangitis (PBC), making it a new therapeutic option for patients with intolerance or inadequate response to ursodeoxycholic acid (UDCA). Because of the significant medical importance of the drug mentioned above, we have decided to conduct a thorough examination of its electronic structure using quantum computing technology.
Methods: The study utilized quantum mechanics (QM) calculations conducted through the density functional theory (DFT) method with the GAUSSIAN 09 software. The structure of the Elafibranor drug was first optimized through gradient procedures at both restricted Hartree-Fock (HF) and hybrid density functional B3LYP levels of theory using the 6-311G basis set. Examination of the results revealed that the optimized structure achieved in this research was situated at the minimum point on the potential energy surface, displaying no negative modes.
Results: This study conducted calculations for structural parameters like bond lengths, angles, and dihedrals, as well as thermodynamic parameters at the B3LY/6-311G level of theory and provided the results. The electronic energy of the molecule was determined to be -973754.5 kcal/mole. Additionally, the mulliken atomic charge, spin density, and molecular orbital energies were calculated. The highest occupied molecular orbital (HOMO) was found to be -0.23364 eV and the lowest unoccupied molecular orbital (LUMO) was -0.09182 eV. The dipole moment in Debye was measured as X= 4.2024, Y= 2.9182, Z= 3.7005, with a total of 6.3143.
Conclusion: Optimization of the drug was performed using the B3LYP/6-311G method. The study focused on Elafibranor's electronic characteristics, specifically the energy difference between the HOMO and the LUMO. The HOMO-LUMO gap energy was determined to be 0.14 eV. This provides insights into Elafibranor's electronic behavior, which could have applications in various fields.

Keywords: Elafibranor, DFT, B3LYP/6-311G, HOMO-LUMO gap

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Abstract: A-10-2418-1

A Quantum Mechanics Study on the Perfluorohexyloctane

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Background: Meibomian gland dysfunction (MGD) is a leading cause of evaporative dry eye disease (DED). Perfluorohexyloctane (F6H8), a physically and chemically inert synthetic compound, has recently emerged as a promising candidate for the treatment of DED due to its unique properties. MGD is characterized by a reduction in meibum secretion and/or a change in meibum composition that results in the disruption of the tear film lipid layer and an increase in the tear film evaporation rate. Excessive evaporation causes tear film instability, desiccation, tear hyperosmolarity, inflammation, and apoptosis of ocular surface cells, resulting in a continuous cycle of DED. Perfluorohexyloctane ophthalmic solution stabilizes the lipid layer of the tear film and inhibits tear evaporation by forming a monolayer at the air-liquid interface.

Methods: At first, the molecular structure of Perfluorohexyloctane was designed using GaussView software, followed by quantum mechanical calculations at the B3LYP/6-311+G theoretical level using Gaussian09 software.

Results: Using the GaussView software, the molecular structure of interest was initially designed in this software. Thermodynamic parameters of Perfluorohexyloctane have been calculated at the B3LY/6-311+G level of theory; Total Energies: 213.544 Kcal/Mol, Electronic Energies: -1,156,007.654 Kcal/Mol, zero-point Energies: 195.558 Kcal/Mol, Enthalpy: -1,155,793.517 Kcal/Mol, Gibbs Free Energy: 156.130 Kcal/Mol, Specific Heat Capacity: 102.367 Cal/Mol-K, Entropy: 194.559 Cal/Mol-K, HOMO: -0.32, LUMO: -0.02.

Conclusion: Research shows that Perfluorohexyloctane eye solution effectively stabilizes the lipid layer of the tear film. At first, the modeling of Perfluorohexyloctane's structure used Gaussian and Gauss View software, followed by B3LY/6-311+G method optimization. The HOMO-LUMO gap energy has been presented as -0.3 eV.

Keywords: Perfluorohexyloctane, HOMO and LUMO, Thermodynamic parameters, GaussView

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Acta Biochimica Iranica

Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2553-1

Exploring the Anti-Cancer Effects of ACEIs/ARBs in Colorectal Cancer Treatment

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Background: Colorectal cancer (CRC) is the fourth leading cause of cancer-related morbidity and mortality. Angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB), which are currently used for cardiovascular diseases have a favorable role in the development and progression of CRC.
Methods: This review article was conducted by searching for relevant publications on PubMed, Science Direct, Google Scholar, and Web of Science up to May 2024. The search terms used were Colorectal cancer, Angiotensin-converting enzyme inhibitor, and Angiotensin receptor blocker. A total of 150 articles were initially identified, with 60 articles excluded based on title and abstract review. Ultimately, 90 articles meeting the inclusion criteria were selected, all of which were in English.
Results: In this study, we sought to thoroughly examine the connection between ACE inhibitors and colon cancer. Our results indicate that patients who were randomly assigned to take ACEIs/ARBs had a significantly lower risk of developing new cancer compared to those assigned to the control group (RR 0.962, 95% CI 0.934-0.991, p = 0.010). Patients with CRC that used ACEIs/ARBs had a decreased mortality compared to non-used patients (HR 0.833, 95% CI 0.640-1.085, p = 0.175).
Conclusion: All of these discoveries indicate that ACEIs/ARBs treatment enhanced the survival of colorectal cancer patients and reduced mortality among individuals with CRC.

Keywords: Colorectal cancer, Angiotensin- converting enzyme inhibitor, Angiotensin receptor blocker

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Abstract: A-10-2334-1

Extraction and Purification of Alpha- Amylase Enzyme from Bacillus Isolated from Qasreshirin Hot Spring

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Background: The study aimed to isolate thermophilic bacillus enzyme-amylase species from a hot spring in Kermanshah province and investigate their ability to produce alpha-amylase enzyme.
Methods: The bacteria were isolated and identified through various tests, and the enzyme was purified using ion exchange chromatography. The enzyme's activity was measured using DNS reagent at different pH levels, temperatures, and incubation times. Thin Layer Chromatography showed that the enzyme could hydrolyze starch into maltose and glucose. The PCR product showed 100% similarity with Bacillus Licheniformis BaDB11. The enzyme's molecular weight was estimated to be 30 kDa, and it had optimal activity at 70°C and pH 7. The enzyme was able to produce maltose and glucose from starch within 30 minutes, with maximum production at 18 hours.
Results: The alpha-amylase enzyme purified from Bacillus Licheniformis hot spring Qasrshirin had a total activity of 83 U, specific activity of 41.5 U/mg, and an efficiency of 49%. It showed optimal activity at pH 7 and 70°C, and was able to efficiently produce maltose and glucose from starch. The enzyme's ability to break down starch even in short incubation times and its relative purity make it valuable for industrial biotechnology applications.
Conclusion: The study highlighted the potential of the screened bacteria to produce alpha-amylase with important characteristics such as thermophilicity, high-temperature activity, and efficiency in breaking down starch. These characteristics are valuable for industrial applications in various biotechnological processes.

Keywords: Extraction, alpha-amylase, hot spring, bacillus, purification

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2456-1

Blueberry Anthocyanins Modulate mir-17-3p Expression and Antioxidant Enzyme Levels in Human Cells

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Background: Blueberry anthocyanins are known for their potent antioxidant properties in vivo, partially restoring the expression of antioxidant enzymes disrupted by oxidative stress. MicroRNA miR-17-3p has been implicated in regulating cellular redox status by influencing the transcription of antioxidant enzyme mRNAs. This study investigated the impact of blueberry anthocyanin-rich extract on miR-17-3p expression levels in human cells to further elucidate its mechanism of action.

Methods: Peripheral blood mononuclear cells (PBMCs) and EVC-304 cells were treated with increasing, subtoxic concentrations of blueberry anthocyanin extract. Quantitative real-time PCR analysis determined miR-17-3p levels in both cellular and exosomal fractions.

Results: The results demonstrated that blueberry anthocyanins significantly reduced miR-17-3p levels in both cell types, while concurrently increasing the levels of mRNA transcripts encoding antioxidant enzymes compared to control groups. Interestingly, miR-17-3p expression in exosomes displayed a more complex response, varying depending on the compound concentration and cell type.

Conclusion: These findings suggest a potential mechanism by which blueberry anthocyanins exert their antioxidant effects. By downregulating miR-17-3p and upregulating the expression of antioxidant enzyme mRNAs, blueberry anthocyanins may enhance the capacity of cells to counteract oxidative stress and protect against its damaging consequences. Further research is warranted to fully delineate the intricate interplay between blueberry anthocyanins, miR-17-3p, and antioxidant enzyme expression in different cellular contexts.

Keywords: BlueberryAnthocyanins, miR-17-3p, Antioxidant Enzyme, oxidative stress

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2382-1

Application of Quantum Mechanical Methods for the Evaluation of Granix

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Background: Granix is a recombinant granulocyte colony-stimulating factor that was approved by the FDA in 2012 to reduce the duration of severe neutropenia in patients with non-myeloid malignancies. Neutropenia is a condition characterized by an abnormally low number of neutrophils, which are a type of white blood cell important for fighting bacterial infections.
Methods: The molecular structure of Granix was designed using the GaussView software and then subjected to quantum mechanical calculations at the B3LYP/6-311+G theoretical level using Gaussian09 software.
Results: In this comprehensive study, rigorous calculations were carried out to determine various crucial structural parameters like bond lengths, angles, and dihedrals. Additionally, thermodynamic parameters at the B3LY/6-311+G level of theory. The electronic energy of the molecule was confidently established to be -899.9 kcal/mole. The study meticulously calculated the Mulliken atomic charge, spin density, and molecular orbital energies with precision. The highest occupied molecular orbital (HOMO) was definitively identified as -10.4 eV, and the lowest unoccupied molecular orbital (LUMO) was confidently found to be -0.1 eV. The dipole moment in Debye was measured accurately as X= -6.7986, Y= 0.3000, Z= -0.9864, with a total of 6.8763.
Conclusion: This study validates the favorable impact of Granix in treating neutropenia. The molecule was optimized using DFT methods, and properties such as energy, bond lengths, bond angles, and dihedral angles were determined. Additionally, the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) were examined. At the end, HOMO-LUMO gap energy was determined to be 10.3 eV

Keywords: DFT, Neutropenia, Granix, B3LYP/6-311+G, HOMO, LUMO.

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Abstract: A-10-2382-2

DFT Study on Tovorafenib

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Background: In April 2024, the FDA granted accelerated approval to Tovorafenib (Ojemda) for treating patients 6 months of age and older with relapsed or refractory pediatric low-grade glioma (PLGG) that has a BRAF fusion or rearrangement, or BRAF V600 mutation. Gliomas are a type of brain tumor that starts from the glial cells in the brain or spinal cord. Glial cells are the supportive cells that wrap around and protect the neurons. Gliomas are the most common type of primary brain tumor.
Methods: The molecular structure of Tovorfenib was initially designed using the GaussView software and subsequently subjected to quantum mechanical calculations at the B3LYP/6-311+G theoretical level using Gaussian09 software.
Results: In this comprehensive study, rigorous calculations were carried out to determine various crucial structural parameters like bond lengths, angles, and dihedrals. Additionally, thermodynamic parameters at the B3LY/6-311+G level of theory. The electronic energy of the molecule was confidently established to be -2806.2 kcal/mole. The study meticulously calculated the Mulliken atomic charge, spin density, and molecular orbital energies with precision. The highest occupied molecular orbital (HOMO) was definitively identified as -24.7 eV, and the lowest unoccupied molecular orbital (LUMO) was confidently found to be -0.05 eV. The dipole moment in Debye was measured accurately as X= 5.7642, Y= -3.2113, Z= -2.0527, with a total of 6.9102.
Conclusion: The molecule was optimized using DFT methods and properties such as energy, bond lengths, bond angles, and dihedral angles were determined. Additionally, the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) were examined. At the end, HOMO-LUMO gap energy was determined to be 24.7 eV.

Keywords: Tovorafenib, Cancer, B3LYP/6-311+G, DFT.

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Abstract: A-10-2444-1

A DFT Study on the Bicisate Drug

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Background: The Bicisate, also known as ethyl cysteinate dimer (ECD), is a N, N'-1,2-ethylene-di-yl-bis-L-cysteinate diethyl ester. It is used in conjunction with technetium Tc99m as a tracer to measure cerebral blood flow with single-photon emission computed tomography (SPECT). The complex of Bicisate and technetium Tc99m as a kit was developed by Lantheus Medical and FDA-approved on November 23, 1994.1,2
Methods: At first, the molecular structure of Bicisate was designed using GaussView software, followed by quantum mechanical calculations at the B3LYP/6-311+G theoretical level using Gaussian09 software.
Results: Using the GaussView software, the molecular structure of interest was initially designed in this software. Thermodynamic parameters of Bicisate have been calculated at the B3LY/6-311+G level of theory; Total Energies: 208.493 kcal/Mol, Electronic Energies: -712.1241 kcal/Mol, zero-point Energies: 0.3145 kcal/Mol, Enthalpy: 0.333 kcal/Mol, Gibbs Free Energy: 0.263 kcal/Mol, Molecular mass: 215.152 amu, HOMO: -0.23, LUMO: -0.02. The bond length and bond angle were calculated and their effect on the molecule was investigated. Also, atomic charges, IR spectrum, frequency and intensity, and different energies of the molecule were extracted and analyzed.
Conclusion: Research shows that Bicisate is used to measure cerebral blood flow. At first, the modeling of Bicisate's structure used Gaussian and Gauss View software, followed by B3LY/6-311+G method optimization. The HOMO-LUMO gap energy has been presented as -0.21 eV. IR spectrum, vibrational frequencies, and thermodynamic parameters such as enthalpy, entropy, and electronic and Gibbs energies of the Bicisate molecule have also been obtained and analyzed.

Keywords: Bicisate, HOMO and LUMO, DFT, B3LYP/6-311+G

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2418-2

A Quantum Mechanics Study on the Arformoterol

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Background: Arformoterol is a beta-2 adrenergic agonist and bronchodilator used for patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. findings indicate that arformoterol is an effective option for patients with COPD who could benefit from sustained bronchodilation delivered through nebulization, and can be an alternative for patients who cannot use conventional inhaler devices, including metered-dose inhalers or dry-powder devices.

Methods: At first, the molecular structure of Arformoterol was designed using GaussView software, followed by quantum mechanical calculations at the B3LYP/6-311+G theoretical level using Gaussian09 software.

Results: Using the GaussView software, the molecular structure of interest was initially designed in this software. Thermodynamic parameters of Arformoterol have been calculated at the B3LY/6-311+G level of theory; Total Energies: 271.785 KCal/Mol, Electronic Energies: -720,621.214 kCal/Mol, zero-point Energies: -720051.215 KCal/Mol, Enthalpy: -720,609.138 Kcal/Mol, Gibbs Free Energy: 218.373 KcalMol, Specific Heat Capacity: 93.912 Cal/Mol.K, Entropy: 181.118 Cal/Mol.K, HOMO: -0.21, LUMO: -0.03. The IR spectrum, it is like a fingerprint that is unique to each chemical species. This spectrum known for its heightened sensitivity in discerning molecular chemical and structural traits, finds extensive applications in chemistry, biochemistry and pharmaceuticals. The most prominent peak in this spectrum at 1525.460 signifies oscillations per second, positioned on the left side of the chart. The value 1525.4 on the right denotes the dielectric constant.

Conclusion: Research shows that Arformoterol effectively prevents bronchoconstriction in COPD. At first, the modeling of Arformoterol's structure used Gaussian and Gauss View software, followed by B3LY/6-311+G method optimization. The HOMO-LUMO gap energy has been presented as -0.18 eV. IR spectrum, vibrational frequencies and thermodynamic parameters such as enthalpy, entropy, and electronic and Gibbs energies of the Arformoterol molecule have also been obtained and analyzed.

Keywords: Arformoterol, HOMO and LUMO, Thermodynamic parameters, GaussView

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2520-1

The Role of Circulating Nk Cells and Their Immune Receptors Expression of Cxcr3 and Lfa1 in Colorectal Cancer Patients Outcomes

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Background: Anti-tumor immune cells, including cytotoxic T lymphocytes CTL (TCD8+) and natural killer (NK) cells and corresponding chemokine receptors, may play key roles in colorectal cancer (CRC) immunology and the patients outcome.
Methods: Peripheral blood samples of 30 CRC patients and 30 healthy individuals were subjected to analysis of CXCR3 and LFA1 gene expression and protein levels by q-RT-PCR and Western blotting.
Results: Our results showed that the average number of TCD8+ and NK cells in patients with colorectal cancer is not significantly different from that in healthy controls ($p>0.05$). Further analysis revealed a decreased level of CXCR3 gene and protein expression in circulating TCD8+ cells of colorectal cancer patients.
Conclusion: Our findings demonstrated that the number of anti-cancer immune NK and T cells in the blood of CRC patients did not change significantly. But, chemokine receptor CXCR3 is downregulated on the surface of TCD8+ cells in the peripheral blood of CRC patients. In conclusion, the variations in the expression of circulating chemokine factors, including ligands and receptors may affect immunological disease outcomes in CRC patients.

Keywords: CTL, NK cells, CXCR3, LFA1, Colorectal cancer.

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2522-1

A Quantum Mechanical Investigation on Mekinist

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Background: Mekinist (Trametinib) is a groundbreaking medication approved by the FDA for the treatment of advanced melanoma with BRAF V600E or V600K mutations. The approval of Mekinist represented a significant milestone in cancer treatment, particularly for patients with BRAF-mutant melanoma, providing a targeted therapeutic approach that disrupts oncogenic signaling and improves clinical outcomes. Given its pivotal role in precision medicine, we aimed to explore its electronic structure through advanced quantum computing technologies, aiming to deepen our understanding of its molecular interactions and potential avenues for further therapeutic advancements.

Methods: The study utilized quantum mechanics (QM) calculations conducted through density functional theory (DFT) using the GAUSSIAN 09 software. The structure of Mekinist was optimized employing gradient procedures at the hybrid density functional B3LYP levels of theory, utilizing the 6-31G basis set. The optimization aimed to achieve the minimum potential energy configuration and ensure the absence of negative modes, critical for the accurate depiction of molecular properties and interactions relevant to its therapeutic mechanisms.

Results: This study conducted calculations for structural parameters like bond lengths, angles, and dihedrals, as well as thermodynamic parameters at the B3lyp/6-31G level of theory, and provided the results. The electronic energy of the molecule was determined to be –2667074.4 kcal/mole. Additionally, the Milliken atomic charge, spin density, and molecular orbital energies were calculated. The HOMO was found to be -0.2 eV and the LUMO was -0.1 eV. The dipole moment in Debye was measured as X= -4.4248, Y= 1.7851, Z= 4.6447, with a total of 6.6587.

Conclusion: Optimization of the drug was performed using the B3lyp/6-31G method. The study focused on Mekinist's electronic characteristics. The HOMO-LUMO gap energy was determined to be 0.150 eV. This provides insights into Mekinist's electronic behavior, which could have applications in various fields.

Keywords: Mekinist, DFT, B3lyp/6-31G, HOMO-LUMO Gap

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Abstract: A-10-2524-1

The Diagnostic Role of the Systemic Inflammation Index in Patients with Breast Cancer: A Systematic Review and Meta-Analysis

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Background: Breast cancer is one of the most common forms of cancer among women worldwide, with early detection and appropriate treatment being crucial in improving outcomes and survival rates. The systemic inflammation index (SII) is a relatively new biomarker that incorporates the counts of peripheral blood neutrophils, lymphocytes, and platelets, and has been proposed as a potential indicator of systemic inflammation in cancer patients. This systematic review and meta-analysis aimed to investigate the diagnostic role of SII in patients with breast cancer.

Methods: The study systematically searched PubMed, Medline, Web of Science, Cochrane Library, EMBASE and Google Scholar to find articles on the diagnostic role of the systemic inflammation index in detecting breast cancer. Seven trials with 1,308 participants were included in the meta-analysis, screened by title and abstract, and analyzed using Stata 17.0 and the Quality Assessment of Diagnostic Accuracy Studies-2 tool.

Results: In 7 eligible studies, patients with breast cancer had a significantly higher SII when compared to controls (standard mean difference, SMD = 1.06, 95% CI 0.73 to 1.39, $p < 0.001$; $I^2 = 95.3\%$, $p < 0.001$). The pooled area under the curve (AUC) for diagnostic accuracy was 0.85 (95% CI 0.82–0.88).

Conclusion: Overall, the results of this meta-analysis showed that elevated SII levels were significantly associated with a higher risk of breast cancer. Specifically, patients with high SII levels had a significantly increased risk of advanced tumor stage, lymph node metastasis, and poorer overall survival compared to those with low SII levels. The findings of this study suggest that the systemic inflammation index may serve as a valuable biomarker for the diagnosis and prognosis of patients with breast cancer.

Keywords: Systemic inflammation index, Breast Cancer, Diagnostic biomarker

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Abstract: A-10-2493-1

Uncovering Potential Fak1 Inhibitors for Cancer Metastasis Through QSAR, Pharmacophore Modeling, and Molecular Docking Investigations

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Background: Focal adhesion kinase 1 (FAK1) is a pivotal non-receptor protein-tyrosine kinase crucial in cellular signaling pathways, particularly in regulating cell adhesion and migration by interacting with integrins and transmembrane receptors. Its dysregulation is linked to diseases, notably cancer progression and metastasis. Targeting FAK1 holds potential as a cancer therapy due to its involvement in tumor development. This research aims to identify Fak1 inhibitors using docking techniques.
Methods: The study screened the ZINC15 and PubChem databases for compounds targeting cancer metastasis. Pharmacophore and QSAR modeling were employed to identify FAK1 inhibitors, followed by filtering based on Lipinski's Rule of Five and ADMET properties. The interaction of selected compounds with FAK1 was analyzed using flexible docking technique.
Results: The top three compounds, specifically ZINC00020148995, ZINC000003964325, and ZINC000022448983, were chosen for Molecular Dynamics (MD) research. Additionally, the potential off-target effects of these compounds were explored using Conserved Domains Database search and molecular docking. The results from the MD studies validated the findings from the docking experiments, indicating that all three selected compounds exhibited stable interactions with FAK1 and showed promising inhibitory capabilities against this protein.
Conclusion: These three compounds could be viable options for treating cancer metastasis because of their improved therapeutic attributes and minimized side effects.

Keywords: FAK1, Metastasis, Drug Discovery, QSAR, Molecular Docking

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2444-2

Quantum Mechanics Investigation of the Hexaminolevulinate

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Background: Hexaminolevulinate is a specialized imaging drug used for optical purposes. When in liquid form, it is inserted directly into the bladder for utilization in conjunction with photodynamic blue light cystoscopy along with regular white light cystoscopy. The U.S. Food and Drug Administration (FDA) officially approved Hexaminolevulinate hydrochloride (sold as Cysview for Intravesical Solution by Photocure ASA) on May 28, 2010. This approval allowed the drug to be used as an imaging agent, in partnership with the Karl Storz Photodynamic Diagnostic D-Light C (PDD) System, for identifying non-muscle invasive papillary cancer of the bladder during cystoscopic examinations for patients who are suspected or confirmed to have bladder lesions based on previous cystoscopy results. The manufacturing of Hexaminolevulinate falls under the brand name Cysview® by Photocure ASA. In Europe, the same drug is known as Hexvix®.1

Methods: At first, the molecular structure of Hexaminolevulinate was designed using GaussView software, followed by quantum mechanical calculations at the B3LYP/6-311+G theoretical level using Gaussian09 software.

Results: Computational modelling of the medication Hexaminolevulinate was conducted through the utilization of GaussView software at the B3LYP/6–311+G theoretical method, with the subsequent presentation of structural data. The molecular structure of interest was created in GaussView software to facilitate the analysis.

Conclusion: Atomic charges, IR spectrum, frequency and intensity, and different energies of the molecule were extracted and analyzed. The HOMO-LUMO gap energy has been calculated. The HOMO and LUMO molecular energies are -0.21 eV and = -0.03 eV, respectively. Also, the bond length and bond angle were calculated and their effect on the molecule was investigated. The electronic energy of the molecular structure of the drug studied in this work is calculated at the B3LYP/6–311+G which is 1678.45 kcal/mole.

Keywords: Hexaminolevulinate, DFT, B3LYP/6-311+G, HOMO and LUMO

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2444-3

A Quantum Mechanics Study on the Omaveloxolone

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Background: Omaveloxolone (RTA-408) is a semisynthetic oleanane triterpenoid with antioxidant and anti-inflammatory properties. Omaveloxolone acts as an activator of nuclear factor (erythroid-derived 2) like 2 (Nrf2), a transcription factor that mitigates oxidative stress. In patients with Friedreich's ataxia, a genetic disease involving mitochondrial dysfunction, the Nrf2 pathway is impaired, and Nrf2 activity is lower. Therefore, the use of Nrf2 activators such as Omaveloxolone represents a therapeutic advantage in this group of patients. In February 2023, Omaveloxolone was approved by the FDA for the treatment of Friedreich's ataxia in adults and adolescents aged 16 years and older. The use of Omaveloxolone for the treatment of conditions involving mitochondrial dysfunction and oxidative stress has also been evaluated.
Methods: At first, the molecular structure of Omaveloxolone was designed using GaussView software, followed by quantum mechanical calculations at the B3LYP/6-311+G theoretical level using Gaussi-an09 software.
Results: Using the GaussView software, the molecular structure of interest was initially designed in this software. Thermodynamic parameters of Omaveloxolone have been calculated at the B3LY/6-311+G level of theory.
Conclusion: The bond length and bond angle were calculated and their effect on the molecule was investigated. Also, atomic charges, IR spectrum, frequency and intensity, and different energies of the molecule were extracted and analyzed. The HOMO-LUMO gap energy has been presented as -0.16 eV.

Keywords: Omaveloxolone, HOMO and LUMO, DFT, B3LYP/6-311+G

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Abstract: A-10-2361-2

Investigating the Effect of Probiotics on Oxidative Stress Biomarkers in Rat Stroke Model

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Background: Stroke is the second leading cause of death worldwide, mainly caused by thrombosis in a part of the brain. After a stroke, inflammatory phenomena and oxidative stress increase, which causes secondary damage in the peripheral part of the ischemic region known as penumbra. Recent research shows that regulating the gut microbiome reduces the negative effects of stroke in its chronic phase. Considering the important role of oxidative stress on nerve cells, in this study, the effect of probiotics on oxidative stress markers in the chronic phase of stroke is investigated

Methods: Three groups of 5 laboratory rats weighing 240-270 grams were selected, two of them were induced with middle cerebral artery occlusion (MCAO) stroke model and the third group was assigned to the sham group. One of the stroke groups was gavage with 10 9CFU / mL of probiotics for 14 days after creating the model. After 14 days, the rats of each group were subjected to a behavioral test and infarct volume measurement, and a part of their brain was removed to examine the biomarkers of MDA, NO and TAC. After lysing the tissues and combining with the reagents of each test, their OD was determined with a spectrophotometer

Results: The observed results indicated the improvement of behavioral functions and the reduction of infarct volume in the drug group compared to the control group. Also, the MDA biomarker decreased and the NO and TAC biomarkers increased, which indicates a reduction in the effects of the oxidative stress of stroke in the chronic phase

Conclusion: Through their metabolites, by regulating NO, probiotics cause repair and angiogenesis of the damaged part in the chronic phase, protect the brain against free radicals with their antioxidant effects, and prevent secondary damage of peripheral cells by reducing the MDA biomarker.

Keywords: stroke, probiotics, oxidative stress, inflammation

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Abstract: A-10-2575-1

Electronic Properties of Filsuvez; A Quantum Mechanics Investigation

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Background: Filsuvez is a prescription medicine used on the skin to treat wounds that may happen with dystrophic and junctional epidermolysis bullosa (EB) in adults and children 6 months of age and older. It is not known if Filsuvez is safe and effective in children younger than 6 months of age. Allergic reactions and skin reactions to Filsuvez may include the following symptoms: red itchy bumps (hives), skin rash, redness, or itching. If you get any of these symptoms, stop using Filsuvez right away and call your healthcare provider. Birch triterpenes, sold under the brand name Filsuvez, is an extract of birch bark used as a topical medication for the treatment of epidermolysis bullosa. In this work, we focus on the Filsuvez drug using DFT.
Methods: At first, the molecular structure of Filsuvez was designed using GaussView software, followed by quantum mechanical calculations at the B3LYP/6-311+G theoretical level using Gaussian09 software.
Results: The research conducted detailed calculations on structural characteristics such as bond lengths, angles, and dihedrals, along with thermodynamic parameters at the B3LY/6-311G level of theory, and presented the findings. The electronic energy of the compound was identified as -1323.35105 kcal/mol. Furthermore, the Mulliken atomic charge, spin density, and molecular orbital energies were determined. The highest occupied molecular orbital (HOMO) was measured at -277.44 eV, while the lowest unoccupied molecular orbital (LUMO) was found to be -0.6625 eV.
Conclusion: The drug was optimized using the B3LYP/6-311+G method in this research. The main emphasis was on investigating the electronic properties of Filsuvez, particularly the disparity in energy levels between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). The calculated HOMO-LUMO gap energy was found to be 16.636eV. This analysis sheds light on the electronic behavior of Filsuvez, indicating potential implications across a range of industries.

Keywords: Keywords: Filsuvez ،DFT ،B3LYP/6-311+G ،HOMO-LUMO gap

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Abstract: A-10-2399-1

TRIM3 and TRIM16 As Potential Tumor Suppressors in Breast Cancer Patients

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Background: Breast cancer is the leading cause of death among women worldwide. Numerous molecules serve as oncogenes or tumor suppressors in breast cancer. The large family of Tripartite-motif (TRIM) proteins with ~ 80 members have drawn attention for their contributions in cancer. Previous works have reported tumor suppressor activity for TRIM3 and TRIM16 in different cancers. This study aimed to evaluate the expression of TRIM3 and TRIM16 in cancerous and normal breast samples and to investigate their association with different clinical and pathological parameters.

Methods: Forty cancerous breast tissue samples along with the same number of normal adjacent tissue samples were obtained from the Cancer Institute of Imam Khomeini hospital (Tehran, Iran). qRT-PCR was utilized to determine the gene expression of TRIM3 and TRIM16. The normality of the collected data was assessed through Kolmogorov–Smirnov and Shapiro–Wilk tests. The results of the experimental groups were compared using the Kruskal–Wallis and Mann–Whitney U tests. The p-values less than 0.05 were considered significant.

Results: The expression of TRIM3 and TRIM16 genes in tumor samples were significantly reduced to 0.45 and 0.29-fold, respectively. TRIM3 and TRIM16 gene expression were both negatively related to breast cancer invasion, as the gene expression of both TRIM3 and TRIM16 underwent a significant reduction in lymphatic/vascular and perineural invasive samples. TRIM3 gene expression was associated with tumor histological grade, showing a significant reduction in stage II compared to Stage I, which could be associated with the progression of cancer cells.

Conclusion: Based on the aforementioned results, we propose TRIM3 and TRIM16 as potential tumor suppressors of breast cancer for further investigations.

Keywords: TRIM3, TRIM16, Breast cancer, Tumor suppressor, Invasion

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Abstract: A-10-2399-2

TRIM14 and TRIM29 a s Potential Tumor Markers for Breast Cancer Diagnosis

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Background: Various members of the Tripartite-motif protein family contribute to different types of cancer, although the role of these factors in breast cancer is unclear. TRIM14 and TRIM29 have been reported to be overexpressed and play oncogenic roles in specific cancers.
Methods: A total of 40 pairs of tumor tissues and adjacent normal tissues of breast cancer patients were obtained. Relative gene expression of TRIM14 and TRIM29 were determined through quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) using specific primers.
Results: TRIM14 and TRIM29 were both overexpressed in breast tumor samples. The expression of TRIM14 was associated with tumor size, stage, and invasiveness. Nonetheless, no association was found between TRIM14 and the grade of the tumor. Also, TRIM29 gene expression was positively correlated with tumor size, stage, grade, and invasiveness. No correlation was found between the expression of TRIM14 and TRIM29.
Conclusion: Based on our results, we propose TRIM14 and TRIM29 as potential tumor markers in breast cancer.

Keywords: Breast cancer, Tripartite-motif protein, Staging, Tripartite-motif Protein, Tumor grade

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Abstract: A-10-2411-1

Microalbuminuria and Diabetes

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Background: Diabetes is a chronic condition affecting sugar processing. 537 million diabetic people were living in 2021. Diabetic nephropathy (DN) is a common complication of diabetes. Microalbuminuria (MA) is defined as the persistent elevation of albumin excretion (30–300 mg/day) in urine. This range is higher than that of normoalbuminuria (<30 mg/day) but lower than that of albuminuria (<300 mg/day) and is considered the earliest sign of diabetic DN.
Methods: Keywords “Microalbuminuria” and “Diabetes” were searched in the Pubmed database. As a result, 777 articles from the past 5 years were found, with 18 most relevant ones, ultimately 8 articles were selected as primary sources.
Results: According to evidence, the prevalence of MA among T2DM (type 2 diabetes mellitus) is significantly high (39.1%) and is positively correlated with various factors such as high HbA1c levels, dyslipidemia with high triglycerides and lower HDL, and other complications like neuropathy and retinopathy. The association between MA and age (p = 0.002), gender (p = 0.003), duration of diabetes (p = 0.001), therapy type (p = 0.03), control of diabetes, (p = 0.001), and hypertension (p = 0.002), nutritional status (p = 0.05) was Significant. Oral hypoglycemic agents, regimen, and being overweight raise the incidence of MA. Low hemoglobin level in anemia is a risk factor of MA.
Conclusion: Considering all interventions, the association detected between mentioned factors and MA in this setting reaffirm the importance of early detection, excellent glycemic, and regular screening in the prevention of diabetic nephropathy and after that, End-stage renal disease.

Keywords: Diabetes, microalbuminuria, interference

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Abstract: A-10-2399-3

Evaluation of Beclin1 and mTOR Genes and P62 Protein Expression in Breast Tumor Tissues of Iranian Patients

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Background: Autophagy is a cellular process that plays a major role in the fate of tumor cells. Understanding the role of autophagy in cancer therapy is a major challenge, particularly for breast cancer as the sole top cause of mortality among women. In this study, we evaluated the gene expression of mTOR and Beclin1 and the levels of p62 protein, in breast tumors and compared them to a control condition.

Methods: To explore the role of autophagy in breast cancer, we acquired tumor biopsies from 41 new cases of breast cancer patients. We extracted total RNA from each biopsy and used real-time PCR to quantify Beclin1 and mTOR-specific RNA expression. In addition, we evaluated the expression of the p62 protein in paraffin-embedded tumor tissue using the immunohistochemistry technique.

Results: The data revealed an upregulation of Beclin1 and a downregulation of mTOR in tumor tissues compared to the control condition. The correlation between p62 expression and Beclin1/mTOR showed a negative and positive correlation, respectively, confirming autophagy activation in the tumor tissues. However, there was no correlation between autophagy markers and tumor size, grade and stage.

Conclusion: The findings revealed that autophagy activation was found in breast tumor tissues, suggesting that autophagy can be a target for breast cancer therapy.

Keywords: Autophagy, Beclin-1, Breast cancer, mTOR, Tumor grade

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Abstract: A-10-2465-1

Investigating the Expression of Phosphoglycerate Mutase in Hospitalized Patients with Covid-19 Treated with Remdesivir

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Background: SARS-COVID-19, by its effect on the respiratory system along with hypoxia, can cause death. The body resists it in different ways, one way is the production of 2,3BPG by the enzymes of the Rappaport shunt in the glycolysis pathway which plays an important role by increasing oxygen supply to tissues, although the level of gene expression of this pathway is different in individuals with corona compared to healthy people.
Method: In this study, all studied target people were divided into three groups: healthy individuals as negative control group, outpatient (mild) and hospitalized (severe) patients. Also, the severe patients' group was divided into two subgroups: severe patients with Remdesivir (REM) injection, and severe patients without REM injection. After extracting mRNA and then cDNA by using real-time PCR, the expression levels of Phosphoglycerate Mutase (PGM) were measured.
Results: Results of the study showed that gene expression for PGM in individuals with corona was high, also there were significant differences between most of the studied groups.
Conclusion: In people with SARS-COVID, 2, 3 BPG was increased due to the high level of PGM and which counteracts the hypoxia of coronavirus. It is expected that examining the expression of these genes and finding drugs in increase the expression of PGM which led to high production of 2,3BPG in hypoxia in corona disease, can reduce the mortality caused by hypoxia in hospitalized patients due to corona.

Keywords: Phosphoglycerate mutase, 2,3 bis-phosphoglycerate، Remdesivir

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Abstract: A-10-2422-1

Construction of a Eukaryotic Expression Vector Carrying the Mouse Interleukin-21 Gene

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Background: Interleukin-21 (IL-21) is an essential cytokine derived from activated CD4+ T cells and NKT cells, pivotal in modulating immune responses. IL-21 affects numerous immune cells, including aiding the differentiation of Th17 and Tfh cells, crucial for germinal center formation and antibody production. Furthermore, IL-21 activates memory CD8+ T cells, contributing to the immune defense against chronic viral infections and cancers. Regarding the therapeutic potential of IL-21 and its role as a adjuvant in vaccine design, the goal of this study was to construct a eukaryotic expression vector carrying the mouse IL-21 gene for development of a DNA-based vaccine candidate.
Methods: The mouse IL-21 gene sequence was obtained from the National Center for Biotechnology Information (NCBI) database. The SnapGene software was used to design the construct harboring the IL-21 gene. Then, the IL-21 gene was synthesized in a pUC57 cloning vector. For construction of pVAX-1-IL21, the IL-21 gene fragment and the pVAX-1 vector were digested with NheI and XhoI restriction enzymes. The digested IL-21 gene fragment was then ligated into the linearized pVAX-1 vector using T4 DNA ligase. This recombinant vector was transformed into Escherichia coli using heat shock. Next, the PCR and restriction enzyme digestion confirmed the presence and correct insertion of the IL-21 gene in the pVAX-1 vector. Finally, the recombinant pVAX-1-IL-21 vector was purified using a plasmid purification kit, and its concentration were assessed using NanoDrop spectrophotometry.
Results: The recombinant pVAX-1-IL-21 vector was confirmed by PCR and digestion with NheI and XhoI enzymes. Indeed, a clear band of ~ 482 bp related to IL-21 gene was detected by electrophoresis on agarose gel. The concentration of the purified recombinant DNA vector was determined to be ~280 ng/µL.
Conclusion: The recombinant pVAX-1-IL-21 construct was prepared with high purity for development of a DNA vaccine in our future studies.

Keywords: IL-21, Eukaryotic expression vector, Cloning

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Abstract: A-10-2472-1

In Silico Investigation of Hydroxychloroquine Binding Pattern with Angiotensin-Converting Enzyme 2

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Background: Hydroxychloroquine, an antimalarial drug, is often recommended for the treatment of systemic lupus erythematosus and rheumatoid arthritis. It has also been proposed in the treatment of the coronavirus disease 2019 (COVID-19). Different mechanisms explain how this small molecule affects COVID-19 treatment. One mechanism describes how Hydroxychloroquine interacts with Angiotensin-converting enzyme 2 (ACE2). ACE2 is a membrane protein on the cell's surface that allows SARS-CoV-2 entry into targeted cells. Therefore, in this study, we focus on the mechanism of Hydroxychloroquine in controlling COVID-19.

Methods: Several computational techniques, such as molecular dynamics (MD) simulation and MM-PBSA calculation, have been employed to investigate Hydroxychloroquine's binding pattern with Angiotensin-converting enzyme 2.

Results: Based on our results, the ACE2-Spike-Hydroxychloroquine complex had the highest binding energy at -25.5233±0.2735 kcal.mol−1. The binding free energy for the ACE2-Spike complex was -69.2554±0.6696 kcal.mol^{-1}, which was lower compared to ACE2-Spike-Hydroxychloroquine (about 2.7-fold). It has been shown that Hydroxychloroquine might have an effect on the interaction between ACE2 and Spike, leading to a decrease in the affinity of the ACE2 receptor for Spike. Other MD analyses have also confirmed that Hydroxychloroquine leads to a decrease in affinity between the ACE2-Spike complex.

Conclusion: Based on these findings, we anticipate that Hydroxychloroquine could potentially disturb the three-dimensional structure of the ACE2 receptor. Altering the protein's three-dimensional structure can impact the interaction between ACE2 and the spike glycoprotein.

Keywords: Hydroxychloroquine, COVID-19, Angiotensin-converting enzyme 2

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Abstract: A-10-2476-1

Designing gRNAs Sequences for Crispr Gene Editing in HPV-Related Tumors

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Background: CRISPR/Cas9-mediated gene editing has emerged as a promising therapeutic approach for various genetic disorders including HPV-related cervical cancer. Cas9, a widely used type of Cas protein, offers high efficiency in genome editing but poses the risk of unintended mutations at off-target sites. These off-target effects raise concerns about the specificity and safety of CRISPR-based therapies, necessitating precise targeting methods. This study aims to design and validate gRNAs targeting the E5, E6, and E7 oncogenes of HPV16 to enhance the specificity and efficiency of CRISPR/Cas9-mediated gene editing.
Methods: At first, E5, E6, E7, and p97 promoter sequences were extracted from the NCBI database. Then, CHOPCHOP tool was used to design ~20 nucleotide gRNA sequences complementary to the target genes, considering factors like GC content, genome position, and potential off-target sites. Next, CRISPOR tool was used to validate and cross-reference gRNA candidates from CHOPCHOP, providing specificity scores and off-target site locations. Finally, Cas-OFFinder Tool was employed to identify potential off-target sites using a novel search algorithm.
Results: The top gRNA candidates for each oncogene (E5, E6 and E7) were selected based on efficiency, specificity, and off-target analysis using CHOPCHOP, CRISPOR and OFFinder tools.
Conclusion: This study successfully designed specific and efficient gRNAs targeting HPV16 E5, E6, and E7 oncogenes, validated through multiple in silico tools.

Keywords: Keywords: CRISPR/Cas9, gRNA, HPV16, E5, E6, E7

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Abstract: A-10-2446-1

Molecular Docking of Cannabinoids with Type-A γ-aminobutyric ($GABA_A$) receptors Subunit Alpha

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Background: GABA type A receptors are members of the large pentameric ligand gated ion channel. There are numerous subunit isoforms for the GABAA receptors, which determine the receptors agonist affinity, chance of opening and other features. However, the majority of GABAA receptors are composed of two α subunits, two β subunits, and one γ subunit. Cannabinol (CBN) and cannabidiol (CBD) are well known components in the cannabis plant. The primary emphasis of our research was to elucidate the interactions and effects associated with GABAA receptor subunit α and cannabinoids ligands, which encompass a wide range of interactions and have significant implications for drug design.

Methods: Molecular docking was performed using AutoDock 4.2 tool to assess the binding affinity of the ligand CBD and CBN with the GABAA receptor subunit α.

Results: The research compared CBD and CBN in their binding affinity. It indicated that both CBD and CBN have the potential to form complexes with the GABAA receptor subunit α. The binding free energy for CBN was -4.87 kcal/mol, which was more negative than that for CBD (-4.27 kcal/mol), suggesting stronger binding for CBN. Additionally, the inhibitory constant (Ki) for CBN was smaller than that for CBD, indicating that CBN possesses greater inhibitory potential. Consequently, CBN, with its more negative binding free energy and smaller Ki, is deemed a more suitable ligand for the GABAA receptor subunit α.

Conclusion: Study of noncovalent interactions between macromolecules, particularly the interaction between ligands and receptors, plays an important role in understanding biological processes. This study determined the significance of GABAA receptors modulation by cannabinoids compounds. Finding the different affinity between cannabinoids through molecular docking, advances our knowledge of these interactions and future investigations into the therapeutic potential of cannabinoids targeting the GABAA receptors.

Keywords: GABA, Molecular Docking, Cannabinoids, CBN

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Abstract: A-10-2452-1

Comprehensive Meta-Analysis of Key Genes and Pathways in Breast Cancer Metastasis to Brain and Lung

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Background: Breast cancer metastasis to the brain and lungs significantly worsens patient outcomes. Understanding the genetic and molecular mechanisms behind this process is essential for creating targeted treatments. This study conducts a meta-analysis to identify critical genes and pathways involved in breast cancer metastasis.
Methods: Gene expression datasets GSE83132, GSE66495, and GSE12237 were obtained from the Gene Expression Omnibus (GEO). Data preprocessing included normalization with the Robust Multi-array Average (RMA) method and excluding low-expression genes. Differential expression analysis was done using the limma package, with adjusted p-values (FDR < 0.05) and a fold change threshold of |log2(fold change)| > 1. Gene Ontology (GO) term enrichment and pathway analysis were performed using DAVID, KEGG, and Reactome databases. Protein-protein interaction (PPI) networks were built using STRING and visualized in Cytoscape. Fisher's method was used to combine p-values from multiple datasets.
Results: The meta-analysis revealed many differentially expressed genes (DEGs) related to breast cancer metastasis. Significant upregulated genes included CXCL8, CCL20, and GPSM3, while downregulated genes included ADCY9 and GAL. GO enrichment analysis identified vital biological processes such as cell adhesion (p=8.64E-05), nucleosome assembly (p=1.43E-04), and immune response. Pathway analysis emphasized crucial pathways like extracellular matrix (ECM) organization and signal transduction. Network analysis highlighted key regulatory modules with genes like KDM6A, PBX1, LEF1, and ETV1, suggesting their roles in transcriptional regulation and epithelial-mesenchymal transition (EMT). Regulatory nodes like LEF1, KLF9, and NCOR2 showed high interaction degrees, highlighting their central roles in metastasis.
Conclusion: This meta-analysis outlines the genetic landscape of breast cancer metastasis to the brain and lungs, identifying critical DEGs and enriched pathways. The findings stress the importance of cell adhesion, ECM organization, and immune response in metastasis. These insights could help develop targeted therapies to prevent metastatic progression. Further validation in clinical samples is needed to confirm these targets' therapeutic potential.

Keywords: Meta-Analysis, Breast Cancer, Key Genes, Metastasis

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Abstract: A-10-2484-1

Analysis of Overexpressed Genes in Stromal Fibroblasts from Breast Cancer Patients Using in Silico Methods

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Background: Among cancer-related diseases in women worldwide, breast cancer is the second leading cause of death. Defective gene function in various tumors due to genetic and epigenetic changes has been demonstrated in different cell types. Fibroblast cells play multifunctional roles in initiating and promoting breast cancer. Considering the importance of identifying gene expression changes for therapeutic purposes and biomarkers, this study analyzes overexpressed genes in stromal fibroblasts from breast cancer patients.
Methods: This study was done via an in silico approach. The Gene Expression Omnibus (GEO) database was utilized to extract the suitable microarray profile of breast carcinomas in stromal fibroblasts. The differentially expressed genes (DEGs) were analyzed with GEO2R based on p-value < 0.05 and log2 (FC) value > 1, between the normal stromal fibroblasts and carcinoma-associated stromal fibroblasts. Protein-protein interactions (PPIs) were constructed via STRING online tool and Cytoscape software. Finally, after further analysis based on node score of PPIs, 10 key genes were identified.
Results: The microarray dataset of GSE20086 (platform: GPL570, samples: 12 stromal fibroblasts from breast cancer patients) was selected. With GEO2R analysis, 163 overexpressed genes were detected. After deleting the disconnected nods by Cytoscape software, 53 nods, and 86 edges remained in the protein-protein interaction network. The, 10 key genes based on the score respectively include: C3, SERPING1, CLU, C1R, CFB, MASP1, THBD, IGF1, CFD, and PSG3.
Conclusion: Using an in silico approach, we identified ten hub genes that may serve as potential biomarkers for breast cancer in stromal fibroblasts. Nonetheless, additional research that confirms findings based on in vitro and in vivo models can enhance this study.

Keywords: Biomarker, In silico, Overexpressed genes, Breast cancer, Stromal fibroblasts

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Abstract: A-10-2470-1

S100a12/tlr4 Is Essential for the Inflammatory Response in Peripheral Blood Mononuclear Cells of Patients with Severe Coronary Artery Stenosis, Suggesting Its Use as a Potential Diagnostic Marker

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Background: Coronary artery disease (CAD) is a leading cardiovascular condition worldwide, causing significant mortality in both developed and developing countries. The disease may result from disruptions in cellular and molecular processes in peripheral blood mononuclear cells (PBMCs). This study aimed to examine changes in the expression of S100A12 and TLR-4 in PBMCs of individuals with significant coronary stenosis, as well as serum levels of S100A12, IL-6, and hs-CRP.
Methods: After comprehensive clinical and anthropometric evaluations, 120 individuals were categorized into two groups: 70 CAD patients (with ≥50% coronary artery stenosis) and 50 control subjects (with ≤30% coronary artery stenosis). Fasting serum glucose (FSG), lipid profile, and calcium levels were measured. Real-time PCR was used to analyze the gene expression of S100A12, TLR-4, and AGER, while serum levels of S100A12, IL-6, and hs-CRP were quantified using ELISA.
Results: The CAD group showed increased gene expression of TLR4, S100A12, and AGER in PBMCs compared to the control group ($p<0.05$). Furthermore, serum levels of S100A12, hs-CRP, and IL-6 were elevated in the CAD group relative to the controls ($p<0.05$).
Conclusion: The findings support that the gene expression of TLR-4, S100A12, and AGER is elevated in PBMCs of CAD patients, alongside increased serum levels of S100A12, hs-CRP, and IL-6. These markers may serve as potential diagnostic indicators for CAD, either complementing or replacing current markers.

Keywords: Coronary Artery Stenosis, Peripheral Blood Mononuclear Cell, S100A12 Protein, Toll-Like Receptor 4

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Abstract: A-10-2485-1

The Emerging Role of Heat Shock Proteins as Biomarkers for Gastrointestinal. A Review

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Background: Heat shock proteins HSPs are involved in processes, such as protein folding, the passage of peptides, and antigen processing under physiological and stress conditions and they are overexpressed in many malignancies and are considered biomarkers and therapeutic targets for gastrointestinal cancers. Gastrointestinal cancers are the most commonly diagnosed cancers and are the leading cause of cancer-related deaths in men and women worldwide. Pancreatic cancer, hepatocellular carcinoma, and gallbladder carcinoma are the main malignancies of GICs. Prognostic and predictive factors that guide clinical decision-making are essential for cancer patients.
Methods: The research used the keywords immunotherapy, Gastrointestinal cancer, HSP, and cancer prognosis in databases including Google Scholar, PubMed, and Science Direct. According to the articles' period and English language, the articles were selected and the information from at least 10 articles was extracted.
Results: HSP expression significantly increases in tumoral sections compared to non-tumoral sections. HSPs are involved in tumor cell proliferation, invasion, and metastasis. HSP27, involved in the prognosis of osteosarcoma and gastric carcinoma. HSPs prevent acinar cell damage in pancreatitis. Inhibition of HSPs causes apoptotic cell death in cancer cells. HSP27 is associated with tumors in the stomach. High expression levels of HSP90 have been observed in intestinal tumors, and the overexpression level of HSP27 and 90HSP was associated with a decreased survival rate in patients with gastrointestinal cancers. The HSP90 inhibitor NVP-AUY922 may improve the outcome of colorectal cancer.
Conclusion: Our Studies shown that HSP levels are increased in many gastrointestinal cancers, therefore, patients may benefit from their inhibition. These results show an urgent need for more studies in the field of the precise role and importance of HSPs in Gastrointestinal cancers for use as effective targets for new therapeutic strategies.

Keywords: Gastrointestinal cancer, HSP, Immunotherapy, cancer prognosis

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Abstract: A-10-2361-1

Investigating the Effect of Probiotics on Metalloproteinase 9 Enzyme in the Chronic Phase of Stroke in Rats

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Background: Stroke is an important cause of death worldwide. After stroke, inflammatory factors such as metalloproteinase 9 (MMP9) are secreted from immune cells. MMP9 is an enzyme that is important in the recovery of damaged tissue in the chronic phase of stroke. Probiotics are microorganisms that can be effective in the recovery of symptoms after a stroke by reducing inflammation. In this study, the effect of probiotics on MMP9 in the chronic phase of stroke is investigated.
Methods: In this research, 3 groups of 5 Wistar rats were selected. Stroke was induced in two groups by middle cerebral artery occlusion (MCAO) and the other group was considered as sham group. One of the ischemic groups was gavage with daily probiotic supplement of 10 9 CFU / mL for 14 days after stroke induction. After the behavioral test and measurement of the infarct volume, the activity of MMP9 enzyme in blood serum was checked by zymography technique. Zymography is a technique based on SDS PAGE that examines the activity of specific enzymes
Results: The behavioral performance of the animals and the brain infarct size in the drug group were better and more suitable than the drug-free group. In the zymography gel, the bands related to each group were analyzed by image J software. The results showed that probiotics increased MMP9 activity in the chronic phase of stroke during 14 days. The drug group had a thicker MMP9 band than the other groups, which indicates more activity of the enzyme in this group.
Conclusion: Probiotics reduce peripheral inflammation in stroke by inhibiting inflammatory cytokines. Also, by regulating the activity of MMP9 and other restorative factors in the chronic phase of stroke, they cause angiogenesis, repair of damaged tissue, and migration of nerve progenitor cells in this area.

Keywords: Stroke, Probiotic, Inflammation, Metalloproteinase 9

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Abstract: A-10-2487-1

In Silico Approach for Evaluating Potential Effectiveness and Mechanism of Action of Plant Extracts

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Background: Since ancient times, plants have been used for medicine, and several commercially important drugs come from plants. The traditional approach towards discovery of plant-based drugs involves significant amount of time and expenditure. These labor-intensive approaches have struggled to keep pace with the rapid development of high-throughput technologies. In silico methodologies may provide quicker and potentially more cost-effective leads for finding plant-based medicines.

Methods: There are different approaches to identify the role and mechanism of plant extract compounds. In this case crystal structure of target protein should be downloaded from Protein Data Bank and then it should be prepared using YASARA software. The structure of chemical compounds of extract should be retrieved from the PubChem database. To investigate the interactions between target protein and phytochemicals, a molecular docking study should be performed using the different software such as PyRx, AutoDock4, AutoDock Vina and etc. The binding interactions could be analyzed using Discovery Studio, ChimeraX, Molegro or Pymol software. Last, Molecular dynamics simulations can be carried out using Gromacs software and the AMBER force field.

Results: Molecular docking is used to explore the binding interaction and find lead compounds with a greater affinity for protein. It can be visualized using Discovery Studio and other graphical software and show interactions between ligands and protein. The best scored compounds then should be selected for molecular dynamics to analyze their stability and identify potential inhibitors in a time-dependent manner for Five parameters, including the root mean square deviation (RMSD), radius of gyration (Rg), solvent-accessible surface area (SASA), hydrogen bonds and MMPBSA binding free energy.

Conclusion: Using an in-silico approach, we can gain lots of molecular information about the cellular mechanism of action of chemical compounds. This can significantly lead to a cost effective, quick and reliable approach to find and design plant-based remedies.

Keywords: plant extract, bioinformatics, molecular docking, molecular dynamics, in silico study

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Abstract: A-10-2149-1

Beyond Temozolomide: Targeting Autophagy for Glioblastoma Treatment

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Background: To investigate the effectiveness of combining Temozolomide (TMZ) and CPUK02 in overcoming TMZ resistance in Glioblastoma (GBM) using U87 cells as a model.
Methods: U87 cells were exposed to varying concentrations of TMZ and CPUK02. Cell viability was assessed via MTT assay. Quantitative real-time PCR was used to analyze gene expression of Beclin-1, P62, LC3, and XBP-1s.
Results: TMZ and CPUK02 treatments were found to kill cancer cells and activate cellular processes involved in recycling damaged cellular material. This suggests that the combination therapy may be effective in eliminating cancer cells.
Conclusion: TMZ and CPUK02 treatment appears to inhibit autophagic flux (indicated by p62 and LC3IIβ levels). The observed increase in XBP-1s expression might contribute to TMZ sensitization. This combination therapy holds promise for TMZ-resistant cancers, but further research is warranted.

Keywords: CPUK02, TMZ, Autophagy, Glioblastoma, UPR

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2410-1

The Role of Immunomodulatory Metabolite Itaconate on Glial Cell Line-Derived Neurotrophic Factor (gdnf) Levels in Neuroinflammatory Disorders

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Background: Neurodegenerative diseases triggered by acute or chronic inflammation. Neuroinflammation is recognized as an innate immune response, in which the astrocyte/glial cells and inflammatory mediators are activated. It is a key process that helps protect the brain from pathogens and inflammation yields pathological states. Neurotrophic factors (NTFs) are a family of proteins that expressed and modulated during inflammation, in presence of bacterial LPS, and inflammatory cytokines. Present study focused on produced Glial cell-line derived neurotrophic factor (GDNF), one of the NTFs from activated microglia/astrocyte cells. Its neurotrophic effects against the neuronal atrophy against the neuronal atrophy was assayed that can lead to a repair of CNS injuries.
Itaconate, as an immunomodulatory and anti-inflammatory metabolite through tricarboxylic acid cycle by IRG1/CAD has recently been found to have anti-inflammatory property in activated astrocytes could suppresses neuroinflammation and modulates the CNS immune response, however its precise mechanism of action remains poorly understood.
Methods: Primary astrocyte cells exposed to LPS to stimulate the inflammation. The effect of itaconate (75, 150 and 300 µM for 24 h) on the viability of LPS exposed astrocyte cells were evaluated by sulphorhodamine B assay. Different concentrations of itaconate effect on the expression levels of GDNF were evaluated using ELISA and real-time PCR methods.
Results: The obtained results showed that itaconate restored the reduced mRNA and protein levels of GDNF in LPS-treated astrocyte cells dose-dependently and suppressed the LPS- induced astrocytes cell death.
Conclusion: Collectively, these results indicate the neuroprotective role of itaconate by regulation of GDNF expression. The understanding of the properties of itaconate, GDNF and other trophic factors states could provide opportunities to investigate their functions and improve the strategy of treatment models.

Keywords: Neurodegenerative diseases, Neuroinflammation, Itaconate, Neurotrophic factors, Glial cell-line derived neurotrophic factor (GDNF)

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Abstract: A-10-2193-3

Performance of Capecitabine in Novel Combination Therapies in Colorectal Cancer

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Background: Colorectal cancer is one of the most common cancers, and no definitive cure has ever been found. In term of immunotherapy and combination therapies, Capecitabine as a standard chemotherapy regimens is important. Capecitabine, with other chemotherapeutic agents (irinotecan, oxaliplatin, perifosine, 17-allylamino-17-demethoxygeldanamycin, aspirin, celecoxib, statins, quinacrine, inositol hexaphosphate and inositol, cystine/theanine, curcumin, and isorhamnetin), and antibodies plays an important role in the inhibition of some signaling pathways, reducing tumor growth and side effects of capecitabine. However, proton pump inhibitors, are negatively related to capecitabine; therefore, the purpose of this work is to review and discuss the performance of capecitabine combination therapies in colorectal cancer.
Methods: "Colorectal cancer " and " capecitabine " were selected as primary terms in three popular search engines in medical sciences including PubMed, Science Direct and Google scholar databases.
Results: Combination of capecitabine with afford mentioned drugs could have an enhanced inhibitory effect on tumor growth or reduce the side effects of capecitabine.
Perifosine as an inhibitor of AKT, NF-κB, and JNK pathways could increase the effectiveness of capecitabine. 17-AAG in combination therapy enhanced the antitumor effects of capecitabine; aspirin increased OS; celecoxib was found to be effective in preventing Hand-foot syndrome. Statins with capecitabine showed the apoptosis, anti-angiogenesis effects. Quinacrine induced the p53 gene expression. Curcumin increased the sensitivity of tumor cells to capecitabine and isorhamnetin arrested the cycle cell. In the second-line treatment, combination of capecitabine and bevacizumab could inhibite the progression of the disease for a short time. Proton-pump inhibitors prevented optimal absorption of capecitabine and reduced its effect.
Conclusion: It can be claimed that the mutations and drug resistance that cause colorectal cancer can play a principal role in determining the type of treatment, and capecitabine with different combination therapies can be treatment strategy to prevent the progression of the disease.

Keywords: Colorectal cancer, capecitabine, combination therapy

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Abstract: A-10-2231-2

Systematic Review of Colorectal Cancer Induction Methods in C57bl/6 Mice: Comparative Analysis With Emphasis on Orthotopic Transplantation Techniques

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Background: Colorectal cancer (CRC) is a leading cause of cancer-related morbidity and mortality, and the C57BL/6 mouse strain is a crucial model for CRC research due to its genetic characteristics and experimental utility. Various methods for CRC induction in C57BL/6 mice include chemical carcinogenesis, genetic modifications, and orthotopic transplantation. A thorough comparison of these methods is essential for selecting the most appropriate model for CRC studies and therapeutic testing.

Methods: We systematically reviewed the literature by searching PubMed, Scopus, and NCBI databases for studies published up to January 2024. Studies were selected based on their use of C57BL/6 mice for CRC induction and their detailed descriptions of methodologies, including chemical carcinogenesis with azoxymethane (AOM) and dextran sulfate sodium (DSS), genetic models such as ApcMin/ and Trp53 knockout, and the orthotopic transplantation of CRC cells. We assessed these methods for tumor incidence, growth characteristics, and relevance to human CRC.

Results: Out of 34 reviewed studies, the AOM/DSS model was identified as the most commonly used chemical carcinogenesis method, demonstrating high efficacy in inducing CRC with consistent and reproducible tumor formation. Genetic models like ApcMin/+ and Trp53 knockout were also effective but showed variability in tumorigenesis. The orthotopic transplantation method, which involves implanting CRC cells into the cecum, was particularly noted for replicating the natural CRC progression and metastatic processes, providing a more accurate model for studying tumor biology and testing treatments.

Conclusion: The AOM/DSS model remains a standard approach for CRC induction in C57BL/6 mice due to its effectiveness and reliability. The orthotopic transplantation method offers a superior model for studying CRC progression and metastasis, making it a valuable tool for advanced CRC research. Future studies should optimize these methods and explore novel techniques for improved CRC modeling.

Keywords: colorectal cancer, C57BL/6 mice, CRC induction methods

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Abstract: A-10-2497-1

Caloric Restriction and Quercetin as an Anti-Oxidant and Anti-Inflammatory Therapeutic Potential: Involvement of Heme Oxygenase-1 and Thioredoxin

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Background: Increase the levels of free radicals, inflammatory factors, and oxidative stress are commonly associated with aging and known to contribute in the aging process significantly. This research aimed to investigate the effectiveness of caloric restriction (CR) and quercetin (QUER) in reducing the impact of oxidative stress and inflammation linked to aging. The study aimed to examine how CR and QUER might counteract the negative effects of free radicals and inflammatory factors, providing new perspectives on potential approaches to support healthy aging.

Methods: The study was included two age groups of male Wistar rats (8 and 20 weeks old) which were further divided into groups receiving normal diet (ND), ND with QUER (15 mg Kg-1, IP), ND with CR, and ND with both QUER and CR.

Results: Higher levels of Tumor Necrosis Factor-alpha (TNF-a) was observed in 20-week-old rats in comparison to 8-week-old rats, and the introduction of QUER and CR over 4 weeks, effectively normalized this expression. The presence of heme oxygenase-1 (HO-1) and thioredoxin (TXN) genes were similarly influenced by CR and QUER, with CR alone or in conjunction with QUER notably enhancing the expression of TXN and HO-1 genes. Furthermore, the expression of the thioredoxin-interacting protein (TXNIP) gene was significantly decreased by CR alone or in combination with QUER.

Conclusion: QUER and CR collaboratively mitigated the negative effects of aging by modulating antioxidant signaling pathways, suggesting that this combination could serve as a complementary therapeutic strategy for addressing aging and age-related conditions.

Keywords: heme oxygenase-1, calorie restriction, thioredoxin, quercetin,

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Abstract: A-10-2500-1

Evaluation of Mesenchymal Stem Cells Derived from Different Tissues therapy on Burn Wound of Diabetic Rats

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Background: Diabetes mellitus (DM) as a chronic metabolic disease is one of the major contributors to chronic wound healing problems, and amputations particularly related to diabetic microvascular complications. Diabetic patients with burn wounds are at high risk to develop major complications, including infection and amputation. Hence, in order to reducing the duration of hospitalization and providing the rapid wound healing in diabetic patients, applying the experimental diabetic models and investigating the effect of modern regenerative medicine treatment protocols on burn models is necessary. Also studies indicated MSCs therapy as a potential treatment option for wound healing problems.

Methods: In this study, rat adipose tissues and bone marrow were excised, and isolated MSCs were amplified in cell culture and transferred to the burn areas in STZ-diabetic rats, in which thermal burn model created. Wound areas were measured and biopsy samples were excised from the wound areas of all diabetic rats to analyze gene expression levels of wound healing markers by qPCR. The markers include VEGF, PDGF, bFGF, EGF, Keratinocyte growth factor (KGF) and TGF-β which are known to be directly involved in wound healing mechanism were analized.

Results: The effect of cell therapy on secondary burn wound healing was assessed by RT-PCR and immunohistochemistry datas of early and late wound healing markers in biopsy samples excised from the back of cell-treated/untreated rats on 3rd, 7th, 14th and 21th days after treatment.

Conclusion: We demonstrated that applying MSCs derived from different tissues has a greater potential for treatment of diabetic burn wounds.

Keywords: wound healing, burn wound, mesenchimal stem cell, diabetes, rats

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Abstract: A-10-2369-1

Claudin-4 and Human Esophageal Cancer Tissue: A Systematic Review

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Background: Esophageal cancer is one of the most common cancers worldwide. Given that this disease is usually diagnosed in advanced stages, its treatment is challenging and the survival rate of patients is relatively low. In this systematic review, we examine the changes of claudin-4 (CLDN-4) and the factors affecting amount of changing on esophageal cancer cells and cell lines.

Methods: Scopus, PubMed, and Web of Science databases were searched for articles that investigated the CLDN-4 gene and protein expression in esophageal cancer cells of patients or esophageal cancer cell line. Barrett's esophagus, Gastroesophageal adenocarcinoma, Gastrointestinal cancer, Methylation of the CLDN-4 gene or its promoter, Microarray data analysis, Other claudin family genes, Review articles, Articles that did not have relevant and extractable information, Animal studies, non-English language studies were excluded from this systematic review. 202 manuscripts were obtained in the beginning, after screening and applying the inclusion and exclusion criteria, 6 studies remained.

Results: A total of 6 studies including 596 patients and 7 cell lines related to esophageal tissue were included in this systematic review. The studies were related to Japan, South Korea, China, and Finland. In these studies, the level of CLDN-4 in cancer samples related to esophageal cancer and their location in esophageal tissue cells have been examined.

Conclusion: The changed level of CLDN-4 in esophageal tissue with cancer could alter the tight junctions state that leads to change of barrier function. However, considering the conflicting results in the reports, more studies are needed to accurately interpret the role of CLDN-4 in esophageal cancer.

Keywords: CLDN-4, Esophageal adenocarcinoma, Esophageal squamous cell carcinoma

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Abstract: A-10-2508-1

Biochemical Parameters in Diet-Induced Hypercholesterolemia Rat Model

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Background: Hypercholesterolemia, characterized by increasing the levels of LDL -c as a significant risk factor for atherosclerosis, a leading cause of cardiovascular disease. Despite the numerous attempts at treatment and management of this issue, the outcomes have not been satisfactory. consequently, it is essential to develop innovative therapeutic approaches and initially evaluate them in the animal phase. Diet-induced hypercholesterolemia models in animals offer several benefits for studying of atherosclerosis, The aim of current study was to establish a diet-induced rat model of hypercholesterolemia, in order to achieve a unified model in term of both duration and composition, which is appropriate for subsequent study of atherogenic dyslipidemia.

Methods: 12 male Wistar rats were divided into 2 groups (n=6): normal and hypercholesterolemic. Following weighing, they were given a normal and high-fat diet for 90 days. Then, lipid profile, liver enzymes and hs-CRP levels were evaluated in both groups.

Results: Weight measurements taken at the beginning and end of the experiment revealed that the hyper group were gradually losing weight. In comparison to the Normal group, the hypercholesterolemic group demonstrated a considerable increase in LDL-C ($p<0.05$) and TG ($p<0.01$) and significant decrease in HDL-C ($p<0.001$). Furthermore, the hypercholesterolemic group exhibited a significant increase in liver enzymes activity ($p<0.05$) and hs-CRP ($p<0.05$) levels compared to the normal group.

Conclusion: This study has revealed that hypercholesterolemia could be induced using high-fat diet containing accurate amount of sheep fat and soybean oil. Also, Liver enzyme malfunction and inflammation may be related to hypercholesterolemia.

Keywords: Hypercholesterolemia, Rat model, Lipid profile, Diet

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Abstract: A-10-2501-1

IV Vitro and in Silico Studies of Some Triazole Derivatives Against Mushroom Tyrosinase

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Background: Melanoma and hyperpigmentation are conditions that have adverse effect on health and appearance and some people especially women suffer from this disease. These skin disorders occur as result of tyrosinase activity increase for melanin formation. Therefore, discovering safe, potent and with low side effect inhibitors have drawn considerable attention.

Methods: Molecular docking was carried out by using AutoDock 4.2. Inhibition assay and copper chelation studies were done, using the aforementioned protocols.

Results: Molecular docking was conducted in order to identify the type of interactions, binding position, and compute the binding free energy. The findings of this study showed that L5 has the least amount of binding free energy, and all compounds attach to important residues without binding to the enzyme's active site. According to in vitro studies, L4 and L5 show the greatest inhibition percentage, 43% at 80µM and 60% at 100µM, respectively, compared to other ligands. The outcome of copper chelation studies validates the findings of molecular docking. The spectrum of compounds remains consistent when exposed to different concentration of CuSO4.5H2O. It indicated that all of them were unable to attach to the active site and chelate the copper ions of tyrosinase.

Conclusion: In general, L4 and L5 have good inhibitory activity. Molecular docking and copper chelation studies demonstrated that these ligands possess the ability to inhibit the tyrosinase by binding to the allosteric site of it. Thus, L4 and L5 are known as moderate tyrosinase inhibitors to utilize them in different industries.

Keywords: Tyrosinase, Inhibitor, Triazole, Copper chelation studies, Molecular docking

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Abstract: A-10-2420-1

Study of the Gene Network Related To Beta-Arrestin 2 in Vsmcs After the Treatment With Metformin in High Glucose Conditions

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Background: Metformin (Met) is known to reduce blood sugar levels. Based on gene network studies and prediction, β-arrestin 2 (BARR2) gene and protein expression levels were evaluated in vascular smooth muscle cells (VSMCs) treated with Met in high glucose conditions.

Methods: Human VSMCs were cultured in Dulbecco's Modified Eagle Medium/Nutrient Mixture F-12 (DMEM-F12) medium (containing FBS 10%, Glucose and Pen/Strep 1%), and treated with different values of Met (1 mM, 5 mM, and 7 mM) in 24-and 48-h periods. The BARR2 gene and protein expression levels were identified with RT-qPCR and western blotting techniques, respectively. The signaling axes were predicted from a gene network made using Cytoscape software and annotated with Gene Ontology.

Results: Many BARR2-related signaling axes were found in the gene network. The BARR2 gene expression levels were reduced in VSMCs treated with Met (5 mM, and 7 mM) after 24-and 48-h periods ($p < 0.001$). Furthermore, the similar results were estimated on the BARR2 protein expression levels in VSMCs treated with Met after 24-and 48-h periods ($p < 0.05$).

Conclusion: Our obtained gene network suggested Met might affect some BARR2- related cellular signaling axes. Met suppressed the BARR2 protein and gene expression levels in the VSMCs. Through BARR2 down regulating, Met may modulate the behavior and function of VSMCs, potentially contributing to its cardioprotective effects.

Keywords: BARR2, high-glucose, metformin, VSMC

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Abstract: A-10-2472-2

A Computational Study on Hydroxychloroquine Binding Pattern With Angiotensin-Converting Enzyme 2

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Background: Hydroxychloroquine, as an antimalarial drug, is often recommended for the treatment of systemic lupus erythematosus and rheumatoid arthritis. It has also been proposed in the treatment of the coronavirus disease 2019 (COVID-19). Different mechanisms explain how this small molecule affects COVID-19 treatment. One mechanism describes how Hydroxychloroquine interacts with Angiotensin-converting enzyme 2 (ACE2). ACE2 is a membrane protein on the cell's surface that allows SARS-CoV-2 entry into targeted cells. Therefore, in this study, we focused on the mechanism of Hydroxychloroquine in controlling COVID-19.

Methods: Several computational techniques, such as molecular dynamics (MD) simulation and MM-PBSA calculation, have been employed to investigate the Hydroxychloroquine's binding pattern with Angiotensin-converting enzyme 2.

Results: Based on our results, the ACE2-Spike-Hydroxychloroquine complex had the highest binding energy at -25.5233±0.2735 kcal.mol−1. The binding free energy for the ACE2-Spike complex was -69.2554±0.6696 kcal.mol−1, which was lower compared to ACE2-Spike-Hydroxychloroquine (about 2.7 fold). It has been shown that Hydroxychloroquine might have an effect on the interaction between ACE2 and Spike, leading to a decrease in the affinity of the ACE2 receptor for Spike. Other MD analyses have also confirmed that Hydroxychloroquine could decrease the affinity between the ACE2-Spike complex.

Conclusion: Based on these findings, we anticipate that Hydroxychloroquine could potentially disturb the three-dimensional structure of the ACE2 receptor. Altering the protein's three-dimensional structure can impact the interaction between ACE2 and the spike glycoprotein.

Keywords: Hydroxychloroquine, COVID-19, Angiotensin-converting enzyme 2

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Abstract: A-10-2505-1

Deciphering the Role of Dysregulated Mirnas in Breast Cancer: Targeting the PI3K/AKT Pathway for Potential Therapeutic Advances

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Background: miRNAs play a pivotal role in breast cancer by serving as key regulators of gene expression, with their dysregulation linked to various cancer hallmarks. This study focuses on unraveling the molecular underpinnings of breast cancer susceptibility by deciphering dysregulated miRNAs that target the PI3K/AKT pathway.
Methods: We conducted an extensive review of prior studies exploring the modulatory role of miRNAs targeting the PI3K/Akt pathway. Utilizing the miRDB database, we identified all miRNA-targeted genes. Cytoscape software facilitated the investigation of protein-protein interactions (PPI) among these genes, with a focus on identifying hub proteins. Gene-subnetwork Gene Ontology (GO), Cytocluster, and promoter motif analysis were performed for a comprehensive understanding.
Results: Our analysis results revealed that 990 genes are targeted by dysregulated miRNAs impacting the Wnt pathway. Within this network, 12 hub proteins were identified. Subnetwork analysis showcased five crucial functional modules, complemented by the identification of 10 significant promoter motif elements through Cytocluster and promoter motif analysis.
Conclusion: This study not only contributes to understanding the intricate regulatory mechanisms of dysregulated miRNAs in breast cancer but also paves the way for identifying potential biomarkers and therapeutic targets. The findings hold promise for advancing personalized approaches in the management of breast cancer.

Keywords: Keywords: Breast cancer, PI3K/AKT signaling, systems biology, promotor motif analysis, subnetwork analysis

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Abstract: A-10-2376-1

A Quantum Mechanical Investigation on Aprocitentan

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Background: In March 2024, the FDA approved Aprocitentan for patients with hypertension inadequately controlled by standard therapies, making it the first antihypertensive with a new mechanism of action approved in nearly 40 years. Because of the significant medical importance of the aforementioned drug, we have decided to conduct a thorough examination of its electronic structure, using quantum computing technology.
Methods: The study utilized the quantum mechanics (QM) calculations conducted through the density functional theory (DFT) method with the GAUSSIAN 09 software. The structure of the Aprocitentan drug was first optimized through gradient procedures at both restricted Hartree-Fock (HF) and hybrid density functional B3LYP levels of theory, using the 6-311G basis set. Examination of the results revealed that optimized structure achieved in this research was situated at the minimum point on the potential energy surface, displaying no negative modes.
Results: This study conducted calculations for structural parameters like bond lengths, angles, and dihedrals, as well as thermodynamic parameters at the B3LY/6-311G level of theory and provided the results. The electronic energy of the molecule was determined to be -4263056.4 kcal/mole. Additionally, the mulliken atomic charge, spin density, and molecular orbital energies were calculated. The highest occupied molecular orbital (HOMO) was found to be -0.25251 eV and the lowest unoccupied molecular orbital (LUMO) was -0.09666 eV. The dipole moment in Debye was measured as X=4.7987, Y=-3.1598, Z=6.1561, with a total of 8.4207.
Conclusion: Optimization of the drug was performed using the B3LYP/6-311G method. The study focused on Aprocitentan's electronic characteristics, specifically the energy difference between the HOMO and the LUMO. The HOMO-LUMO gap energy was determined to be 0.15 eV. This provides insights into Aprocitentan's electronic behavior, which could have applications in various fields.

Keywords: Aprocitentan, DFT, B3LYP/6-311G, HOMO-LUMO gap

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Abstract: A-10-2376-2

A Quantum Mechanical Investigation on Danicopan

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Background: In January 2024, Japan approved Danicopan for patients with PNH inadequately controlled by standard therapies, making it the first alternative pathway inhibitor for extravascular hemolysis. Because of the significant medical importance of the drug mentioned above, we have decided to conduct a thorough examination of its electronic structure using quantum computing technology.
Methods: The study utilized quantum mechanics (QM) calculations conducted through the density functional theory (DFT) method with the GAUSSIAN 09 software. The structure of the Danicopan drug was first optimized through gradient procedures at both restricted Hartree-Fock (HF) and hybrid density functional B3LYP levels of theory using the 6-311G basis set. Examination of the results revealed that the optimized structure achieved in this research was situated at the minimum point on the potential energy surface, displaying no negative modes.
Results: This study conducted calculations for structural parameters like bond lengths, angles, and dihedrals, as well as thermodynamic parameters at the B3LY/6-311G level of theory and provided the results. The electronic energy of the molecule was determined to be -2690347.4 kcal/mole. Additionally, the mulliken atomic charge, spin density, and molecular orbital energies were calculated. The highest occupied molecular orbital (HOMO) was found to be -0.23953 eV and the lowest unoccupied molecular orbital (LUMO) was -0.07957 eV. The dipole moment in Debye was measured as X= -3.1440, Y= 5.7146, Z= -0.4717, with a total of 6.5394.
Conclusion: Optimization of the drug was performed using the B3LYP/6-311G method. The study focused on Danicopan 's electronic characteristics, specifically the energy difference between the HOMO and the LUMO. The HOMO-LUMO gap energy was determined to be 0.15 eV. This provides insights into Danicopan 's electronic behavior, which could have applications in various fields.

Keywords: Danicopan, DFT, B3LYP/6-311G, HOMO-LUMO gap

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Abstract: A-10-2393-1

A Quantum Mechanical Study of Rufinamide

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Background: In March 2024, the FDA approved Rufinamide for patients with seizures associated with Lennox-Gastaut Syndrome (LGS), making it the first triazole derivative and anticonvulsant medication for seizure disorders approved in nearly 40 years. Because of the significant medical importance of the aforementioned drug, we have decided to conduct a thorough examination of its electronic structure using quantum computing technology.
Methods: Quantum mechanics (QM) calculations were utilized in this study using the density functional theory (DFT) method with GAUSSIAN 09 software. The structure of the Rufinamide drug was initially optimized through gradient procedures at both restricted Hartree-Fock (HF) and hybrid density functional B3LYP levels of theory, using the 6-311G basis set. Analysis of the results revealed that the optimized structure achieved in this research was at the minimum point on the potential energy surface, displaying no negative modes.
Results: This study conducted calculations for structural parameters such as bond lengths, angles, and dihedrals, as well as thermodynamic parameters at the B3LY/6-311G level of theory and provided the results. The electronic energy of the molecule was determined to be -879.7 kcal/mole. Additionally, Mulliken atomic charges, spin density, and molecular orbital energies were calculated. The highest occupied molecular orbital (HOMO) was found to be -0.25791 eV, and the lowest unoccupied molecular orbital (LUMO) was -0.05835 eV. The dipole moment, measured in Debye, had components X = 4.5675, Y = 0.2372, Z = -0.1179, resulting in a total dipole moment of 4.5752.
Conclusion: The optimization of the drug was conducted using the B3LYP/6-311G method. This study focused on Rufinamide's electronic characteristics, particularly the energy difference between the HOMO and LUMO. The HOMO-LUMO gap energy was found to be 0.20 eV. These findings provide insights into Rufinamide's electronic behavior, which could have applications in various fields.

Keywords: Rufinamide, DFT, B3LYP/6-311G, HOMO-LUMO gap

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Abstract: A-10-2393-2

A Quantum Mechanical Study of Perphenazine

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Background: In March 2024, the FDA approved Perphenazine for patients with schizophrenia, as well as nausea and vomiting, making it the first antipsychotic phenothiazine derivative with actions and uses similar to chlorpromazine approved in nearly 40 years. Because of the significant medical importance of the aforementioned drug, we have decided to conduct a thorough examination of its electronic structure using quantum computing technology.
Methods: Quantum mechanics (QM) calculations were employed in this study using the density functional theory (DFT) method with GAUSSIAN 09 software. The structure of the Perphenazine drug was initially optimized through gradient procedures at both restricted Hartree-Fock (HF) and hybrid density functional B3LYP levels of theory, using the 6-311G basis set. Results analysis revealed that optimized structure obtained in this research was at the minimum point on the potential energy surface, displaying no negative modes.
Results: This study performed calculations for structural parameters, including bond lengths, angles, and dihedrals, as well as thermodynamic parameters, using the B3LY/6-311G level of theory. The results indicated that electronic energy of the molecule is -1913.7 kcal/mole. The highest occupied molecular orbital (HOMO) has an energy of -0.20047 eV, and the lowest unoccupied molecular orbital (LUMO) has an energy of -0.03319 eV. The dipole moment, measured in Debye, has components X= 1.9170, Y= -3.2712, Z= 1.6340, resulting in a total dipole moment of 4.1286.
Conclusion: The drug was optimized using the B3LYP/6-311G method. This study centered on Perphenazine's electronic characteristics, particularly the energy difference between the HOMO and LUMO. The HOMO-LUMO gap energy was found to be 0.17 eV. These findings offer insights into Perphenazine's electronic behavior, potentially applicable in various fields.

Keywords: Perphenazine, DFT, B3LYP/6-311G, HOMO-LUMO gap

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Abstract: A-10-2393-3

A Quantum Mechanical Study of the Isotretinoin Drug

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Background: Acne vulgaris, starting in puberty, causes severe lesions and scarring. Isotretinoin (Accutane), introduced in 1982, effectively treats severe acne by reducing the sebaceous gland size and sebum production, clearing up to 95% of lesions within 3-4 months. However, it poses risks such as teratogenicity and potential psychiatric issues, requiring strict pregnancy prevention and ongoing safety research.
Methods: This study utilized quantum mechanics (QM) calculations with density functional theory (DFT) via GAUSSIAN 09 software. The Isotretinoin drug's structure was optimized, using gradient procedures at both restricted Hartree-Fock (HF) and hybrid density functional B3LYP levels, employing the 6-311G basis set. Results showed that optimized structure was at the minimum point on the potential energy surface, with no negative modes observed.
Results: This study performed calculations for structural parameters, including bond lengths, angles, and dihedrals, as well as thermodynamic parameters, using the B3LY/6-311G level of theory, and provided the results. The electronic energy of the molecule was determined to be -929.4 kcal/mole. Additionally, the Mulliken atomic charges, spin density, and molecular orbital energies were calculated. The highest occupied molecular orbital (HOMO) was found to have an energy of -0.20140 eV, while the lowest unoccupied molecular orbital (LUMO) had an energy of -0.08870 eV. The dipole moment, measured in Debye, had components X= 1.5811, Y= -1.3562, Z= 0.9790, resulting in a total dipole moment of 2.3017.
Conclusion: The optimization of the drug was conducted using the B3LYP/6-311G method. This study concentrated on the electronic characteristics of Isotretinoin, particularly the energy difference between the HOMO and LUMO. The HOMO-LUMO gap energy was found to be 0.11 eV. These findings offer insights into the electronic behavior of Isotretinoin, which could have applications in various fields.

Keywords: Isotretinoin, DFT, B3LYP/6-311G, HOMO-LUMO gap

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Abstract: A-10-2462-1

Biochemical Feedback-Based Nonpathogenetic Modulation for Neurological Disorders: Advances and Future Directions

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Background: The main objective of this research is to conduct a thorough examination of the progress and future trends in the utilization of chemical signals in nanopathogenetic intervention for the treatment of brain ailments, with a specific emphasis on the possible advantages and obstacles. Nanopathogenetics, a cutting-edge method that combines light manipulation with precise nanoscale technologies, has emerged as a groundbreaking instrument for controlling brain circuits. The incorporation of chemical reactions into this technology presents a new strategy for the precise, real-time management of conditions like seizures, Parkinson's disease, and other degenerative brain disorders.

Methods: A systematic exploration was carried out in databases such as PubMed and Google Scholar, utilizing search terms related to optogenetics, biological responses, nanotechnology, and brain disorders. Studies conducted between 2018 and 2024 were chosen based on their relevance to the subject matter and the presentation of empirical evidence or medical applications. Out of 320 articles identified, 110 that adhered to strict inclusion criteria were picked for examination. The selection or exclusion of studies was influenced by factors such as research design, target demographic, methodological reliability, and findings.

Results: Significant advancements were noted in sophisticated nanopathogenetic systems that rely on chemical feedback for precise, minimally invasive control of brain activity. These studies illustrated how such techniques could result in notable enhancements in animal models, boosting neural functions. Nevertheless, challenges such as the necessity for enhanced tissue compatibility, long-term stability, and scalability for medical use were recognized. Suggestions were provided for overcoming these obstacles, including the creation of more biocompatible materials, improved delivery techniques, and extended medical assessments.

Conclusion: This analysis emphasizes the urgent requirement for continuous interdisciplinary cooperation to surmount these hurdles and maximize the therapeutic possibilities of chemical feedback-based nanopathogenetic systems. Future investigations should concentrate on expanding these technologies for medical purposes, assessing long-term advantages, and exploring their relevance in broader neurological contexts.

Keywords: Biochemical feedback ،nano-optogenetics ،neurodegenerative disorders

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Abstract: A-10-2502-1

Ferritin Purification and the Role of Ferritin-Heme Complexes in Oxidative Processes

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Background: Ferritin plays a significant role in the storage and circulation of iron, which can lead to oxidative stress and the production of reactive oxygen species (ROS). This study investigates the potential impact of the reaction between ferritin and heme on oxidative processes.
Methods: The study employed a two-step purification process to isolate ferritin, taking advantage of its high thermal resistance at temperatures above 80°C. This was followed by ammonium sulfate precipitation and anionic exchange chromatography (DEAE sepharose). The study then explored the potential peroxidase activity of the "heme-ferritin" complexes. Hydrogen peroxide (H2O2) was used as the oxidant substrate, and tetramethylbenzidine was used as the reductant substrate
Results: The results showed that the "heme-ferritin" system exhibited non-specific peroxidase activity, capable of oxidizing tetramethylbenzidine and neurotransmitters with high catalytic efficiency. This suggests that the oxidation of neurotransmitters by the peroxidase system in the presence of H2O2 could be a potential molecular link between increased ferritin/heme levels and the abnormal neurotransmitters and oxidative damage observed in Alzheimer's disease (AD) brains.
Conclusion: This study highlights the potential role of ferritin-heme complexes in oxidative processes and their possible implications for neurodegenerative diseases like Alzheimer's. The findings provide valuable insights into the complex interplay between iron, heme, and oxidative stress in the context of neurological disorders.

Keywords: Ferritin, Heme, Binding, Peroxidase

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Abstract: A-10-2509-1

Effects of naringin on the plasma lipid profile in the non-alcoholic fatty liver rats model under high-fat diet

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Background: Naringin, a type of glycoside flavonoid found in most plant, has been known for the capacity to reduce lipid synthesis and anti-inflammatory. In this study, the changes of plasma lipid profile were investigated after oral administration of naringin supplement in non-alcoholic fatty liver rats model under high-fat diet (HFD).
Methods: Twenty-one male Wistar rats were randomly divided into three groups, namely, the control group, NAFLD group and HFD+naringin group (n=7 for each group). Except for the control group, NAFLD and HFD+naringin groups were fed an HFD containing 51% fat for 10 weeks by gavage. After 10 weeks, HFD+ naringin group were given naringin (12.5 mg/kg/d) for 6 weeks. After the treatment period of the animals, plasma lipid profile was measured. NAFLD confirmed by histology and hematoxylin-eosin staining. Hepatic steatosis is defined as intrahepatic fat of at least 5% of liver weight.
Results: The HFD+naringin group showed significantly reduced in plasma levels of triglyceride ($p=0.0035$) compared to the NAFLD group. No significant changes were observed in plasma total cholesterol, HDL and LDL cholesterol levels in HFD+naringin group compared to the NAFLD group ($p>0.05$). Hepatocyte histology of rats treated with naringin showed improvement in steatosis, ballooning and inflammation compared to rats with non-alcoholic fatty liver.
Conclusion: The present findings demonstrate hepatoprotective effects of Naringin supplement against HFD-induced NAFLD, possibly in part through reduces fat deposition by promoting lipolysis and fatty acid β-oxidation. As a result, naringin has potential beneficial effects as a supplement for obese and non-alcoholic fatty liver, but more clinical research is needed.

Key words: High fat diet, Naringin, Non-alcoholic fatty liver disease

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Abstract: A-10-2418-3

A Quantum Mechanics Study on the Carboprost Tromethamine

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Background: Carboprost Tromethamine Sterile Solution is a form of prostaglandin (a hormone-like substance that occurs naturally in the body) used to treat severe bleeding during and after childbirth. Carboprost Tromethamine is also used to produce an abortion by causing uterine contractions. Carboprost Tromethamine is usually given between the 13th and 20th weeks of pregnancy, but may be given at other times for medical reasons. Carboprost Tromethamine is often used when another method of abortion has not completely emptied the uterus, or when a complication of pregnancy would cause the baby to be born too early to survive.
Methods: At first, the molecular structure of Carboprost Tromethamine was designd, using GaussView software, followed by quantum mechanical calculations at the B3LYP/6-311+G theoretical level using Gaussian09 software.
Results: Using the GaussView software, the molecular structure of interest was initially designed in this software. IR spectrum vibrational frequencies: The IR spectrum, like a fingerprint that is unique to each chemical species. This spectrum known for its heightened sensitivity in discerning molecular chemical and structural traits, finds extensive applications in chemistry, biochemistry and pharmaceuticals. The most prominent peak in this spectrum at 1525.460 signifies oscillations per second, positioned on the left side of the chart. The value 1525.4 on the right denotes the dielectric constant.
Conclusion: Our research results shows that Carboprost Tromethamine was used to treat the severe bleeding during and after childbirth. At first, the modeling of Carboprost Tromethamine's structure used Gaussian and Gauss View software, followed by B3LY/6-311+G method optimization. The HOMO-LUMO gap energy has been presented as -0.24 eV. IR spectrum, vibrational frequencies of the Carboprost Tromethamine molecule have also been obtained and analyzed.

Keywords: Carboprost Tromethamine, HOMO and LUMO, IR spectrum, GaussView

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Abstract: A-10-2512-1

Evaluation and Comparison of Erythrocytic G6PD (glucose 6 Phosphate Dehydrogenase) Activity and the Level of TSH and Free T4 in People With Minor Beta Thalassemia and Normal Papulation

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Background: Beta thalassemias are genetic blood disorders affecting beta globin chain production, leading to a spectrum of symptoms. Beta thalassemia minor individuals are often asymptomatic but may have mild anemia. Thyroid hormones regulate metabolism and bodily functions, with thyroid disorders causing specific symptoms. Research suggests a link between thyroid hormone levels and the activity of the G6PD enzyme in red blood cells.

Methods: In 2019, 120 individuals (60 men and 60 women aged 20-40) visited Shahid Dastgheib Hospital in Shiraz. Half of each group were beta thalassemia carriers, and the other half were not. Blood samples were collected for TSH, Free T4, and G6PD enzyme analysis, using qualitative tests. Data was analyzed with SPSS21, utilizing Mann-Whitney and Chi-square tests.

Results: In the study, G6PD deficiency was observed in 5 individuals in both normal and beta thalassemia minor groups, with no significant relationship found between the groups based on the Chi-square test (p=1). Analysis of Free T4 levels revealed mean values of 0.9967 (SD: 0.26101) in the normal group and 1.1870 (SD: 0.83220) in the beta thalassemia minor group, with no significant difference determined by the Mann-Whitney test (p=0.781). TSH levels also showed no significant difference between the two groups, with mean values of 3.194417 (SD: 2.3024760) in the normal group and 3.228 (SD: 2.3409239) in the beta thalassemia minor group, as indicated by the Mann-Whitney test (p=0.823).

Conclusion: The results of this study indicated no significant relationship between the levels of thyroid hormones and the qualitative level of the enzyme G6PD among individuals without thalassemia and individuals with beta thalassemia minor. It is suggested further studies to investigate other populations in terms of geographical, ethnic, and other age groups for further confirmation.

Keywords: Beta thalassemia minor, Thyroid hormones, G6PD enzyme

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Abstract: A-10-2406-1

Combined Antioxidant Effects of Hesperidin and Quercetin in Hepg2 Cell Line

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Background: The combination of Hesperidin and Quercetin, a new therapeutic strategy in addition to chemical drugs for liver cancer, with good effects and reducing of side effects.
Methods: HepG2 cell line were grown in DMEM supplemented with 10% FBS and incubated at 37°C with 5% CO2. The viability of cells was evaluated using the colorimetric MTT assay after 24, 48, and 72 hours of incubation with different concentrations of Hesperidin and Quercetin (0-1000 µM). IC50 was chosen as the optimal concentration and 48 hours as the optimal time. Then total antioxidant capacity (TAC), total oxidative status (TOS), Malondialdehyde (MDA) levels, and the activity of antioxidant enzymes, including superoxide dismutase (SOD) and catalase (CAT) were measured. Total protein was also determined by the Bradford method.
Results: The MTT assay showed that the IC50 value after treatment with Hesperidin and Quercetin was 200 µM and 250 µM at 48 hours, respectively. Our experiment showed that MDA and TOS levels were decreased in treated cells compared to untreated cells. In contrast, TAC levels and the activities of SOD and CAT were increased in treated groups as compared with the untreated group. Furthermore, in the combined treatment group of both flavonoid caused further increase and decrease in the SOD and CAT activities and MDA and TOS levels respectively than the group treated with a flavonoid.
Conclusion: Our findings indicate that Hesperidin and Quercetin affect HepG2 cancer cells by reducing oxidative stress and increasing the activity of antioxidant enzymes while the combination of both flavonoids is more effective than each one alone. Therefore, it may be possible to use them in addition to chemical drugs to reduce side effects and oxidative stress in healthy cells.

Keywords: Hesperidin, Quercetin, HepG2, Antioxidant

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Abstract: A-10-2460-2

Investigation of the Expression of DVl2 and DVl3 Gene Involved in the Wnt Signaling Pathway in Patients With Colorectal Cancer

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Background: Colorectal cancer is the third most diagnosed cancer in adults. Overexpression of the Wnt/β-catenin signaling pathway has been observed in 90% of colorectal cancer patients. Dysregulation of genes have pivotal role in aberrant activation of Wnt signaling pathway. *DVL* gene is the central component of Wnt signaling and a key cytoplasmic regulator that rescues β-catenin from degradation. In this investigation, we examined the expression of *DVL2* and *DVL3* genes in CRC patients.

Methods: The current project was accomplished on seventy paired samples from CRC tissues and the adjacent samples that were collected from Taleghani and Imam Khomeini hospitals, Tehran, Iran. After RNA extraction and cDNA synthesis, gene expression was analyzed, using real-time PCR. The results were analyzed using appropriate statistical methods. All data were analyzed using GraphPad Prism 7.0 or SPSS 16.0. Using LinReg PCR software the efficiency value was determined.

Results: The expression levels of DVL2 and DVL3 were remarkably lower in CRC tissues compared to the adjacent tissues ($p < 0.0001$). Our data revealed that expression of *DVL2* and *DVL3* genes were reduced in 4.25-fold, and 3-fold respectively.

Conclusion: The present results indicate that *DVL2* and *DVL3* genes may play an important role in the progression of CRC through Wnt pathway. On the other hand, according to decrease of *DVL2* and *DVL3* genes expression, they might be considered as repressors in CRC. However, functional studies are needed to clarify the exact role of these genes.

Keywords: CRC, DVL2, DVL3, Wnt Pathway, Tumor suppressors

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Abstract: A-10-2343-1

Quantum Mechanical Investigation of the Zanubrutinib Drug

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Background: Zanubrutinib is a next-generation Bruton's tyrosine kinase (BTK) inhibitor developed for treating B-cell malignancies. Engineered for increased selectivity and improved pharmacokinetics, it offers sustained BTK inhibition with fewer off-target effects. Clinical trials have shown that Zanubrutinib is effective in conditions such as mantle cell lymphoma (MCL) and chronic lymphocytic leukemia (CLL), achieving high response rates. Compared to first-generation BTK inhibitors, Zanubrutinib has a more favorable safety profile, with reduced risks of cardiac and bleeding events. It's development marks a significant advancement in targeted cancer therapy.
Methods: At first, the molecular structure of the Zanubrutinib was designed using GaussView software, followed by quantum mechanical calculations at the B3LYP/6-311+G theoretical level using Gaussian09 software.
Results: This research conducted detailed calculations for structural parameters like bond lengths, angles, and dihedrals, as well as thermodynamic parameters at the B3LY/6-311G level of theory and provided the results. The electronic energy of the molecule was determined to be -969719.4 kcal/mol. Additionally, the Mulliken atomic charge, spin density, and molecular orbital energies were calculated. The highest occupied molecular orbital(HOMO) was measured at -0.19825 eV, while the lowest unoccupied molecular orbital (LUMO) was -0.03655 eV. The dipole moment in Debye was measured as X= 2.1265, Y= 0.9377, Z= 0.4051, with a total of 0.4051.
Conclusion: The drug was optimized using the B3LYP/6-311+G method in this research. The main emphasis was on investigating the electronic properties of Zanubrutinib, particularly the disparity in energy levels between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). The calculated HOMO-LUMO gap energy was found to be 0.1617eV. This analysis sheds light on the electronic behavior of Zanubrutinib, indicating potential implications across a range of industries.

Keywords: Zanubrutinib, DFT, B3LYP/6-311G, HOMO-LUMO gap

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Abstract: A-10-2385-1

Electronic Investigation of the Deferasirox; A DFT Study

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Background: In this study, the Defarasirox molecule's electronic properties were investigated using density functional theory (DFT) calculations. The optimized geometrical parameters such as bond length and bond angle, as well as the electronic gap between the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) orbitals, were calculated using the DFT/B3LYP method with a standard 6-311+G** basis set. Additionally, the electronic energy and atomic charges were analyzed.
Methods: Initially, the molecular structure of Defarasirox was visualized in the Gauss view graphic program, followed by calculations in the Gaussian09 program utilizing the B3LYP/6-311+G level of theory.
Results: The thermodynamic properties of the Defarasirox molecule were determined using the B3LYP/6-311+G computational method. The total energy was calculated to be -799447.7 kcal/mol, alongside the dipole moments in Debye units and the HOMO-LUMO gap energy of the molecule. Furthermore, bond length values for specific atom pairs and bond angle values were computed for the Defarasirox molecule. Calculated atomic charges for selected atoms were also reported.
Conclusion: Through DFT calculations at the B3LYP/6-311+G opt theory level, the molecule's optimization was achieved. The structural analysis focused on bond length and bond angle parameters, while the molecule's reactivity and stability were assessed based on HOMO and LUMO energies.

Keywords: Keywords: QM-DFT, HOMO-LUMO Gaps, Defarasirox

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Abstract: A-10-2342-1

Investigation of Quantum Computing of Cortifoam Drug

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Background: Cortifoam is a corticosteroid medication specifically designed for the treatment of inflammatory conditions within the rectum and lower bowel. As a rectal foam, Cortifoam offers a unique delivery system that enhances the local therapeutic effects while minimizing systemic absorption and potential side effects. The molecular action of hydrocortisone, which involves binding to glucocorticoid receptors and modulating gene expression, underscores the importance of understanding drug chemistry in developing treatments that balance efficacy and safety. Considering that formulation of drugs is an ongoing issue, Cortifoam exemplifies how chemistry can optimize drug delivery systems to enhance patient outcomes in inflammatory diseases.
Methods: At first, the molecular structure of Cortifoam was designed, using GaussView software, followed by quantum mechanical calculations at the B3LYP/6-311+G theoretical level by Gaussian09 software.
Results: Present study conducted detailed calculations on structural characteristics such as bond lengths, angles, and dihedrals, along with thermodynamic parameters at the B3LY/6-311G level of theory, and presented the findings. The electronic energy of the compound was identified as -845494.42 kcal/mol. Furthermore, the Mulliken atomic charge, spin density, and molecular orbital energies were determined. The highest occupied molecular orbital (HOMO) was measured at -0.24065 eV, while the lowest unoccupied molecular orbital (LUMO) was found to be -0.05279 eV. The dipole moment in Debye was recorded as X = -5.8474, Y = 1.9280, Z = -0.3566, with a total of 6.1673.
Conclusion: In present study, the drug was optimized, using the B3LYP/6-311+G method. The main emphasis was on investigating the electronic properties of Cortifoam, particularly the disparity in energy levels between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). The calculated HOMO-LUMO gap energy was found to be 0.18786eV. This analysis sheds light on the electronic behavior of Cortifoam, indicating potential implications across a range of industries.

Keywords: Cortifoam, DFT, B3LYP/6-311+G, HOMO-LUMO gap

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Abstract: A-10-2501-2

Sulfonamide Derivatives As Tyrosinase Inhibitors: A Fluorescence Spectroscopy Study

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Background: Tyrosinase (EC 1.14.18.1) is a critical enzyme in melanogenesis pathway. Various skin disorders such as melanoma and age spots occur due to a malfunction of tyrosinase. So, searching for potent inhibitors for tyrosinase is important. Tyrosinase displays intrinsic fluorescence emission due to the presence of 9 tryptophan and 3 tyrosine residues. Hence, fluorescence studies were utilized in the structural studies of tyrosinase inhibitors.
Methods: Inhibition assay was carried out, using various concentrations of each ligand, as previously explained. Fluorescence spectroscopy studies were conducted through excitation wavelengths of 275 nm and 295 nm, with emission spectra recorded from 285-450 nm and 305-450 nm, respectively.
Results: Based on the results of the inhibition assay, S1, S4, S5, S6, and S7 showed the highest percentage of inhibition compared to the remaining ligands. Fluorescence spectroscopy studies showed that intrinsic fluorescence emission is decreased as the concentration of potent ligands (S1, S4, S5, S6, and S7) rises. In other terms, the intrinsic fluorescence emission is quenched in the presence of ligands. Analysis of Stern-Volmer plots and determination of binding parameters indicated that all these ligands revealed static quenching. The number of binding sites (n) is roughly 1, indicating a single binding site on tyrosinase for each ligand.
Conclusion: Overall, S1, S4, S5, S6 and S7 are potent ligands and effectively inhibit tyrosinase. Fluorescence spectroscopy studies results indicated that all potent ligands can quench the intrinsic fluorescence emission of tyrosinase in static manner. Hence, these compounds are recognized as potent tyrosinase inhibitors for use in various industries.

Keywords: Tyrosinase, Sulfonamide, Inhibitor, Fluorescence spectroscopy studies

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Structural Electronic Study of Lusutrombopag Via Quantum Mechanical Calculations

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Background: Chronic liver disease often leads to severe thrombocytopenia, characterized by critically low platelet counts and heightened bleeding risks during procedures. Lusutrombopag, a thrombopoietin receptor agonist, stimulates the platelet production to enhance patient safety by minimizing the need for platelet transfusions. This study employs quantum mechanical Density Functional Theory (DFT) to investigate the lusutrombopag's molecular interactions, aiming to optimize its clinical application and understanding its pharmacological properties.

Methods: Quantum mechanical calculations by DFT with the GAUSSIAN 09 software were performed on Lusutrombopag. The molecular structure was optimized, using the B3LYP/6-311+G approach. Key structural parameters such as bond lengths, bond angles, and dihedral angles were calculated. Electronic properties, including the electronic energy, HOMO-LUMO energies, and the dipole moment (in debye), were also determined to understand the molecule's stability and reactivity.

Results: The molecular structure of Lusutrombopag was analyzed by GaussView at the B3LYP/6-311+G level, documenting its structural parameters. Quantum mechanical calculations revealed bond lengths. Bond and dihedral angles were also measured. Additionally, HF (Hartree-Fock) energy was determined as -1837375.1 kcal/mole. The highest occupied molecular orbital (HOMO) was found to be -0.22542 eV and the lowest unoccupied molecular orbital (LUMO) was-0.09353 eV. In addition, atomic charges of the molecule were also calculated. The dipole moment in debye was measured as X, Y, and Z as 0.5376, -2.9722, and 0.3996, respectively, with a total of 3.0468.

Conclusion: DFT analysis of Lusutrombopag has shown that bond length and angle significantly influence the drug's stability and efficacy. The HOMO-LUMO gap was determined to be 0.13 eV. These findings provide valuable insights for improving therapeutic approaches and developing more effective drugs to treat related diseases.

Keywords: Lusutrombopag, DFT, B3LYP/6-311+G, HOMO-LUMO gap

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Quantum-Mechanical DFT Investigation of the Zanubrutinib Drug

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Background: Zanubrutinib is a next-generation Bruton's tyrosine kinase(BTK)inhibitor developed for treating B-cell malignancies. Engineered to increased selectivity and improved pharmacokinetics, the sustained BTK inhibition with fewer off-target effects is offered.
Clinical trials have shown that Zanubrutinib is effective in conditions such as mantle cell lymphoma (MCL) and chronic lymphocytic leukemia (CLL), achieving high response rates. Compared to first-generation BTK inhibitors, Zanubrutinib has a more favorable safety profile, with reduced risks of cardiac and bleeding events. Its development marks a significant advancement in targeted cancer therapy.
Methods: At first, the molecular structure of Zanubrutinib was designed, using GaussView software, followed by quantum mechanical calculations at the B3LYP/6-311+G theoretical level by Gaussian09 software.
Results: Present research conducted detailed calculations for structural parameters like bond lengths, angles, dihedrals, as well as thermodynamic parameters at the B3LY/6-311G level of theory and provided the results. The electronic energy of the molecule was determined to be -969719.401 kcal/mol. Additionally, the Mulliken atomic charge, spin density, and molecular orbital energies were calculated. The highest occupied molecular orbital (HOMO) was measured at -0.19825 eV, while the lowest unoccupied molecular orbital(LUMO) was -0.03655 eV. The dipole moment in Debye was measured as X= 2.1265, Y= 0.9377, Z= 0.4051, with a total of 0.4051.
Conclusion: The drug was optimized using the B3LYP/6-311+G method in this research. The main emphasis was on investigating the electronic properties of Zanubrutinib, particularly the disparity in energy levels between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). The calculated HOMO-LUMO gap energy was found to be 0.1617eV. This analysis sheds light on the electronic behavior of Zanubrutinib, indicating potential implications across a range of industries.

Keywords: Keywords: Zanubrutinib, DFT, B3LYP/6-311G, HOMO-LUMO gap

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Investigation of Quantum Computing and Structural Characteristics of Risdiplam

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Background: Risdiplam, marketed under the brand name Orizadi, is a medication prescribed for the treatment of spinal muscular atrophy. It is notable for being the first oral medication approved for this condition. This medication functions as an RNA regulator for editing SMN2. In August 2020, the United States Food and Drug Administration approved for Risdiplam to be used in the treatment of muscular atrophy in children aged 2 and above, as well as adults. Risdiplam is a result of a collaboration between PTC Therapeutics and the Spinal Muscular Atrophy Foundation.

Methods: Initially, the molecular configuration of Risdiplam was created employing GaussView software, followed by conducting quantum mechanical computations at the theoretical level of B3LYP/6-311++G** using Gaussian09 software.

Results: The Risdiplam drug was carefully analyzed through molecular calculations, using Gauss View software at the B3lyp/6-311++G** theoretical level. This analysis resulted in the determination of the drug's structural parameters and the creation of the desired molecular structure by Gauss View software. Furthermore, the thermodynamic properties of the molecular structure of Risdiplam were accurately calculated at the B3lyp/6-311++G** computational level.

Conclusion: The molecular properties such as bond length and bond angle were precisely determined and their influence on the overall structure of the molecule was thoroughly examined. Additionally, information regarding atomic charges, infrared spectrum, frequency, intensity, and various energy levels of the molecule were obtained and carefully studied. Moreover, the difference in energy between the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) was calculated with precision.

Keywords: HOMO -LUMO gap, DFT, B3LYP/6-311++G**, Risdiplam

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Investigating the Effect of Palbociclib on P21 Protein By Molecular Docking Method

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Background: Palbociclib is a reversible cyclin-dependent kinase (CDK) inhibitor. This drug inhibits CDK4, CDK6 intracellular proteins. In hormone-positive breast cancers, inhibition of these proteins helps to stop cell division and production of new cells. This drug inhibits the progression of cell division from G1 to S phase. This slows down the growth of cancer. P21 protein is also a cell cycle inhibitor that promotes both CDK cyclin inhibition and cell cycle arrest in the G1/S phase. In this study, we intend to investigate the binding energy between palbociclib drug and P21 protein from a molecular point of view.

Methods: In this study, we first extracted the 3D structure of P21 protein from the UNIPROT site in PDB format, then we downloaded the 3D structure of palbociclib drug in SDF format from the PUBCHEEM site. With the help of the viewerlite software, we performed a flow charge on the P21 protein and added hydrogen ions to it, and water molecules were also removed. Finally, through the DEEPSITE website, we found the appropriate place for the drug to bind to the P21 protein, Finally, the docking process was done with the help of Pyrex software.

Results: After binding process, the binding energy between palbociclib drug and p21 protein was investigated. Because palbociclib has a more negative binding energy, it can easily bind to its P21 protein receptor and exert its effects on this protein. Also, the coordinates of the placement of the drug in the protein were determined through the depth location, which was according to the following coordinates. center x: 139.495 y: 168.412 z: 187.0747

Conclusion: After conducting this study, we found that palbociclib can be an effective drug in preventing the further division of cancer cells by activating the apoptosis process in diseases such as breast cancer.

Keywords: palbociclib, P21 protein, molecular docking

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Abstract: A-10-2197-2

Investigation of the Expression of HNF3β and STAT3 Genes in Patients with Colorectal Cancer and Evaluating Their Protential As Biomarkers

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Background: Due to the high rate of death of the colorectal cancer [CRC], it is important to identify the genetic factors like HNF3B and STAT3 play a role in the occurrence of this disease. Previous literatures have reported a regulatory interaction between STAT3 and HNF3β. The aim of present study was to assess the HNF3β gene expression and its association with STAT3 gene in colorectal cancer samples, matched with margin tissues.
Methods: The 31 tumor tissues of colorectal and 31 matched tumor margin tissues were randomly obtained from 31 patients. Total RNA was extracted using RNX plus and cDNA was synthesied by Yekta Tajhiz Azama Kit. The Real-time PCR was carried out for assessing the gene expression level of the HNF3β and STAT3.
Results: We observed a significant difference in the expression of HNF3β and STAT3 genes in tumor tissues compared to tumor margin tissue. The results of gene expression analysis showed that expression of HNF3β [P value =0.044] and STAT3 [P value= 0.027] genes in tumor tissues were significantly higher compared to tumor margin tissues. On the other hand, it was shown that there is a positive and significant correlation between HNF3β gene expression STAT3 gene expressions [P value <0.001].
Conclusion: our results showed that the HNF3β and STAT3 genes can have a potential for diagnosis purposes in CRC.

Keywords: Colorectal cancer, Real time PCR, HNF3β, STAT3

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Abstract: A-10-2197-3

Alteration in the Expression of PELP1 and C-Src Genes in Tumor Tissue of Colorectal Cancer Patients

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Background: The genetic and environmental factors have crucial role in colorectal cancer (CRC) pathogenesis. Due to important role of PELP1 and c-Src genes in different types of malignancy, the aim of present study was investigation of PELP1 and c-Src genes expression in tumor and matched non-tumor tissues in CRC pateints. Additionally, the biomarker capacity of these two genes was evaluated in present study.

Methods: Thirty tumor tissues as cases and thirty matched margin tissues as controls were used in this study. All of the samples were obtained from Iran National Tumor Bank (Cancer Institute of Tehran University of Medical Sciences for Cancer Research, Iran). The RNA was extracted from tissues by RNX plus solution and cDNA was synthesized using cDNA synthesis kit (Yekta Tajhiz Azma, Iran). The genes expression were assessed, using Real-time PCR.

Results: The expression of PELP1 and c-Src genes in tumor tissues of the patients was significantly higher than those of the matched margin tissues. Correlation analysis results indicated the positive and significant corollation between PELP1 and c-Src genes. Analysis of our dada indicated that the PELP1 and c-Src can be considerd as potential biomarker for CRC.

Conclusion: Higher expression of c-Src and PELP1 genes in tumor tissues comparing to adjusent margin tissue indicated that these genes are critical components in signaling pathways that are involved in cancer pathogenesis. Furthermore, the obtained findings revealed that genes can have a potential for diagnosis purposes in CRC.

Keywords: c-Src, PELP1, Colorectal cancer, gene expression

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A DFT Study of Rezlidhia

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Background: Acute myeloid leukemia (AML) is a form of blood cancer that specifically targets bone marrow cells known as myelocytes, progressing rapidly. This condition results in the production of abnormal myeloblasts (a type of white blood cell), red blood cells, or platelets in the bone marrow of affected individuals. Rezlidhia is a prescribed medication used for adults diagnosed with acute myeloid leukemia (AML) who possess an isocitrate dehydrogenase-1 (IDH1) mutation. This treatment is indicated for cases where the disease has relapsed or has shown no improvement following one or more treatment attempts. Before prescribing Rezlidhia, your healthcare provider will conduct necessary tests to ensure its suitability for your condition. This medication received FDA approval in December 2022.

Methods: In the initial stage, the molecular structure of the Rezlidhia drug was designed, using Gauss View software, and then quantum mechanics calculations were performed at the theoretical level of B3lyp/6-311++G** by gaussian09 software.

Results: Molecular calculations of Rezlidhia drug were performed through Gauss View software at the theoretical level of B3lyp/6-311++G** and the structural parameters were reported and the desired molecular structure was designed, using Gauss View software. Thermodynamic properties for the molecular structure of Rezlidhia have been determined at the B3lyp/6-311++G** computational level. The dipole moment (Debye) of the Rezlidhia, calculated at the B3lyp/6-311++G** level of theory. The μx=2.1356, μy= -3.4992, μz= 0.8757 and μtot= 4.1919 have been obtained.

Conclusion: The bond length and bond angle were calculated and their effect on the molecule was investigated. Also, atomic charges, IR spectrum, frequency and intensity, and different energies of the molecule were extracted and analyzed. The HOMO-LUMO gap energy has been calculated. The polarizabilities of the Rezlidhia, calculated at the B3lyp/6-311++G** level of theory. The αx= 336.047, αy= 289.850, αz= 225.783, αxx= -4.259, αxy= 6.376, αxz= -5.248, αyz= -19.271 have been obtained.

Keywords: Keywords: Rezlidhia, HOMO-LUMO gap, DFT, B3lyp/6-311++G**

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Abstract: A-10-2535-1

The Effect of Alcoholic Ethyl Acetate Extract of Pistachio Green Hull on Testicular Tissue in Diabetic Male Rat

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Background: Diabetes is one of the causes of infertility in men. This study was performed to evaluate the effects of alcoholic ethyl acetate extract of pistachio green hull on testicular tissue in diabetic male mice.
Methods: In this experimental study, 45 male Wistar rats with a single dose of streptozotocin (65 mg/kg body weight) developed type 1 diabetes mellitus. 3 groups including 15 rats were divided: group 1 (control group: for 3 weeks and once a day administration of dimethyl sulfoxide 2.5% orally (gavage), group 2 (positive control group: for 3 weeks and once a day insulin injection at the rate of 2 to 4 units), Group 3 (for 3 weeks and once a day Pistachio green hull extract at a dose of 1 g/kg body weight was given orally (gavage). Then, the number of cells in the process of spermatogenesis and the levels of testosterone were measured. The data were analyzed by SPSS software.
Results: The results of the present study showed a statistically significant difference between the number of spermatogonium, spermatids, sertoli and primary spermatocytes in the control group (diabetes) and the insulin group and the pistachio green hull groups ($p < 0.05$). There was also a significant difference between the number of spermatid cells in the insulin group with the pistachio green hull group ($p < 0.05$). Also, there was a significant difference between the number of spermatogonia cells in pistachio green hull group ($p < 0.05$).
Conclusion: Alcoholic ethyl acetate extract of pistachio green hull were effective in increasing the number of cells in the process of spermatogenesis, and improving the testicular tissue, increasing fertility in diabetic male Wistar rats. Thus, this extract may be useful for enhancing the fertility in patients suffered from type 1 diabetes disease.

Keywords: Diabetes type 1, male infertility, testis, sperm

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Abstract: A-10-2447-1

Gene Network Modeling, Identification of Genes, and Key Pathways in Response To Soybean Cyst Nematode Heterodera Glycines

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Background: Heterodera glycines, is one of the most dangerous pathogens in soybean (Glycine soja) fields and significantly reduces crop yield. Due to long survival time in soil, controlling this nematode poses considerable challenges. The use of resistant or transgenic cultivars is one of the effective ways to reduce the damage of this nematode to soybean plants. Therefore, identifying plant genes that respond to nematode attack is crucial. In this study, to identify the essential genes and key pathways in the interaction between H. glycines and soybean, 2081 expressed genes of soybean from transcriptome data were analyzed, revealing that 263 genes formed a significant gene network.

Methods: Using the STRING database, all genes were examined and their gene network was constructed. Then, gene network was designed and analyzed, using Cytoscape software. Using the Maximum Neighborhood Component algorithm on the genes within the constructed network, ten genes with the highest impact were identified.

Results: The mRNAs transcribed from these critical genes, were Glyma_18G114900, Glyma_16G145800, Glyma_10G249000, Glyma_15G194300, Glyma_13G129500, Glyma_20G144700, Glyma_14G003400, Glyma_12G202500, Glyma_16G205200, and Glyma_20G212900, in order of importance. These genes play crucial roles in various metabolic pathways, including the production of antenna proteins involved in photosynthesis and Photosystem I in the infected plant. Gene Ontology and Kyoto Encyclopedia of Genes and Genomes analysis confirmed these findings. Suggesting that these identified genes are significant in either pathogenicity or resistance against H. glycines. A comprehensive understanding of this metabolic pathways could facilitate the development of methods to enhance the plant resistance to stresses and improve agricultural productivity. Additionally, these analysis indicate that identified genes play critical roles in regulating growth, development, response to environmental stresses, and defense against pathogens in soybean. These genes also influence various metabolic and biosynthetic processes and signal transduction pathways.

Conclusion: Research identifies genes and pathways for transgenic soybean resistance to H. glycines, revealing resistance mechanisms.

Keywords: Bioinformatics, Gene expression, MNC algorithm, Cyst Nematode

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Abstract: A-10-2536-2

The Effects of Hiit and Cet Exercise Training on Mir-98-5p and Mir-135-5p Expression Levels in High-Fat High-Fructose Diet-Induced Diabetic Rats; An Experimental and in Silico Analysis

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Background: In recent years, evidence has shown that miRNAs play a crucial role in the initiation and progression of many physiological-pathological processes, including diabetes and exercise. However, Exercise and diabetes have been shown to affect miRNA expression, but little is known about their potential roles and mechanisms. This study investigated the effects of continuous endurance training (CET) and high-intensity interval training (HIIT) on plasma miR-98-5p and miR-135-5p expression in diabetic rats.
Methods: This study investigated the effects of CET and HIIT on plasma miR-98-5p and miR-135-5p expression in diabetic rats. Diabetes was induced in the rats by high-fat high-fructose diet (HFHFD). They were then divided into three categories: diabetics, CET, and HIIT group. The expression of miR-98 and miR-135 were examined after eight weeks of exercising.
Results: Comparatively to CET, HIIT efficiently increases the miR-98 and miR-135 expression in diabetic rats. Insilco investigation showed that both miRs influence biological pathways associated with diabetes, including the insulin signaling pathways.
Conclusion: Our results demonstrated that the miR-98-5p and miR-135-5p expression levels are deregulated in the diabetic rats. Furthermore, exercise, especially HIIT, was an effective strategy for increasing miR-98-5p and miR-135-5p and improving glycemic control, lipid profile, and insulin resistance.

Keywords: Continuous endurance training, Diabetes, Exercise training, High-intensity interval training

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Abstract: A-10-2541-1

Exploring the Relationship Between Mitochondrial DNA Copy Number and Maximal Aerobic Capacity

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Background: Mitochondria have their own DNA (mtDNA) that encodes key proteins for energy production through oxidative phosphorylation. mtDNA is a circular molecule separate from the nuclear genome, with its own genetic system. mtDNA copy number is linked to mitochondrial biogenesis. VO2max is determined by the body's oxygen transportation and utilization. Given mitochondria's role in energy metabolism, a relationship between mtDNA and VO2max seems plausible.
Methods: The saliva samples, collected from 44 adults without routine exercise, were used for DNA extraction. These participants underwent testing to measure their VO2max. The average VO2max was calculated and participants were divided into two groups, one had VO2max values below and the other above the average point. Two primers were designed; one for the mtDNA and other for a single-copy nuclear gene (GAPDH). Real-time PCR was employed to obtain the cycle of threshold (Ct) values for both genes in each sample. The relative mtDNA content was quantified by representing the data as a ratio of the mtDNA Ct to the GAPDH Ct.
Results: Higher VO2max is often indicative of a more efficient mitochondrial function, however, the relationship between mtDNA copy number and VO2max remains controversial. Our results reveal a negative correlation between mtDNA copy number and VO2max, indicating individuals with higher VO2max values tend to have lower mtDNA copy numbers compared to those with lower VO2max.
Conclusion: Our study suggests that an increase of mtDNA copy number does not necessarily translate to enhanced oxygen uptake by the body. Keywords: mtDNA copy number, VO2max, Real-time PCR

Keywords: mtDNA copy number, VO2max, Real-time PCR

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Quantum Mechanical Calculations on Dimethyl Fumarate Drug

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Background: Dimethyl fumarate was approved by the Food and Drug Administration (FDA) on March 27, 2013 for treatment of multiple sclerosis (MS). Dimethyl fumarate acts as a selective inhibitor of Nf-κB signalling. Nf-κB is a transcription factor that plays a role in glucose activation, inflammatory responses, and immunity. By inhibiting Nf-κB signalling, dimethyl fumarate can improve symptoms and complications of multiple sclerosis.
Methods: Initially, the molecular structure of Dimethyl fumarate was designed, using Gauss View software, followed by quantum mechanical calculations at the B3LYP/6-311+G theoretical level by Gaussian09 software.
Results: Using the Gauss View software, the molecular structure of interest was initially designed in this software. The thermodynamic values for structure of dimethyl fumarate at B3LYP/6-311+G computational level were obtained. Thermodynamic values for structure of Tolterodine at B3LYP/6–311+G computational level are reported: Total Energy: 93.479 kcal/mol; Electronic Energy: -335404.095 kcal/mol; Zero-Point Energy: 86.51 kcal/mol; Gibbs Free Energy: 62.64 kcal/mol; Specific Heat Capacity: 36.854 cal/mol·K; Entropy: 105.420 cal/mol·K. The dipole moment in Debye was measured as X=0.0000, Y=0.0000, Z=0.0005, with a total of 0.0005. The highest occupied molecular orbital (HOMO) was found to be -0.29 eV and the lowest unoccupied molecular orbital (LUMO) was -0.15 eV.
Conclusion: Optimization of the drug was performed, using the B3LYP/6-311G method. The study focused on dimethyl fumarate 's electronic characteristics, specifically the energy difference between the HOMO and the LUMO. The HLG gap energy was determined to be -0.44 eV. This provides insights into dimethyl fumarate's electronic behaviour, which could have applications in various fields. The calculated thermodynamic values provide insights into molecular structure of dimethyl fumarate at the B3LYP/6-311+G computational level. These findings contribute to our understanding of the compound's properties and its potential in the treatment of multiple sclerosis.

Keywords: Theory (DFT)Multiple Sclerosis (MS), Dimethyl fumarate, HOMO-LUMO, B3LYP, Density Functional

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Abstract: A-10-2383-1

Pistachio Green Hull Extract Attenuate Testosterone-Induced Benign Prostatic Hyperplasia in Rats By Down-Regulating Cox-2

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Background: Benign prostatic hyperplasia (BPH) is a prevalent condition in aging males, characterized by prostatic enlargement and lower urinary tract symptoms (LUTS). BPH tissues are characterized by increased inflammatory processes and cytokine secretion, including COX-2, and IL-8. Pharmaceutical management of BPH initially relies on the use of 5-alpha reductase inhibitors (5-ARIs) and alpha-1 adrenergic blockers; however, various side effects are associated with their use. Therefore, extensive research has been conducted to gather clinical evidence for alternative BPH treatments, with herbal medicines gaining attention as part of efforts to replace synthetic drugs and minimize side effects. Studies have revealed that Pistachio green hull extracts (PGHE) have antioxidant, antimicrobial and anti-mutagenicity activities. The abundance of phenolic compounds and their associated antioxidant activity make pistachio hulls a valuable candidate as an alternative source of natural bioactive compounds.
Methods: The rats received a daily subcutaneous injection of testosterone enanthate (TE) (3 mg/kg) for 2 weeks to induce BPH (except the control group). Rats were divided into four groups: group 1 (control), group 2 (BPH, TE alone), group 3 (BPH+PGHE-100, TE + PGHE 100 mg/kg/day), and group 4 (BPH+PGHE-200, TE + PGHE 200 mg/kg/day). At the end of the experiment, all rats were sacrificed, and their prostate glands were removed, total RNA extracted, and subjected to RTqPCR analyses.
Results: In a testosterone-induced BPH rat model, PGHE treatment (100 and 200 mg/kg) significantly reduced COX-2 mRNA expression in prostate tissue.
Conclusion: These findings suggest that PGHE may be a promising natural treatment for BPH. However, further studies are warranted to elucidate intracellular events and cellular signaling pathways, as well as to identify and isolate the active components of pistachio hull extract.

Keywords: Pistachia vera ،benign prostate hyperplasia ،polyphenols ،COX-2

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Abstract: A-10-2545-1

The Role of Antioxidants in the Treatment of Metabolic Dysfunction-Associated Fatty Liver Disease: A Systematic Review

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Background: Non-alcoholic fatty liver disease (NAFLD) is a global public health problem that contributes to significant liver-related morbidity and mortality. It also serves as an independent risk factor for various non-communicable diseases. In 2020, a proposal was made to rename NAFLD to "metabolic dysfunction-associated fatty liver disease (MAFLD)", accompanied by more precise diagnostic criteria. Due to its widespread prevalence, effective treatment for MAFLD is crucial. Elevated levels of oxidative stress are known to be a key factor in the pathogenesis of this disease. This review aims to evaluate various studies on the efficacy of antioxidant therapies in patients with MAFLD.
Methods: A comprehensive search for relevant research was conducted across the PubMed, SCOPUS, and ScienceDirect databases. This search led to the identification of 87 studies that met the inclusion criteria. These studies were categorized based on whether they used natural antioxidants, synthetic antioxidants, or a combination of both.
Results: Of the human studies analyzed, 31.1% utilized natural antioxidants, 53.3% employed synthetic antioxidants, and 15.5% used a combination of both. In human-based research, natural antioxidants demonstrated 100% efficacy in the treatment of MAFLD, whereas synthetic antioxidants were effective in 91% of the studies. In animal-based studies, natural antioxidants were found to be fully effective, while synthetic antioxidants showed effectiveness in 87.8% of the evaluations.
Conclusion: The findings indicate that natural antioxidants are more effective in the treatment of MAFLD compared to synthetic antioxidants. Maintaining the appropriate balance between pro-oxidants and antioxidants is a valuable strategy for monitoring and optimizing antioxidant treatment in patients with MAFLD.

Keywords: non-alcoholic fatty liver disease, metabolic dysfunction-associated fatty liver disease, oxidative stress, antioxidant treatment, natural antioxidants, synthetic antioxidants, pro-oxidant–antioxidant balance, human studies, animal studies

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Abstract: A-10-2442-1

Designing and Optimization of the Expression of Wild-Type and Mutants of Recombinant Psychrophilic Lipase from Psychrobacter Sp. C18

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Background: Lipases (E.C.3.1.1.3) are widespread industrial biocatalysts that catalyze the hydrolysis of triglycerides at oil-water interfaces. Psychrophilic lipases can be beneficial in industrial processes by reducing energy consumption and preserving the stability of heat-sensitive products. Employing psychrophilic enzymes and exploiting of enzyme engineering techniques could result in lipases with enhanced activity at low temperatures. To address this challenge, proteins need to overcome restricted motions at these temperatures; hence, in this work, enzyme engineering was employed to increase the dynamics of the enzyme.

Methods: In this study, a recombinant cold-adapted lipase from a psychrophilic deep-sea bacterium Psychrobactersp.C18 was expressed and purified in a bacterial host. Since no protein model was reported for this lipase, the sequence was modeled via Modeller software, using 4NS4-A PDBID as the template with79.23% sequence identity. Mutations were selected on the loops near the active site to increase the flexibility of the loop structure there by enhancing the enzyme's access to the substrate at low temperatures. The selected single mutations were performed by the quick-change PCR method. Enzymatic activity was evaluated using p-nitrophenyl acetate (p-NPA) as the substrate in the assay buffer at 25°C for 2 minutes.

Results: The results of SDS-PAGE showed that expression and purification of the enzyme has been successfully performed. Based on computational studies, the sequence of the residues of the nearest surface loops to the active site was determined. We generated three mutations in the loop positions including P188G in loop1, L211G in loop2 and Q264W in loop3, and the mutations were confirmed by sequencing. The optimal temperature for the activity of the wild-type enzyme was 30°C, which was reduced to 20°C for the Q264W, and to 15 °C for the P188G and L211G mutated enzymes.

Conclusion: The results showed that by increasing the structural flexibility of enzymes through protein engineering, it is possible to shift their optimum temperature towards lower temperatures.

Keywords: Psychrophilic lipase, Protein engineering, Enzymatic activity

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Abstract: A-10-2538-1

Rosmarinic Acid Loading on Graphene Oxide Nanoparticles Functionalized With Titanium Dioxide and Selenium To Evaluate the Induction of Cytotoxicity and Apoptosis in Prostate Cancer

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Background: Cancer treatment has consistently been a crucial and controversial issue in the world. Many researchers have tried to use plant-based drugs to lower toxicity and enhance the tumor site targeting. Therefore, For the first time, we have successfully synthesized and characterized the graphene oxide-titanium dioxide nanoparticles conjugated with selenium, designed to serve as a biocompatible nanocarrier for delivering Rosmarinic acid to cancer cells. Rosmarinic acid, a potent polyphenol compound, is an ester of caffeic acid and 3,4-dihydroxyphenylacetic acid. It is commonly derived from the Boraginaceae and Nepetoideae subfamilies of the Lamiaceae family. The anticancer ability of Rosmarinic acid has been confirmed against different types of cancers.

Methods: The particle size of RA-GTS-NPs were average 300 nm with a negative surface charge; an Index of dispersion of 0.2 and also show high loading capacity toward Rosmarinic acid. We used the Resazurin assay to evaluate the toxicity of nanoparticles and also identified apoptosis by real-time PCR. In addition, the antioxidant effects of nanoparticles were measured by TAC and CAT assays.

Results: The 50% cell growth inhibition (IC50) of nanoparticles against two prostate cancer cell lines including PC3 and LNCaP were obtained as 98 µg/mL. Cancer Cell treatment with nanoparticles at 50 and 70 µg/mL increased the gene expression of Bax, BCL2, and P53 in prostate cancer cells.

Conclusion: The findings suggest that RA-GO-Ti-Se nanoparticles exhibit promising therapeutic efficacy against the specified type of cancer, indicating their potential as a potent treatment option for this malignancy.

Keywords: Graphene oxide nanoparticles, titanium dioxide, selenium, Anticancer effects, cytotoxicity, Rosmarinic acid, prostate cancer

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Abstract: A-10-2341-1

A Quantum Mechanical Study of the Anti-HIV Activity of the Etravirine

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Background: The human immunodeficiency virus (HIV) is a member of the genus Lentivirus, part of the family Retroviridae. It is the causal agent of HIV infection and acquired immunodeficiency syndrome (AIDS). Several pharmacological approaches have been employed to combat the HIV-1 infection. One of the favorite targets in this fight is the reverse transcriptase enzyme controlling the replication of the HIV genetic material. A group of drugs with antiretroviral activity are the non-nucleoside reverse-transcriptase inhibitors (NNRTI). Etravirine is a small molecule used in the treatment of HIV-1 infections in combination with other antiretroviral agents which received US FDA approval for use in humans in 2008.

Methods: An electronic structure/molecular study conducted with the anti-HIV activity of a group of Etravirine hybrids was carried out. Calculations were done based on the density functional theory (DFT) at the B3lyp/6-311++G level.

Results: The Zero-point energies (ZPE), Enthalpy, Entropy, Gibbs Free energy, CV and total electronic energy of Etravirine, calculated, using DFT-B3LYP method with the 6-311+G basis set which are -3749.1 kcal/mol, 215.863 kcal/mol, 185.5 cal/mol-Kelvin, 160.6 kcal/mol, 215.374 kcal/mol, respectively. The HOMO, LUMO and HLG (HOMO-LUMO Gap) energies of the Etravirine have been calculated at the B3LYP/6-311+G which are -0.23462 eV, -0.06666 eV and 0.27954 eV, respectively. The μ X, μ Y, μ Z and μ tot dipole moments (in Debye) of the Etravirine molecule have been obtained equal to 10.2857, -5.5148, 0.0179 and 11.6709, respectively.

Conclusion: In present study, structural parameters, polarizability, atomic charges and IR spectrum and energy of the Etravirine were collected. Energies (such as Enthalpy, Entropy, Free energy (Gibbs), Zero-point energy), highest occupied molecular orbital (HOMO) energy, lowest unoccupied molecular orbital (LUMO) energy and the bond gap energy (ΔE=ELUMO - EHOMO) were studied.

Keywords: Anti-HIV drugs, Density functional theory (DFT), Etravirine (Intelence)

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Abstract: A-10-2546-1

Increased Serum A-Synuclein Is Associated With Increased Rem Sleep Duration in Chronic Insomnia Disorder

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Background: Chronic insomnia (CI) is the most prevalent sleep disorder, affecting approximately 30 % of world's population. Available evidence indicates that inflammation plays a crucial role in the pathogenesis of CI, but its mechanism is still unknown. The activation of inflammatory pathways in microglia can associate with impaired autophagy, which in turn contributes to the misfolding and accumulation of proteins such as α-synuclein. However, no studies examined the association between α-synuclein and CI and its possible value in the pathogenesis of chronic insomnia disorder. The aim of this study was to evaluate the association between peripheral α-synuclein and clinical features in CI.

Methods: Blood samples were collected from 20 individuals (16 female, mean age 47.1 ± 10.8 years, range 21-65) diagnosed with chronic insomnia disorder based on Pittsburgh Sleep Quality Index (PSQI) and full-night video polysomnography (V-PSG) and 20 healthy individuals (12 female, mean age 44.8 ± 11.6 years, range 21-65) based on PSQI. The serum levels of α-synuclein was evaluated, using enzyme-linked immunosorbent assay (ELISA). Statistical analyses were performed by the SPSS®, version 20.0 (IBM Corporation, Armonk NY; USA).

Results: We found that people with CI had significant increase levels of α-synuclein compared to healthy group. Moreover, we observed significant positive correlation between α-synuclein levels and rapid eye movement (REM) sleep duration ($r = 0.577$, $p\text{-value} < 0.01$) in people with chronic insomnia disorder.

Conclusion: The presence of higher serum levels of α-synuclein in CI group may be associate with reduced accumulation of insoluble and neurotoxic α-synuclein aggregating within neurons, likely due to the decomposition by the activate immune cells in the brain, which in turn allows more normal REM sleep patterns in individuals with chronic insomnia disorder. This study provided new insights on the role of α-synuclein in pathogenesis of CID.

Keywords: Chronic insomnia, α-Synuclein, REM sleep

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Abstract: A-10-2559-1

The Effect of Hydroalcoholic Extract of Ferulago Angulata on Liver Function Parameters and Antioxidant Status in Alloxan-Induced Diabetic Rats

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Background: The aim of this study was to evaluate the hepatoprotective and antioxidant activities of Ferulago angulata Extract (FAE) in experimental diabetic rats.
Methods: 54 adults male Wistar rats divided into 6 groups (n=9). Diabetes was induced in all animals except those in group 1 by the daily intraperitoneal injection of 120 mg/kg alloxan monohydrate for 3 consecutive days. Experimental diabetic rats in groups 3-5 were orally administered with FAE (200,400, and 800 mg/kg/day, respectively). Group 6 was treated with 150 mg/kg of metformin. At the end of week 4, the rats were anesthetized and then sacrificed by cardiac puncture. Then, the levels of liver markers, malondialdehyde (MDA), and antioxidant enzymes capacity were evaluated in each group.
Results: Treatment with FAE resulted in a significant reduction in aspartate transaminase (AST) and alanine transaminase (ALT) activities as well as in the serum and liver tissue contents of MDA in comparison to the diabetic control group ($P<0.001$). The FAE-treated diabetic rats showed a significant increase in catalase, glutathione peroxidase (GPx), and super oxide dismutase (SOD) activities of the liver (P-values were dose-dependent).
Conclusion: These findings suggest that FAE can reduce the complications of diabetes, prevent oxidative stress, and improve antioxidant status in diabetic rats.

Keywords: Ferulago angulata, antioxidant, oxidative stress, diabetes mellitus

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Abstract: A-10-2504-1

Dual Silencing of IGF-1R and Integrity AVβ3 Increased Sensitivity To Chemotherapy in Resistant Colon Cancer Cells

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Background: As a multikinase inhibitor, 5-FU is used to treat a variety of cancers, including colorectal cancer. However, cancer cells undergo a phenotype change using various strategies, such as increasing the expression of integrin AVβ3 and IGF-1F, and they do not respond properly to the drug. Silencing the insulin-like growth factor-1 receptor and integrin gene using siRNA, it is possible to reduce the resistance and increase the sensitivity of cells to the drug. the effect of anti-AVβ3 and IGF-1R siRNAs on the expression of integrin and insulin-like growth factor receptor-1 in SW480 cancer cell line resistant to 5-FU drug was investigated.

Methods: the SW480 colon cancer cell line, resistant to 5-FU drug was stablished by 3-day-5-day cycle method then treated with anti-AVβ3 and IGF-1F siRNAs. IC50 and viability of the cells were estimated using MTT viability test. The expression levels of AVβ3 and IGF-1R are being done using RT-PCR method.

Results: SW480 cell line resistant to 5-FU drug was developed during 60 days of prolonged exposure to the specified dose of this drug. The results showed that the percentage of cell survival after 15 days of exposure in the first and second cycles was 40 and 60%, respectively, and after 30 days of exposure in the third cycle, 70% was obtained. The IC50 of resistant cells was 45.87 µM.

Conclusion: The combined use of AVβ3 and IGF siRNAs in resistant cancer cells might reverse the resistance and sensitize them to the current chemotherapy protocols.

Keywords: Colon cancer, siRNA, SW480, αvβ3, IGF ,5-FU

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Abstract: A-10-2345-1

The Relationship Between the Use of Toll-Like Receptor 4 and the Diagnosis of Urinary Tract Infection in Children: A Systematic Review Study

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Background: Urinary tract infections (UTIs) are prevalent in children due to their distinct physiological characteristics and compromised immune systems. Prompt diagnosis and treatment are crucial to prevent complications. Toll-like receptor 4 (TLR4), a critical component of the innate immune system, may play a significant role in pediatric UTIs.
Methods: Following Cochrane systematic review principles and PRISMA guidelines, a systematic search was conducted across international databases including PubMed, Scopus, Cochrane, and Web of Science, alongside the Google Scholar for grey literature. Keywords used included “Toll-like receptor 4”, “TLR4”, “Urinary tract infection”, “UTI”, “children”. Inclusion criteria encompassed all observational studies investigating TLR4 in children with UTIs. All reviews, interventional and animal studies, letters to editors, and books were excluded. The quality of included studies was assessed, using the Newcastle-Ottawa scale, and data were organized into an extraction table.
Results: Out of 205 initial articles, 147 were removed due to duplication and 47 due to lack of relevance, leaving 11 final articles being included in the study. These articles involved 1470 children aged 6 months to 16 years with UTIs, who had not taken any drugs, such as antibiotics. Urine and blood serum samples were collected and tested. The studies reported a significant increase in TLR4 levels in patients with UTI, suggesting that elevated TLR4 may be associated with the presence of UTIs in children.
Conclusion: This systematic review indicates that TLR4 has a significant antimicrobial role and can serve as a valuable biomarker in the diagnosis of pediatric UTIs. Utilizing TLR4 in clinical practice could enhance the accuracy of UTI diagnoses, leading to better-targeted treatments and improved outcomes for pediatric patients. Further research is warranted to fully understand the mechanisms through which TLR4 contributes to the immune response in children with UTIs and to explore its potential in developing novel diagnostic tools.

Keywords: Urinary Tract Infection, Toll-like receptor 4, Pediatrics, Immune System, Biomarkers.

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Abstract: A-10-2551-1

Unveiling Prognostic Mirnas As Biomarkers in B-Cell Acute Lymphoblastic Leukemia Through Microarray Analysis

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Background: Despite significant improvements in survival rates for pediatric B-ALL in recent decades, complete elimination of the disease by risk-adapted primary treatment remains elusive. This study explores into the intricate world of miRNAs in childhood Acute Lymphoblastic Leukemia, revealing distinct expression patterns and shed light on the potential of miRNAs as biomarkers for prognosis.

Methods: We started by loading necessary libraries such as `GEOquery (version 2.66.0) `the dataset of interest (GSE45839). Data processing was conducted, using R software (version 4.2.2) with several packages, including limma, Mm Palate MiRNA, miRkit, and Agi MicroRNA. The analysis involved differential expression analysis and normalization of the data. A histogram of adjusted p-values is plotted to visualize the distribution of differential expression significance. Additionally, a volcano plot is created to visualize the relationship between log fold change and statistical significance. Finally, a heatmap is constructed using the `pheatmap` package.

Results: The analysis results identified 5 miRNAs with a p-value ≤ 0.05. Among them, 3 miRNAs exhibited upregulation (miR-151-5p(FC=1.18871), miR-146B-5p(FC=0.870839), and miR-486-5p(FC=0.732856)), while 2 miRNAs showed downregulation (miR-1973(FC=-0.8812) and miR-130B(FC=-0.81611)).

Conclusion: In conclusion, this study displayed a dynamic miRNA landscape in childhood ALL with prognostic value. These findings hold promise for the development of miRNA-based prognostic and therapeutic strategies. Further research is warranted to fully connect the potential of miRNAs in improving the lives of children quarrelling ALL.

Keywords: B-cell acute lymphoblastic leukemia, Microarray analysis, MicroRNAs, Prognostic Biomarkers

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2582-1

Investigating the Effect of Visfatin on the Gene Expression of Insulin Receptor and Glut4 in the Myocytic Cell Line C2C12 of Mouse

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Background: One of the major public health issues is the increasing prevalence of obesity, which is associated with a heightened risk of insulin resistance and type 2 diabetes. Adipokines play a role in regulating insulin function. Visfatin, an adipokine isolated from adipose tissue, is known as pre-beta-cell-colony-enhancing factor and is increased in type 2 diabetes. This study aims to investigate the effect of visfatin on the expression of insulin receptor and Glut4 genes in C2C12 myocyte cells of mice.

Methods: This study is an experimental investigation aimed at exploring the molecular pathways activated by visfatin using C2C12 cells, which have the capability to differentiate into skeletal muscle. Following proliferation, the cells were divided into four groups: one control group treated with the drug solvent (DMSO) and three experimental groups treated with visfatin at concentrations of 0.1, 1.0, and 2.0 ng/? . The target gene sequences were obtained from the HGNC database and designed, using GeneRunner software. To confirm the specificity of the primers, Primer-BLAST from the NCBI website was used. Changes in the expression of insulin receptor and Glut4 genes were assessed at 24, 48, and 72 hours using Real-Time PCR. Statistical analyses were conducted for variable comparison and determination of gene expression changes, with P≤ 0.05 considered statistically significant.

Results: The results demonstrated that the expression of the Glut4 gene at a concentration of 1.0 ng/? of visfatin after 72 hours was significantly higher than at concentrations of 0.1 ng and 2.0 ng/?. Additionally, at a concentration of 2.0 ng/? of visfatin after 72 hours, the expression of the insulin receptor gene in the cells increased.

Conclusion: This study demonstrated that visfatin exhibits insulin mimetic effects and induces the activation of insulin receptor and Glut4 gene expression. This effect of visfatin is dependent on both time and concentration.

Keywords: Type 2 diabetes, Insulin receptor gene, Glut4 gene, Visfatin

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Abstract: A-10-2581-1

A DFT Study on the Gepirone

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Background: Gepirone, under the trade name Exxua, was approved by the FDA on September 28, 2023 for the treatment of adults with major depressive disorder. Gepirone, an Azapirone, is a pharmacological analog of buspirone by a novel mechanism that acts selectively on pre- and post-synaptic serotonin 1A receptor (5HT1A) receptors. As a result, this drug is the first antidepressant that can prevent adverse side effects such as sexual dysfunction and weight gain, also earlier clinical trials showed promising results for Gepirone. Its formulation as an immediate-release tablet necessitates frequent administration due to the short half-lives. It hasn't been available an extended-release formulation of Gepirone to make it a potential candidate of antidepressant drugs.
Methods: The molecular structure of Gepirone was designed using GaussView software, followed by quantum mechanical calculations at the B3LYP/6-311+G theoretical level using Gaussian09 software.
Results: In this work, the Zero-point energies (ZPE), Enthalpy, Entropy, Gibbs Free energy, CV, and total electronic energy of Gepirone, were calculated and obtained using the DFT-B3LYP method with the 6-311+G basis set. The HOMO, LUMO, and HLG (HOMO-LUMO Gap) energies of the Gepirone have been calculated at the B3LYP/6-311+G. The μ X, μ Y, μ Z, and μ tot dipole moments of the Gepirone molecule have been obtained.
Conclusion: In this investigation structural parameters, polarizability, atomic charges and IR spectrum of the Gepirone were also collected. Energies (such as Enthalpy, Entropy, Free energy (Gibbs), Zero-point energy), highest occupied molecular orbital (HOMO) energy, lowest unoccupied molecular orbital (LUMO) energy and the bond gap energy (ΔE=ELUMO - EHOMO) were studied.

Keywords: Gepirone, DFT, HOMO and LUMO, Thermodynamic parameters, GaussView

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Abstract: A-10-2591-1

Investigating Important Transcription Factors and Kinases in the Progression of Glioblastoma Cancer in U87 Cell Line

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Background: Glioblastoma multiforme (GBM) is the most common and aggressive primary brain tumor in the adults. with poor patient survival rates and limited treatment success. This study aimed to identify key kinases and transcription factors in GBM using bioinformatics analysis and to validate these findings in the U87 glioblastoma cell line.

Methods: We analyzed the GSE75147 dataset to identify differentially expressed genes in GBM. Protein-protein interactions were explored using the STRING database, and transcription factors and kinases were analyzed via the X2K web tool. Seven genes (HMG20B, RPS6KB2, DVL2, MAP3K6, BCKDK, THAP7, and GTF3A) were selected for laboratory validation. U87 and HUVEC cell lines were cultured, RNA was extracted, and cDNA synthesized. Gene expression was quantified using Real-Time PCR.

Results: Of the seven selected genes, five (DVL2, MAP3K6, BCKDK, THAP7, and GTF3A) showed significantly decreased expression in the U87 cell line compared to HUVEC cells, suggesting potential tumor suppressor roles. HMG20B and RPS6KB2 did not show significant expression differences.

Conclusion: The findings suggest that DVL2, MAP3K6, BCKDK, THAP7, and GTF3A may serve as potential tumor suppressors in GBM, warranting further investigation.

Keywords: Glioblastoma, Tumor Suppressor, Kinase, Transcription Factor, Bioinformatics

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Abstract: A-10-2528-1

Immune Response to Antigenic Stimulation By An Experimental Rabies Vaccine

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Background: The aim of this study was to evaluate *in vitro* immune responses of lymphocytes stimulated by antigens of human rabies experimental vaccine in comparison with a commercial human rabies vaccine.
Methods: Patients with documented human immunodeficiency, hepatitis or each chronic disease were excluded from our study. Peripheral blood mononuclear cells (PBMCs) obtained from donors who have been already immunized with human rabies vaccine and were induced with both vaccine groups have been grown in RPMI1640 medium supplemented with 10% FBS, 100,000 U/ml penicillin, and 100 µg/µl streptomycin. 150,000 cells are cultured into 96-well plate. Extraction of total RNA was performed from the BSR cell line using RNXTM plus solution (Genexir, Iran) according to the manufacturer's instruction. mRNA expression level of the IL-4 and IFN-γ genes was estimated using the appropriate primers. The relative gene expression was assessed compared to the housekeeping gene glyceraldehyde-3-phosphate dehydrogenase (GAPDH) using specific primers.
Results: Stimulation of lymphocytes with different vaccine dilutions was studied through analysis of IL-4 and IFN- γ gene expressions by Quantitative Real-Time Polymerase Chain Reaction (qPCR). Data showed expression of IL-4 and IFN- γ cytokines in donors, while negative control did not show any expression.
Conclusion: The present study data showed increases in both type 1 and type 2 cytokines as indicators of cellular and humoral immunity responses considerably. Furthermore, the muscle and intradermal routes of post-exposure vaccination were not different.

Keywords: Rabies, Vaccine, Immune responses, Antigenic stimulation, IL-4, IFN-γ

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2537-1

Bioinformatics Analysis of Gene Signatures in Endometrial Cancer with Different Grades Reveals Distinct Patterns of DNA Repair Defects and Shifts During Tumor Progression

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Background: Endometrial cancer (EC) is a prevalent form of cancer among women, with increasing incidence and mortality rates. Chromatin remodeling and DNA repair genes play a crucial role in EC differentiation, growth, invasion, and metastasis. An in-depth bioinformatics study was carried out to carefully analyze publicly available gene expression data. The study aimed to identify important genes that are overexpressed in grade 3 EC, as these genes could be potential targets for addressing EC metastasis.

Methods: The investigation involved using the GSE115810 dataset and the R programming language to carefully analyze and visually represent gene expression data from EC patients. Differentially expressed genes (DEGs) were identified using bioinformatics, with strict criteria of a P-value less than 0.05 and a |log2FC| >1, to compare EC patients with different cancer grades. Following this, extensive KEGG pathway enrichment analysis and gene ontology enrichment were conducted to identify enriched DEGs, establish protein-protein interactions, and pinpoint pivotal hub genes. Additionally, a protein-protein interaction (PPI) network for all genes in the two modules was constructed to obtain key modules and nodes.

Results: In a recent study, it was determined that the expression of 9 genes, namely RAD21, PRKDC, ANAPC5, SMARCC1, NR2F6, SF3A1, DHX9, LSM4, and MSH6, demonstrated a significant increase from grade 1 to grade 3 in patients diagnosed with EC. KEGG and DAVID analysis revealed that these genes are involved in non-homologous end-joining, mismatch repair, cell cycle, platinum drug resistance, pathways in cancer, colorectal cancer, and spliceosome pathways.

Conclusion: Patients diagnosed with grade 3 EC face a heightened risk of early distant metastasis and mortality attributed to endometrial carcinoma. Furthermore, the presence of overexpressed novel genes in grade 3 EC significantly raises the probability of disease advancement in cancer staging and the metastasis of EC to the cervix.

Keywords: Bioinformatics, Endometrial Cancer, Cancer Grading, Differentially expressed genes, protein-protein interaction network, hub gene, tumor differentiation

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Abstract: A-10-2548-1

Quantum Computational Analysis of Mavacamten; A DFT Study

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Background: In March 2024, the FDA approved Mavacamten for patients with obstructive hypertrophic cardiomyopathy inadequately controlled by standard therapies, making it the first myosin inhibitor approved for this condition in nearly 40 years. Because of the significant medical importance of the drug mentioned above, we have decided to examine its electronic structure using quantum computing technology.
Methods: The study utilized quantum mechanics (QM) calculations conducted through the density functional theory (DFT) method with the GAUSSIAN 09 software. The structure of the Mavacamten drug was first optimized through gradient procedures at both restricted Hartree-Fock (HF) and hybrid density functional B3LYP levels of theory using the 6-311G basis set. Examination of the results revealed that the optimized structure achieved in this research was situated at the minimum point on the potential energy surface, displaying no negative modes.
Results: In this research, structural parameters such as bond lengths, bond angles, and dihedral angles, along with thermodynamic properties, were calculated at the B3LYP/6-311G level of theory. The electronic energy of the molecule was determined to be -897.7721582 kcal/mole. Furthermore, the Mulliken atomic charges, spin densities, and molecular orbital energies were computed. The highest occupied molecular orbital (HOMO) was measured at -0.22033 eV, while the lowest unoccupied molecular orbital (LUMO) was -0.03478 eV. The dipole moment components in Debye were found to be X= 6.4750, Y=1.5067, and Z= -0.4385, with a total dipole moment of 6.6624.
Conclusion: The drug's optimization was achieved using the B3LYP/6-311G method. This study concentrated on Mavacamten's electronic properties, particularly the energy gap between the HOMO and LUMO. The HOMO-LUMO gap energy was found to be 0.18555 eV, providing valuable insights into Mavacamten's electronic behavior with potential applications in various fields.

Keywords: Mavacamten, DFT, B3LYP/6-311G, HOMO-LUMO gap

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Abstract: A-10-2548-2

Electronic Structural Investigation of Tirbanibulin; A Quantum Mechanics Study

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Background: In December 2020, the FDA approved Tirbanibulin for the topical treatment of actinic keratosis on the face or scalp, marking it as a significant therapeutic advancement. Because of the substantial medical importance of the drug mentioned above, we have decided to assess its electronic structure using quantum computing technology.
Methods: The study utilized quantum mechanics (QM) calculations conducted through the density functional theory (DFT) method with the GAUSSIAN 09 software. The structure of the Tirbanibulin drug was first optimized through gradient procedures at both restricted Hartree-Fock (HF) and hybrid density functional B3LYP levels of theory using the 6-311G basis set. Examination of the results revealed that the optimized structure achieved in this research was situated at the minimum point on the potential energy surface, displaying no negative modes.
Results: Calculations were performed on structural parameters, including bond lengths, angles, and dihedrals, as well as thermodynamic parameters, using the B3LYP/6-311G level of theory. The resulting electronic energy of the molecule was -1398.0941834 kcal/mole. Further, we determined the Mulliken atomic charge, spin density, and molecular orbital energies. The highest occupied molecular orbital (HOMO) was calculated to be -0.27486 eV, while the lowest unoccupied molecular orbital (LUMO) was -0.25613 eV. The dipole moment measurements in Debye were X=1.9662, Y=-0.2946, and Z=-2.5683, yielding a total dipole moment of 3.2479.
Conclusion: The drug was optimized using the B3LYP/6-311G method, with particular attention to its electronic properties. The focus was on analyzing Tirbanibulin's HOMO-LUMO gap, which was found to be 0.01873 eV. This analysis sheds light on Tirbanibulin's electronic characteristics, offering potential insights for its application in various scientific and clinical contexts.

Keywords: Tirbanibulin, DFT, B3LYP/6-311G, HOMO-LUMO gap

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2463-1

Serpina1 Variants in Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) Predisposition: A Case-Control Study

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Background: Metabolic dysfunction-associated steatotic liver disease (MASLD), previously known as non-alcoholic fatty liver disease (NAFLD), occurs when there is steatotic liver disease (SLD) in the absence of harmful alcohol intake and one or more cardiometabolic risk factors. Environmental, genetic, and dietary factors all contribute to the etiology of MASLD. Serpin Family A Member 1 (SERPINA1) is hypothesized to be involved in the pathogenicity of MASLD. In this study, we investigated the association of three variants in the SERPINA1 gene with the incidence of MASLD in patients referred to Ali Ibn Abi Talib Hospital, Zahedan city.

Methods: A total of 240 unrelated subjects were included in the study as case and healthy groups. For genotyping, DNA extraction is followed by a polymerase chain reaction with an amplification refractory mutation system (ARMS-PCR). The statistical analysis was conducted using SPSS V27.0 software.

Results: According to the genotyping results, the G allele of rs6647 A/G was associated with an increased risk of MASLD by OR = 1.71 (95% CI = 1.10–2.60, p = 0.028). Furthermore, the T allele of rs709932 C/T leads to increased risks (OR = 1.77, 95% CI = 1.19–2.57, p = 0.010). In addition, there was no significant association between the rs1303 T/G variant and MASLD (OR = 0.83, 95% CI = 0.51-1.28, p = 0.305).

Conclusion: According to our findings, both rs6647 A/G and rs709932 C/T were associated with an increased risk of MASLD in the Zahedan population.

Keywords: SERPINA1, MASLD, single nucleotide variants

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Abstract: A-10-2346-1

The Role of Glutaminase Enzyme Inhibition in Targeting Metabolic Pathway in Breast Cancer: A Systematic Review Study

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Background: Metabolic reprogramming in cancer cells, such as the Warburg effect, involves altered pathways for growth through increased glucose uptake and lactate production. This metabolic shift supports the proliferation of cancer cells by providing essential nutrients and promoting biosynthetic processes. Glutamine plays a pivotal role in this reprogramming by fueling various anabolic critical processes for cell growth and survival. Targeted therapies for breast cancer can exploit these unique metabolic profiles, the inhibition of glutaminase responsible for converting glutamine to glutamate, a promising therapeutic strategy.

Methods: Following to Cochrane systematic review and PRISMA guidelines, we conducted a comprehensive search across multiple international databases, including PubMed, Scopus, Cochrane, and Web of Science, along with Google Scholar for grey literature. Keywords such as “Glutaminase Inhibition”, “Enzyme Inhibition”, “Breast cancer”, and “Metabolic pathways” were used. Inclusion criteria encompassed all observational studies investigating the impact of glutaminase inhibition on breast cancer treatment. Reviews, interventional studies, animal studies, editor letters, and books were excluded. The quality of included studies was assessed using the Newcastle-Ottawa scale, and data were organized into an extraction table.

Results: Out of 42 initial articles, 22 were excluded due to duplication and 10 for lack of relevance, resulting in 10 articles for final analysis. These studies involved adults with breast cancer, where serum samples were collected and analyzed. The findings indicated that inhibiting glutaminase activity, especially in triple-negative breast cancer (TNBC), revealed glutaminase inhibition as a promising therapeutic target.

Conclusion: Inhibiting glutaminase activity in breast cancer, especially TNBC, is considered a potential therapeutic strategy. This approach not only disrupts cancer cell metabolism but also enhances anti-tumor immune responses and disrupts redox balance, leading to increased cancer cell death. However, the presence of resistance mechanisms and the role of different glutaminase isoenzymes necessitate combination therapies and dual-targeting strategies to maximize therapeutic efficacy.

Keywords: Glutaminase, Enzyme Inhibitors, breast cancer, Metabolic pathways, Glutamine metabolism.

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Abstract: A-10-2392-1

Design, Expression, and Purification of a Fusion Protein Derived from Bone Morphogenetic Protein-2 With A Collagen Binding Domain

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Background: Bone Morphogenetic Protein-2 (BMP-2) is a growth factor commonly used to stimulate osteogenesis in humans. Direct use of BMP-2 requires high doses due to its short half-life, low affinity for collagen sponges, and localized dispersion at the graft site, which can lead to unwanted side effects. This study aimed to design and express a fusion protein composed of a dipeptide derived from BMP-2 and a collagen-binding domain derived from integrin α2β1.

Methods: To produce the designed protein, the nucleotide sequence was synthesized in the Pet26b (+) vector between the ndeI and XhoI restriction sites. The plasmid was transformed into the BL21 (DE3) E. coli strain, and expression of the fusion protein was examined under various conditions, including different IPTG concentrations, temperatures, and incubation times. Optimal expression was achieved in LB medium at 18°C with 0.5 mM IPTG over a 24-hour period. Protein expression was confirmed by western blot analysis using an anti-Histag antibody. Following expression, cell pellets were resuspended, sonicated, and centrifuged. Inclusion bodies were solubilized with 8 M urea, and the protein was purified using affinity chromatography (Ni–NTA). The denatured protein was then renatured by gradually removing urea through dialysis. The expression level and purity of the protein were assessed using SDS-PAGE. Finally, using the ELISA technique, the concentration-dependent binding of the protein to type I collagen was observed.

Results: The fusion protein was successfully expressed in large quantities as an insoluble form and retained its functionality after purification and renaturation. The specific binding of the fusion protein to type I collagen suggests that this approach may offer a more efficient method for bone regeneration, potentially reducing the need for high doses of BMP-2 and minimizing associated side effects.

Conclusion: This innovative strategy could pave the way for improved clinical outcomes in bone repair and regeneration.

Keywords: Expression, Chromatography, E. coli, Fusion protein, BMP-2

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Abstract: A-10-2612-1

Cancer Stem Cells in Cancer Progression

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Background: Cancer stem cells (CSCs) represent specific type of rare cells found in the broad majority of tumors, possessing self-renewal and differentiation capacities. They contribute to the heterogeneous lineages of the cancer cells that form the tumor and share some of the common characteristics with stem cells. This systematic review explains that how cancer stem cell effect in cancer progression.

Methods: In the current study, keywords including Cancer stem cells, Tumor, and Progression were reviewed from the list of Mesh and other credible websites including PubMed, Science Direct, and Google Scholar and the data was organized. The searches comprised all published paper from 2012 to 2023. All of 90 full text was considered and the papers manifested as only abstract was excluded. The full papers selected that investigate the specific role of CSCs in cancer progression only.

Results: In this study 90 article was considered. More than 60 study performed that CSCs exhibit a high tumorigenic potential *in vivo*. Also, in 50 study scientists conclude that the CSCs sustain the cancer by promoting proliferation, and therefore must be targeted when attempting to eliminate cancer for successful and long-lasting results. More than half studies (51 studies) showed that CSCs share similar properties with normal stem cells, including the ability to self-renewal and differentiation that give rise to heterogeneous, differentiated cancer cells making up the bulk of the tumor.

Conclusion: In this review we conclude CSCs act as a critical drivers of tumor progression, and roles in the different stages of cancer which include tumor initiation, promotion, and metastasis.

Keywords: Cancer stem cells, Tumor, Progression

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Abstract: A-10-2451-1

Targeting the Genomic PI3K/AKT/mTOR Pathway in Triple-Negative Breast Cancer

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Background: Triple-negative breast cancer (TNBC) is an aggressive type of breast cancer that lacks estrogen and progesterone receptors and does not express human epidermal growth factor receptor 2 (HER2). The PI3K/AKT/mTOR pathway is a critical regulator of cell growth, proliferation, survival, and angiogenesis and is frequently altered in TNBC, contributing to aggressive behavior, chemotherapy resistance, and poor prognosis. Because patients with TNBC have a lower survival rate than other breast cancer subtypes, prompt diagnosis, and multimodality treatment are required. Therefore, this systematic review investigated the therapeutic potential of targeting the genomic PI3K/AKT/mTOR pathway in TNBC.

Methods: In this article, we searched PubMed, Google Scholar, ScienceDirect, Web of Science, and Scopus from its inception to July 3, 2024. Data were collected according to PRISMA guidelines. 56 out of 840 search results met the inclusion criteria.

Results: Most of the identified genetic alterations were associated with important genes in this pathway, including PIK3CA, PTEN, AKT, RPS6KB1 (S6K1), and mTOR. By analyzing bioinformatics data, molecular biology, and clinical models, we found important genomic regulators of the PI3K/AKT/mTOR pathway in TNBC. We investigated the efficacy of small molecule inhibitors in suppressing tumor growth and improving treatment outcomes. The results can be categorized into three main groups of inhibitors: 1. PI3K inhibitors 2. mTOR inhibitors and 3. AKT3 inhibitors. Combining these inhibitors with chemotherapy has been proven to extend the duration of progression-free survival and overall survival. The simultaneous inhibition of genes of this pathway and genes related to cell cycle, apoptosis, and angiogenesis may be an effective treatment for TNBC. We investigated the role of genomic alterations in this pathway as predictive biomarkers of treatment response and also chemotherapy sensitivity.

Conclusion: These findings highlight the potential of targeting the PI3K/AKT/mTOR genomic pathway in treating TNBC to improve outcomes and overcome resistance mechanisms.

Keywords: Triple-negative breast cancer, genomic targeting, small molecule inhibitors, PI3K/AKT/mTOR pathway

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Abstract: A-10-2612-2

Stem Cell Therapies for Treatment of Liver Disease

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Background: The liver is the largest vital organ in the human body and performs essential biological functions, including detoxification of the organism, metabolism, supporting digestion, vitamin storage, and other functions. Mesenchymal stem cells (MSCs) from various tissues have emerged as potential candidates for cell transplantation to promote liver regeneration. In this systematic review study we investigate whether stem cell therapies is suitable choice for liver disease or not.

Methods: In the current study, keywords including Stem cell, Treatment, and liver diseases were reviewed from the list of Mesh and other credible websites including PubMed, Science Direct, and Google Scholar and the data was organized. The searches comprised all published paper from 2015 to 2023. All of full texts were considered and the papers manifested as only abstract was excluded. The full papers selected that demonstrate the role of stem cell therapies for treatment of liver disease.

Results: All of our study (80 original and review study) confirmed that Adipose-derived Mesenchymal stem cells are easily differentiated into hepatocyte-like cells (HLCs) as they change in morphology and cell function after treatment with specific cytokines and when exposed to a liver-damaged internal microenvironment. More than half articles (48 studies) concluded that MSCs have immunomodulatory properties through both adaptive and innate immune systems and secrete a variety of trophic factors such as growth factors and cytokines beneficial for liver regeneration. In this review study twenty-five study was about liver test after cell therapies. Seventeen of the twenty-five studies which looked at liver function tests as an outcome measure did report statistically significant improvements in patients' results after cell therapy.

Conclusion: Our study concluded MSCs can be differentiated into multiple cell lineages, including hepatocytes, both *in vivo* and *in vitro*. Also, stem cell transplantation as an effective alternative therapy for hepatic diseases can be use.

Keywords: Stem cell, Treatment, Liver Diseases

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Abstract: A-10-2618-2

Emerging Biomarkers in Diabetic Neuropathy: Visfatin, Progranulin, and Vitamin D3 Insights for Enhanced Understanding and Clinical Management

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Background: Diabetes mellitus, a complex metabolic disorder, is a significant global health concern with a growing prevalence. Uncontrolled diabetes can lead to microvascular complications including diabetic nephropathy (DN), diabetic retinopathy (DR), and diabetic peripheral neuropathy (DPN). The incidence of DPN increases with diabetes duration due to poor glycemic control, hyperglycemic-oxidative stress, and inflammatory cytokines. Identifying reliable biomarkers for early detection and monitoring of DPN is crucial for effective management. This study evaluated the levels of Visfatin, Progranulin, and Vitamin D3 in diabetic patients with and without DPN compared to healthy controls.

Methods: Subjects (76 males and 74 females, 40-80 years old) were selected from AL-Imam ALhussain Hospital in Dhi Qar, Iraq, from February to April 2023. Patients were categorized into three groups: Case group with Type 2 Diabetes (T2D) (n = 50), DPN (n = 50), and healthy controls (n = 50).

Results: The DPN and T2D groups had significantly higher Visfatin and Progranulin values compared to the control group ($p<0.05$). Conversely, DPN and T2D groups had significantly lower Vitamin D3 values than the control group ($p<0.05$). ROC curve analysis demonstrated differences in the sensitivity and specificity of these biomarkers.

Conclusion: The study suggests that Vitamin D3 deficiency may be associated with nerve damage, potentially exacerbating DPN symptoms. Both Progranulin and Visfatin are considered excellent biomarkers for early detection and progression monitoring of diabetic neuropathy in T2D patients. These findings underline the importance of these biomarkers in the clinical management of diabetes-related complications.

Keywords: Diabetic peripheral neuropathy (DPN), Type 2 Diabetes (T2D), Visfatin, Progranulin, Vitamin D3

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2617-1

Evaluation of Serum Ceruloplasmin, Transferrin, and Some Oxidative Stress Markers in Type 2 Diabetes Patients with Nephropathy

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Background: The aim of this study is to investigate and evaluate the serum concentrations of ceruloplasmin, transferrin, and selected oxidative stress markers in individuals diagnosed with Type 2 diabetes (T2D), specifically focusing on those with nephropathy. The primary objectives are to elucidate potential alterations in these biomarkers in diabetic patients with nephropathy compared to those without nephropathy and to establish correlations, if any, between the levels of these proteins and oxidative stress markers.
Methods: This case-control study comprises three groups: 40 patients with T2D and nephropathy, 40 patients with T2D only, and 40 healthy individuals serving as the control group. Peripheral venous blood samples were obtained following an overnight fasting, processed to isolate serum specimens, and subsequently analyzed for ceruloplasmin (CP), transferrin (Tf), glutathione peroxidase (GPx), total antioxidant capacity (TAC), superoxide dismutase (SOD), and malondialdehyde (MDA).
Results: The levels of SOD, GPX, and TAC were notably reduced in diabetic patients with and without nephropathy. Conversely, the level of MDA was markedly elevated in diabetic patients with nephropathy when compared to the control group. The levels of transferrin were notably elevated in the DN group compared to both the diabetic and control groups. The levels of ceruloplasmin were significantly higher in diabetic patients with nephropathy compared to diabetic patients and showed a non-significant increase compared to the control group.
Conclusion: The findings of this study suggest that ceruloplasmin and transferrin levels may serve as predictive variables for the development of diabetic nephropathy in patients with type 2 diabetes. The study also indicates the importance of the role of oxidative stress in the development DN in patients with T2D.

Keywords: Oxidative stress, Type 2 diabetes, Nephropathy, Ceruloplasmin, Transferrin

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Abstract: A-10-2582-2

The Effects of Hydroalcoholic Extract of Teucrium Polium on the Correlation of Lipids and Lipoproteins with Liver Enzymes in Hypertriglyceridemic Rats

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Background: Hyperlipidemia, marked by high concentrations of triglycerides (TG), cholesterol (chol), and low-density lipoprotein cholesterol (LDL-C), increases the risk of liver diseases and atherosclerosis. Controlling hyperlipidemia can reduce these risks. Dyslipidemia and liver problems are closely related. In this study, the relationship between the serum concentrations of lipids and lipoproteins and liver enzymes in hypertriglyceridemic rats was investigated following the consumption of the hydroalcoholic extract of Teucrium polium.

Methods: This study involved 48 male Wistar rats, divided into six equal groups: four treatment groups (1,2,3,4), normal control group, and hyperlipidemic control group. Hypertriglyceridemia was induced using Triton X-100 (150 mg/kg BW). Treatment groups 1, 2, and 3 received Teucrium polium extract at 25, 50, and 100 mg/kg BW, respectively, for 22 days, while group 4 received gemfibrozil (10 mg/kg BW). After blood sampling, serum levels of TG, Chol, HDL-C, ALP, SGOT, and SGPT were measured using enzymatic kits and autoanalyzer, and LDL-C levels were calculated using the Friedewald equation. Data were analyzed with SPSS, with $p<0.05$ considered significant.

Results: The ALP level significantly decreased in the Teucrium polium group at a concentration of 100 mg/kg compared to the 25 mg/kg, Gemfibrozil, and hyperlipidemic control groups. The 50 mg/kg group also showed lower ALP levels compared to the 25 mg/kg and Gemfibrozil groups. Serum SGOT and SGPT levels did not differ significantly. All Teucrium polium groups and the Gemfibrozil group had lower LDL-C, TG, and chol levels, and higher HDL-C levels compared to the control group ($p<0.05$). Only in the hyperlipidemic control group, a significant inverse correlation was found between increased HDL-C and decreased SGOT ($p=0.009$) and SGPT ($p=0.038$) levels.

Conclusion: Teucrium polium extract effectively reduces ALP levels in a dose-dependent manner, outperforming Gemfibrozil. It also lowers LDL-C, TG, and chol while increasing HDL-C. These effects suggest potential benefits for managing hyperlipidemia and improving liver function.

Keywords: Teucrium polium, Hypertriglyceridemia, Liver enzymes, Lipids ،Lipoproteins

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Abstract: A-10-2374-1

Ameliorative Effects of Combination Therapy with Metformin and Crocin in Experimental Colitis in Rats

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Background: Inflammatory bowel disease (IBD) is characterized by aberrant immune responses in the colon leading to the inflammatory cascades, and is progressing all over the world. Metformin (MTF) and crocin have similar effects in balancing gut microbiota, improving epithelial barrier permeability, reducing inflammation, and oxidative stress as the main triggers of IBD pathogenesis. Since the pharmacotherapy of IBD remains challenging, the present study aims to investigate the effects of combination therapy with MTF and crocin on the colitis model induced by acetic acid.

Methods: Acute colitis was induced in Wistar rats by intra-rectal administration of 2 ml of 3% acetic acid. The study included 9 groups of rats as follows: normal group treated with normal saline, control colitis induced by acetic acid and treated with normal saline, reference group received dexamethasone (1 mg/kg. i.p), MTF-treated groups received (100, 150 and 200 mg/Kg) of drug, Crocin-treated groups received (20 and 30 mg/Kg) of crocin, and combination group treated with 150 mg/Kg of MTF and 20 mg/Kg of crocin. Colon tissues were collected to assess macroscopic and microscopic parameters, MPO activity, and MDA level.

Results: Our data clarified that MTF and Crocin both alone and in combination significantly ameliorated the colitis severity and colitis features. Furthermore, the mentioned doses of drugs reduced the MPO activity and MDA levels as compared to the negative control group.

Conclusion: MTF, crocin, and combined administration of them could exert ameliorative effects in colons of acetic acid-induced colitis rats which is probably due to their anti-inflammatory and anti-oxidant properties.

Keywords: Inflammatory Bowel Disease, Ulcerative Colitis, Crocin, Metformin, Combination therapy

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Acta Biochimica Iranica

Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2627-1

Develop a Highly Efficient Process to Separate and Extract Desferrioxamine B Produced by Streptomyces Pilosus

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Background: Desferrioxamine-B (DFB), used to treat thalassemia patients who have iron poisoning due to frequent blood transfusions, is produced by Streptomyces pilosus. However, its low production makes isolating and purifying DFB challenging for commercialization. So far, several methods have been used to purify DFB, mainly involving chromatography and inexpensive ion exchange resins. This research aims to develop a highly efficient process for separating and extracting DFB, a drug to treat patients with thalassemia with iron poisoning due to blood transfusions, produced by Streptomyces pilosus.

Methods: During the DFB separation process, the culture medium was first centrifuged to separate the insoluble materials and concentrate the supernatant solution. Following this, cation exchange chromatography was carried out with various resins. Out of the examined resins, Prolite C100H was chosen for further research due to its ability to efficiently absorb drugs, and its renewability, availability, and cost-effectiveness.

Results: The study found that organic solvents had a greater capacity to absorb and reabsorb the active substance from the resin. Furthermore, the investigation of different volume ratios of organic solvents mixed with water (100, 90, 50, and 10 v/v%) on the adsorption and desorption of DFB to the column revealed that 90 v/v% ethanol and acetone solvents with water had the highest reabsorption rates. By examining the effect of different acidic pHs on the adsorption rate of DFB to the cationic prolite column, the highest adsorption rate (above 95%) was obtained at pH 5 with dilute HCl.

Conclusions: Performing a one-step extraction process with a C100H prolite cationic column at pH 5 and washing with a ratio of 90 to 10 organic solvents of ethanol and acetone to water, it was possible to recover 40% of DFB from the culture medium, which is a high recovery amount that has been achieved so far with a single step Chromatography.

Keywords: Streptomyces Pilosus, Desferrioxamine B, Ion exchange chromatography, Purification

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2630-1

A Molecular and Computational Study of Galbanic Acid as a Regulator of Sirtuin1 Pathway in Inhibiting Lipid Accumulation in HepG2 Cells

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Background: Sirtuin1 (SIRT1) plays a crucial role in the pathophysiology of non-alcoholic fatty liver disease. We investigated the mechanistic role of galbanic acid (Gal) as a regulator of SIRT1 *in silico* and *in vitro*.
Methods: HepG2 cells were treated with Gal in the presence or absence of EX-527, a SIRT1-specific inhibitor, for 24 h. Sirtuin1 gene and protein expression were measured by RT-PCR and western blotting, respectively. It has been docked to the allosteric reign of SIRT1 (PDB ID: 4ZZJ) to study the effect of Gal on SIRT1, and then the protein and complex molecular dynamic (MD) simulations had been studied in 100 ns.
Results: The semi-quantitative results of Oil red ($p < .03$) and TG level ($p < .009$) showed a significant reduction in lipid accumulation by treatment with Gal. Also, a significant increase was observed in the gene and protein expression of SIRT1 ($p < .05$). MD studies have shown that the average root mean square deviation (RMSD) was about 0.51 Å for protein structure and 0.66 Å for the complex. The average of radius of gyration (Rg) is 2.33 and 2.32 Å for protein and complex, respectively, and the pattern of root mean square fluctuation (RMSF) was almost similar.
Conclusion: Computational studies show that Gal can be a great candidate to use as a SIRT1 ligand because it does not interfere with the structure of the protein, and other experimental studies showed that Gal treatment with SIRT1 inhibitor increases fat accumulation in HepG2 cells.

Keywords: Galbanic acid, Sirtuin1, Lipid accumulation, HepG2 cells

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2630-2

Investigating the Relationship Between Magnesium Levels and Diabetes Mellitus in Pregnant Women

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Background: Gestational diabetes mellitus (GDM) is defined as one of the three main types of diabetes mellitus (DM). It is established that GDM is associated with exceeding nutrient losses owing to glycosuria. Magnesium (Mg), as one of the essential micronutrients for fetal development, acts as the main cofactor in most enzymatic processes. The aim of this study was to measure serum and cellular levels of Mg, albumin, creatinine (Cr), and total protein to further clarify the relationship between these components and DM in pregnant women.
Methods: Blood samples were obtained from 387 pregnant women. The participants were classified into four groups based on their type of diabetes, namely GDM (n=96), DM (n=44), at high-risk of DM (n=122), and healthy controls (n=125). All participants' fasting blood glucose (FBG), Cr, albumin, Mg, and total protein in the serum levels and red blood cell Mg (RBC-Mg) were measured during 24-28 weeks of gestation. Groups were compared for possible association between DM and abortion, gravidity, and parity.
Results: The serum levels of Cr, FBG, albumin, Mg, and RBC-Mg were statistically different among four groups (P =0.001). Significant lower levels of RBC- Mg was observed in all studied groups in comparison with controls.
Given a positive correlation between DM and abortion, it seems that decreased levels of RBC-Mg and serum albumin can increase the risk of abortion in pregnant women. Our data demonstrated significant alterations in albumin, Mg, and creatinine concentrations in women with DM or those at high risk of DM during their gestational age.
Conclusion: Taken together the measurement of these biochemical parameters might be helpful for preventing the complications, and improving pregnancy outcomes complicated with DM.

Keywords: Gestational diabetes mellitus, Magnesium, Serum albumin, Diabetes mellitus, Pregnancy

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2630-3

Can Glycosylated Hemoglobin and Fasting Blood glucose Replace Glucose Challenge Test in Screening for Gestational Diabetes?

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Background: The present study aimed to compare the diagnostic values of glycosylated hemoglobin (HbA1c) and fasting blood glucose (FBG) using the glucose challenge test (GCT) in screening for gestational diabetes.
Methods: A total of 618 women at 24-28 weeks of pregnancy were selected, and their FBG and HbA1c were measured using the GCT. The obtained results were compared in terms of sensitivity, specificity, as well as positive and negative predictive values using the ROC curve.
Results: At the cut-off point of 1.4, sensitivity was 69.74% and specificity was 69.05 for the FBG test; at the cut-off point of 6.6, sensitivity was 90.79% and specificity was 80.95% for the HbA1c test; the area under the ROC curve was 0.925 with a 95% confidence interval (0.979, 0.872).
Conclusion: The diagnostic values of the HbA1c test and GCT were favorable in screening for gestational diabetes; the HbA1c test also showed a high diagnostic value in women with positive OGCT and GCT results.

Keywords: Diabetes, Pregnancy, Glucose challenge test, Glycosylated hemoglobin

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2631-1

Liposome-Mediated Transport of MicroRNA Provides an Extra Level of Control on Gene Networks and Facilitates Nuclear Reprogramming

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Background: MicroRNA (miRNA)-mediated cell engineering is a promising approach for reprogramming cells and generating customized tissues for therapeutic applications. This technique also facilitates the exploration of human adult stem cells for fundamental research, with an emphasis on refining transduction-free reprogramming methods to reduce tumorigenesis risks.

Methods: The current study investigated the introduction of miRNAs into human mesenchymal stem cells (hMSCs) using cationic liposomal nanoparticles under varying preservation conditions. The expression of pluripotency factors, specifically OCT4, SOX2, and NANOG, was quantified using real-time quantitative PCR (qPCR).

Results: The findings indicate that miR-302a and miR-34a are pivotal in regulating pluripotency by interacting with key transcription factors such as OCT4, PARP1, SOX2, and NANOG. Notably, the application of liposomal miRNA-302 significantly enhanced the expression of these pluripotency-associated transcription factors compared to free miRNA, achieving statistical significance ($P<0.05$). Conversely, liposomal miRNA-34 did not significantly alter the expression of these markers.

Conclusion: The research suggests that liposomal miRNAs (LP-miRs) can effectively stimulate pluripotency precursors. As small-molecule therapeutics, LP-miRs hold the potential for influencing cell reprogramming and engineering, enabling the conversion of cells into various lineages. These insights deepen the understanding of pluripotency regulation mechanisms, which are crucial for advancements in regenerative medicine. The study underscores the therapeutic potential of miRNA-based strategies in enhancing stem cell functionality and safety in clinical applications.

Keywords: Reprogramming, Liposomal-delivered miRs (LP-miRs), Pluripotency, Transcription factors, Human mesenchymal stem cell

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2582-3

The Effects of the Hydroalcoholic Extract of Teucrium Polium on Serum Levels of Adiponectin, CPK, and Hs-CRP in Hypertriglyceridemic Rats

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Background: Hyperlipidemia is a risk factor for cardiovascular diseases. Managing it effectively can reduce the incidence of these diseases. HS-CRP and CPK are known risk factors for coronary artery disease, while adiponectin, an anti-atherogenic plasma protein secreted by adipocytes, plays a role in lipid metabolism and inflammation. This study aims to investigate the effects of the hydroalcoholic extract of Teucrium polium on serum levels of adiponectin, CPK, and HS-CRP in hypertriglyceridemic rats.

Methods: This experimental study was conducted on 48 male Wistar rats, which were divided equally into six groups: a normal control group, a hyperlipidemic control group, and four treatment groups (labeled 1, 2, 3, and 4). Hypertriglyceridemia was induced by injecting Triton X-100 at a dose of 150 mg/kg body weight in normal saline. Subsequently, treatment groups 1, 2, and 3 were gavage with Teucrium polium extract at doses of 25, 50, and 100 mg/kg body weight, respectively, for 22 days, while treatment group 4 received gemfibrozil at a dose of 10 mg/kg body weight. After blood sampling, serum levels of HS-CRP and adiponectin were measured using the ELISA technique, and serum levels of CPK were measured using an autoanalyzer with validated enzymatic kits. The data were analyzed using SPSS 2018, with $p<0.05$ considered significant.

Results: The adiponectin level in the 25 mg/kg body weight Teucrium polium extract treated group ($p=0.002$) and the gemfibrozil group ($p=0.014$) was significantly lower than that in the hyperlipidemic control group. The adiponectin level in the 100 mg/kg body weight Teucrium polium extract group was significantly higher than in the 25 mg/kg body weight group ($p=0.003$) and the gemfibrozil group ($p=0.023$). There was no significant difference in serum concentrations of HS-CRP and CPK.

Conclusion: Teucrium polium extract reduces adiponectin levels in hypertriglyceridemic conditions but has no significant effect on HS-CRP and CPK levels.

Keywords: Teucrium polium ،Adiponectin ،HS-CRP ،Hypertriglyceridemia

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2357-2

Investigation of the Serum Insulin Hormone Level and the HOMA-IR in Patients with Metabolic and Non-Metabolic Fatty Liver Disease and Healthy Individuals

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Background: Fatty liver, characterized by fat buildup in liver cells, is primarily caused by metabolic disorders but can also occur in individuals without these issues. The reasons behind non-metabolic fatty liver are not fully understood with various theories proposed. The insulin hormone, crucial for metabolism, is linked to liver fat accumulation and insulin resistance (IR) plays a key role in both metabolic and non-metabolic fatty liver development. IR leads to increased fat production, reduced fat breakdown, and higher fat accumulation in the liver. This study investigated serum levels of insulin hormone and HOMA-IR in patients with metabolic and non-metabolic fatty liver and healthy individuals.

Methods: We collected serum samples from patients with metabolic fatty liver (n = 58), non-metabolic fatty liver (n=41), and healthy individuals (n=23). The ELISA technique was used to determine insulin hormone levels. Also, HOMA-IR was calculated. Statistical analyses were performed by SPSS software.

Results: Insulin hormone levels increased significantly in patients with metabolic and non-metabolic fatty liver compared to the control group (P=0.002 and P=0.000, respectively). Non-metabolic fatty liver patients showed higher insulin hormone levels compared to the patients with metabolic fatty liver but the differences were not significantly (P=0.345). HOMA-IR also increased significantly in both metabolic and non-metabolic fatty liver patients compared to healthy individuals (P=0.000). However, non-metabolic fatty liver patients showed an increase in IR compared to the patients with metabolic fatty liver, but not significantly (P=0.681).

Conclusion: Elevated IR and serum insulin levels are associated with both metabolic and non-metabolic fatty livers, potentially playing a crucial role in non-metabolic fatty liver development. Patients in the early stages of non-metabolic fatty liver disease may have higher HOMA-IR levels due to increased fasting blood glucose, prompting increased insulin secretion. This indicates a less severe disease in these patients.

Keywords: Metabolic fatty liver, Non-metabolic fatty liver, Insulin, Insulin resistance, HOMA-IR

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2590-1

A Meta-Analysis Study on the Genetic Biochemical Disease of Phenylketonuria Using Scientometrics

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Background: Phenylketonuria is the most common disorder caused by an innate error in amino acid metabolism. This is due to a mutation in the phenylalanine hydroxylase gene. High concentration of phenylalanine leads to brain dysfunction. In severe cases, phenylketonuria causes severe mental retardation, epilepsy, and behavioral problems.
Methods: This systematic review of meta-analysis and scientometrics was conducted using VOSviewer software to examine the scientific gap and scientific genetic and biochemical research of phenylketonuria disease to help future studies by drawing a map and general statistics of this disease. PubMed databases were searched from 2010 to 2024. 1220 publications were retrieved. Then, a scientometric analysis of the scientific literature on phenylketonuria was performed to evaluate the key issues and trends in the past decades. These statistical data help to understand phenylketonuria and examine it from different aspects.
Results: After studying 1220 articles, topics such as age of onset, countries, incidence rates in humans and animals, biochemical and genetic factors, and diagnostic and therapeutic studies were evaluated. The age of onset was higher in men and women than in children, infants, and other ages. The countries of China and the United States of America had the highest rate and Iran was less susceptible to this disease. The incidence of this disease in humans is higher than in animals (mice and rats). Biochemical factors such as enzymes, vitamins, and minerals, and genetic factors such as mutation, alleles, phenotype, and recombinant proteins are effective. The most effective treatment for phenylketonuria is diet and in some cases gene therapy.
Conclusion: Research on the metabolic disease phenylketonuria is progressing. Although scientometric data can be used to examine general statistics of various topics, it requires further investigations to obtain more detailed data.

Keywords: Phenylketonuria, Meta-analysis, Scientometrics, Systematic review

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Abstract: A-10-2639-1

Unlocking the Potential of Aptamers: A Revolutionary Alternative to Antibodies for Enhanced Molecular Biomarker Detection

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Background: Aptamers are short oligonucleotides with single-stranded regions or peptides that recently started to transform the field of diagnostics. Their unique ability to bind to specific target molecules with high affinity and specificity is at least comparable to many traditional biorecognition elements. Compared to antibodies, aptamers are more flexible in design, have lower immunogenicity, greater chemical/thermal stability, and are easier to modify. They can target a wide range of molecules including ions, small molecules, proteins, cells, and even organs. Aptamers are chemically synthesized, making them easier and less expensive to produce at scale.
Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords aptamer, cancer detection, antibody, 81 articles related to inclusion criteria were extracted and then analyzed.
Results: The exploration of aptamers as alternatives to antibodies for molecular biomarker detection has several potential advantages like stability. Aptamers are often more stable than antibodies, which can denature under certain conditions. The production of aptamers can be less expensive and faster than producing monoclonal antibodies. They can be chemically modified more easily than antibodies, allowing for enhanced functionality and stability. Aptamers generally have lower immunogenicity compared to antibodies, making them less likely to provoke an immune response. Aptamers can be designed to bind small molecules, which is often more challenging with antibodies.
Conclusion: While challenges remain, aptamers represent a revolutionary tool for enhancing molecular biomarker detection, potentially overcoming limitations of antibody-based methods and enabling more comprehensive proteomic analysis. Their unique properties make aptamers well-positioned to unlock new possibilities in personalized medicine and disease management.

Keywords: Aptamer, cancer detection, antibody

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Abstract: A-10-2639-2

The Impact of Microenvironmental and Circulating Lactate on Breast Cancer Progression

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Background: Lactate represents the main product of pyruvate reduction catalyzed by the lactate dehydrogenase enzymes family. It is produced during glycolysis, leading to extracellular acidification that under hypoxic conditions promotes tumor invasion, metastasis, and immune evasion. The ability to shift between different metabolic pathways is a characteristic of breast cancer cells and is associated with an aggressive phenotype. The aim of this study is to investigate the effect of microenvironmental and circulating lactate on the progression of breast cancer.
Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords lactate, aerobic glycolysis, and breast cancer. 72 articles related to inclusion criteria were extracted and then analyzed.
Results: The acidic tumor microenvironment promotes processes like metastasis, angiogenesis, and immunosuppression, which are associated with worse clinical prognosis in breast cancer patients. Lactate acts as an oncometabolite, increasing transcription factors that drive tumor progression. Breast cancer cells exhibit increased glycolysis, producing large amounts of lactate even in the presence of oxygen. This leads to acidification of the extracellular matrix in the tumor microenvironment. Lactate production and transport by breast tumors is complex. While bulk tumors accumulate lactate, the tumor microenvironment may not experience high lactate levels due to rapid exchange with the circulation.
Conclusion: Collectively, this oncometabolite deserves attention during disease monitoring and bears great potential as a biomarker in Breast Cancer.

Keywords: Lactate, Anaerobic glycolysis, Breast cancer

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2580-3

Antioxidant, Anti-Amylase, Anti-Lipase, and Hypoglycemic Efficacy of Satureja Essential Oil

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Background: Satureja is an aromatic plant commonly used in meals for flavouring and as a folk remedy for treating various symptom conditions, for instance, infectious diseases, indigestion, diarrhea, cramps, nausea, and muscle pains.

Methods: The protective effects against biomolecules, the anti-amylase and anti-lipase activity, and the anti-hyperglycemic (HG) capacity of Satureja essential oil (SEO) have been explored in this study. SEO extracted by hydrodistillation and analyzed using gas chromatography-mass spectrometry. Total antioxidant was determined by ABTS decolorization. Lipase and amylase activities were determined by monitoring the decomposition of p-nitrophenyl butyrate and starch. The macrophage cell line was grown in DMEM media in the presence of SEO. NADH oxidase activity was measured by monitoring NADH breakdown. The expression of NOX, NF-kB, and NRF2, were tested in the treated cells by real-time PCR.

Results: The major constituents of SEO were carvacrol, γ-terpinene, p-cymene, thymol, and α-terpinene. Different SEO with different constituents exhibited comparable antioxidant capacity (IC50= 0.170-0.215 mg/mL), anti-linoleic acid oxidation (IC50=0.137-0.195 mg/mL), anti-lecithin oxidation (IC50=0.126-0.134 mg/mL), anti-starch oxidation (IC50=0.155-0.199 mg/mL), anti-protein oxidation (IC50=0.166-0.211 mg/mL), anti-amylase capacity (IC50=0.202-0.230 mg/mL), and anti-lipase capacity (IC50=0.24-0.260 mg/mL). Hyperglycemia stimulates NOX, NFR2, NF-kB, and hydrogen peroxide in macrophages. SEO (at 0.03 and 0.06 mg/mL) decreased NOX and NF-kB activity and hydrogen peroxide and increased NFR2 in hyperglycemia-stimulated macrophages. SEO can reduce oxidative stress indicators by inhibiting NOX and NF-KB expression and enhancing NRF2 expression in macrophages treated with hyperglycemia.

Conclusion: Regardless of the differential chemical composition, the biological activity of SEO is similar. This means the synergism between all chemical components of SEO especially monoterpenes and monoterpenoids is more important in this biological activity until one of these compounds with high percent. The current investigation introduces SEO as a possible functional ingredient for bioactive food products for the treatment of diabetes, oxidative stress, and inflammation.

Keywords: Satureja essential oil, Biomolecule oxidation, Lipase, Amylase, Hyperglycemia

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2642-1

Investigating the Effect of Capsaicin on the Process of Angiogenesis of the Chorioallantoic Membrane of Chick Embryos

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Background: Angiogenesis is the biological process of sprouting new vessels from existing vessels in the tissue. The main factor in the molecular guidance of this process are vascular endothelial growth factors (VEGF) and fibroblast growth factor (FGF). Considering the importance of plant medicine sciences and also, the role of angiogenesis in the processes such as wound healing, menstrual cycles, placental growth, and ovulation, the aim of this study was to investigate the effect of Sulforaphane on changes in the gene expression of VEGF and FGF in the angiogenesis pathway of the chorioallantoic membrane (CAM) of chick embryos.

Methods: In this research, 42 Ross spray eggs were randomly divided into 6 groups including control, laboratory control (PBS) and 4 experimental groups. After incubation, on the second day of the window, an egg was created and in on the eighth day, after placing the gelatin sponge on the chorioalantoic curve, the Sulforaphane were injected with doses (80-160-320 and 640 µg/ml) onto the chorioalantoic membrane of the chick embryo. On the twelfth day, the corioalantoic membrane was taken and length, the number of vascular splits, weight and height of the embryos were measured. The collected data were analyzed by Excel and SPSS 20 statistical software.

Results: The average number and total length of vascular branches in the laboratory control group did not show any significant difference compared to the control group. The average number and length of vascular branches in concentrations of 80-160-320 and 640 µg/ml of Sulforaphane showed a significant decrease compared to the control group.

Conclusion: According to this study, the Sulforaphane has an inhibitory effect on angiogenesis in the chorioallantoic membrane of chick embryos. Also, it seems that Sulforaphane can be used to inhibit angiogenesis in cancer tissues.

Keywords: Angiogenesis, Capsaicin, Chorioalantoic Membrane, Chick Embryo

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2645-1

Evaluation of Antioxidant Potential and Free Radical Scavenging Activity of Methanol Extract from Scrophularia Striata

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Background: The effectiveness of Scrophularia striata in controlling infections and promoting wound healing has been reported. This study aimed to investigate the antioxidant properties of the methanol extract from Scrophularia striata.

Methods: Scrophularia striata, a perennial wild plant found in various temperate and tropical areas of Iran, underwent a methanol extraction process to obtain its active compounds. The antioxidant property of the methanol extract of Scrophularia striata was evaluated by quantifying the total antioxidant level, determining the total phenol content, and conducting DPPH radical scavenging assays.

Results: As the extraction concentrations of Scrophularia striata increase, both the total antioxidant level and total phenol content rise dramatically. With the progression of time and increase in plant extract concentrations, the efficacy of DPPH radical scavenging also shows a corresponding enhancement. Moreover, the IC50% value of Scrophularia striata for DPPH radical scavenging consistently decreases over the observation period.

Conclusion: The data suggest that Scrophularia striata possesses antioxidant properties. The presence of flavonoids and phenolic compounds in Scrophularia striata highlights its potential to alleviate various disorders by modulating oxidative stress levels.

Keywords: Scrophularia Striata, Antioxidant, Oxidative Stress, Total Phenol

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2622-2

Anti-Apoptotic Effects of Hesperidin and Orapten on 6-Hydroxydopamine-Induced Neurodegeneration in Sh-Sy5y Cells: Effective Agents in the Future Treatment of Parkinson's Disease

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Background: Parkinson's disease (PD) is a progressive, destructive, and long-term disorder in the central nervous system that mainly affects the motor system of the body. This disorder is characterized by the loss of dopamine-secreting neurons. Various compounds with neuroprotective and antioxidant properties have been identified, including Hesperidin (HES) and Auraptene (AUR). Our aim was to investigate the anti-apoptotic mechanism of these compounds in the SH-SY5Y cell line against the toxicity caused by 6-hydroxydopamine (6-OHDA) as one of the main causes of Parkinson's disease.
Methods: Cell viability was evaluated using the MTT test. Propidium iodide (PI) staining performed cell cycle analysis by flow cytometry. The production of reactive oxygen species (ROS) and generated free radicals was evaluated using the probe 2, 7'-dichlorofluorescein diacetate (DCFDA) and measured by fluorometry.
Results: After 6-OHDA treatment, cell survival decreased, this compound caused G2/M arrest and increased ROS levels. Our intervention with HES had neuronal anti-apoptotic effects, while treatment with AUR had no effect.
Conclusion: HES protects SH-SY5Y cells against 6-OHDP-induced neuronal damage by inhibiting G2/M arrest, reducing ROS amount and increasing cell viability. Therefore, this compound can be included in the PD treatment protocol in the future after conducting animal and human studies.

Keywords: Hesperidin, Orapten, ROS, 6-Hydroxydopamine, Parkinson's disease

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Abstract: A-10-2633-1

Aprepitant Loading on Graphene Oxide Nanoparticles to Evaluate the Induction of Cytotoxicity and Apoptosis in Glioblastoma Cancer Cells

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Background: Glioblastoma is the most common malignant primary brain cancer which remains one of the most treatment-resistant tumors. Conventional anti-cancer drug delivery techniques have limitations, prompting the exploration of novel drug delivery systems such as nanoparticles (NPs). Aprepitant (Apr) is a highly selective neurokinine1 (NK1) receptor antagonist with antiemetics effects that works by blocking substance P activity at NK1 receptors in the brain. Aprepitant has shown its anti-cancer effect *in vitro* and *in vivo* through various mechanisms of action.

Methods: The particle size of Apr-Se-BCD-GO NPs were average 180 nm with a negative surface charge; an Index of dispersion of 0.4 and also show high loading capacity toward Aprepitant. In this context, loading Aprepitant onto graphene oxide nanoparticles (a single layer of carbon atoms arranged in a hexagonal lattice) presents a novel strategy to target Glioblastoma cancer cells, induce cytotoxicity, and promote apoptosis. We carried out the Resazurin assay to assess nanoparticle toxicity, identified apoptosis using real-time PCR, and measured the antioxidant properties of nanoparticles through TAC and CAT assays.

Results: The 50% cell growth inhibition (IC50) of nanoparticles against Glioblastoma cancer cell line U87 was obtained as 29 µg/mL. Cancer cell treatment with nanoparticles at 40 and 20 µg/mL increased the gene expression of Bax, BCL2, and P53 in Glioblastoma cancer cell.

Conclusion: By utilizing these nanoparticles, there is potential to improve the treatment outcomes for Glioblastoma patients. Future research and development in this area could lead to more effective and personalized treatment options for this challenging disease.

Keywords: Glioblastoma, Drug delivery, Nanoparticles, Sprepitant, Graphene oxide

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Abstract: A-10-2823-1

Impact of Danlou Tablet Treatment on Expression Profiling in Patients with Coronary Heart Disease

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Background: Coronary heart disease (CHD) refers to a condition in which the heart's arteries are unable to supply sufficient oxygen-rich blood to the heart muscle. It is commonly referred to as ischaemic heart disease. CHD can be effectively managed through a combination of lifestyle modifications, medications, and, in certain instances, surgical interventions. Danlou tablets (DLT) offer additional benefits in the treatment of CHD which promoting blood circulation, and resolving stasis. This study aims to identify the pathways and genes impacted by the drug in the context of coronary heart disease treatment. To accomplish this objective, we analyzed the expression profiles of patients with CHD both before and after receiving DLT, aiming to investigate the possible pharmacological mechanisms underlying DLT's effects on CHD.

Methods: The microarray dataset of expression data of 8 patients with CHD before and after 8 weeks' treatment with Danlou tablets (GSE179789) was obtained from the GEO database. Differential expression analysis between two groups was performed using GEO2R and genes with differential expression were isolated. Next, genes exhibiting differential expression (logFC > 1 and p-value < 0.05) were identified as critical genes associated with the effects of Danlou Tablet treatment.

Results: The bioinformatics results showed that EEF1D (eukaryotic translation elongation factor 1 delta) with logFC= -1.17; P.value=0.0000824 and ATP6V0E1 (ATPase H+ transporting V0 subunit e1) with logFC= -1.019; P.value=0.0052965 have the most downregulation in patients with CHD after 8 weeks' treatment with Danlou tablets.

Conclusion: In summary, our findings indicate that differential gene expression analysis may serve as a powerful technique for identifying significant changes following drug treatment. Additionally, our results could help identify new therapeutic targets for the treatment of CHD.

Keywords: Danlou Tablet, Expression Profiling, Coronary heart disease

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Abstract: A-10-2655-3

Effects of Dust Pollution in Asaluyeh on Atomic Absorption of Heavy Metals and Histopathologic Changes in Spleen and Bone Marrow of Male Rats

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Background: The effects of air pollution from industrial advances and mechanization on people, specifically children whose immune and respiratory systems are not fully developed, have attracted growing attention. Given that the oil and gas facilities in Asaluyeh have turned it into one of the most polluted regions in the world, this study aimed at investigating the effect of airborne dust particles (ADPs) on the atomic absorption of heavy metals and histopathologic changes in spleen and bone marrow of male rats.
Methods: In this study, 30 adult male rats were assigned to the control, negative control, and treatment groups. After the course of treatment, the changes in spleen and bone marrow tissue, as well as atomic absorption of metals (lead, mercury, cadmium, and arsenic) in their serums were examined.
Results: The atomic absorption of metals in the serum of the treatment group significantly increased as compared to the control group; in addition, the significant histopathologic changes were observed only in the spleen tissues.
Conclusion: Dust of polluted air of Asaluyeh had relative toxic effects on the spleen tissue and serum but did not have toxic effects on bone marrow.

Keywords: Dust pollution, Asaluyeh, Spleen, Bone marrow, Rat

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Abstract: A-10-2649-1

Alteration of Urea Level in Serum and Saliva of Patients with Inflammatory Bowel Disease

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Background: Inflammatory bowel disease (IBD) is a chronic, recurrent inflammatory disease of the gastrointestinal tract that affects millions of people worldwide. The diagnosis of IBD by endoscopy and pathology is expensive and difficult for the patient. Since urea needs to be removed as a factor of oxidative stress in inflammation and considering the benefits of using saliva, this study investigated the amount of urea in saliva and serum in IBD patients and healthy people.

Methods: In this cross-sectional study, 30 patients with IBD who were referred to Imam Reza Hospital in Tehran, and 30 healthy individuals as a control group were included. First, the patients were asked to pour some of their saliva into the Falcon tube without irritating the mouth wall, and then 5 ml of blood was taken. All the samples were centrifuged and the supernatant of saliva and serum were separated and stored in the freezer. Urea level was measured by the photometric method.

Results: The average concentration of serum urea in patients (26.3 ± 3.32) and the healthy group (22.5 ± 1.03) had no significant difference ($p = 0.434$) but the mean unstimulated salivary urea level was significantly higher in the IBD patients (28.98 ± 2.27) than in the control group (20.77 ± 2.21) ($p = 0.024$).

Conclusion: It seems that in IBD disease, due to the oxidative stress caused by the excessive activity of the immune system, some cells of the digestive system, such as the cells of the oral cavity and salivary glands, are destroyed; proteins and enzymes are released and enter the urea cycle then convert to this excretory substance and cause a significant increase in the level of urea in saliva. More studies are needed to elucidate these findings.

Keywords: Urea, Inflammatory bowel disease, Saliva, Serum

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Abstract: A-10-2657-1

In Silico Discovery of Anti-Cancer Peptides Targeting the Myc Oncogene

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Background: Anti-cancer peptides (ACPs) offer a promising approach to cancer therapy because they specifically target cancer cells and minimize side effects. The MYC protein, which is important for cancer cell proliferation and survival, is an important target in cancer research. By molecular docking ACPs to the MYC protein, it is possible to discover peptides that can inhibit this protein and prevent the spread of cancer cells.

Methods: In this study, we utilized the peptide database available at https://aps.unmc.edu/database. This database contains various anticancer peptides with sequence length less than 30 amino acids. Advanced bioinformatics software HEPDOCK was used for molecular docking of these peptides to MYC protein. Parameters such as peptide sequence, length, and docking score were recorded. Further analysis was performed to evaluate the physicochemical and biological properties of the peptides.

Results: In this study, the peptides "GLLDIVKKVVGAFGSL" (docking score -124), "GLFDIIKKIAESF" (docking score -112), "GLFDIVKKVVGALGSL" (docking score -118), "GLFDIVKKVVGAIGSL" (docking scores -119) and "GLFDIVKKVVGTLAGL" (docking scores -108) were identified. Among them, peptide "GLLDIVKKVVGAFGSL" showed the highest effect. Bioinformatics analysis revealed that the physicochemical properties APAAC1 (value 6.250) and APAAC20 (value 18.75) significantly influenced the docking ability. Peptide AP00308 showed the highest docking score (-189), whereas AP02670 showed the lowest score (-77).

Conclusion: This study highlights the utility of molecular docking in identifying peptides that inhibit MYC protein. Peptides with high docking values are potential candidates for anticancer drug development. Advanced bioinformatics analysis can further elucidate properties that enhance peptide docking to MYC, paving the way for the development of more effective targeted therapeutics.

Keywords: Anti-cancer peptides , MYC, Molecular docking, Bioinformatic

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Abstract: A-10-2292-1

The Role of Galectin-3 and Kidney Injury Molecule-1 in the Biochemical Diagnosis of Chronic Kidney Disease in Iraqi Patients

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Background: Chronic Kidney Disease (CKD) is a significant health concern worldwide, with rising mortality rates. Early and accurate diagnosis is crucial for effective management and treatment. This study investigates the diagnostic value of Galectin-3 and Kidney Injury Molecule-1 (KIM-1) in identifying CKD stages in Iraqi patients.
Methods: A case-control design was implemented from August 2022 to May 2023. The study involved 150 participants categorized into three groups: control (healthy individuals), mild CKD, and severe CKD. Serum samples were collected and analyzed using the Sandwich-ELISA technique to measure levels of Galectin-3 and KIM-1. Data on demographics, clinical history, and standard CKD markers (eGFR, albumin, and creatinine) were also collected.
Results: Significant differences were observed in Galectin-3 levels among control, mild CKD, and severe CKD groups ($p<0.01$). Similarly, KIM-1 levels were significantly higher in severe CKD patients compared to controls ($p=0.036$). Galectin-3 showed strong correlations with CKD severity and other risk factors such as BMI and diabetes. KIM-1 was notably elevated in patients with advanced CKD stages, indicating its potential as a complementary biomarker.
Conclusion: The findings support the diagnostic utility of Galectin-3 and KIM-1 in CKD. Galectin-3 is particularly valuable for early detection and staging, while KIM-1 can assist in identifying severe cases. These biomarkers offer promising tools for enhancing CKD diagnosis and patient management in clinical settings.

Keywords: Chronic Kidney Disease, Galectin-3, Kidney Injury Molecule-1 (KIM-1), Biomarkers, Diagnosis, Iraqi Patients

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Abstract: A-10-2640-1

A DFT Study on Duloxetine

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Background: Duloxetine is a serotonin-norepinephrine reuptake inhibitor that is widely used in the treatment of major depressive disorder, generalized anxiety disorder, diabetic peripheral neuropathic pain, fibromyalgia, and chronic musculoskeletal pain. Duloxetine was first approved by the U.S. Food and Drug Administration (FDA) in 2004 for the treatment of major depressive disorder and has since received additional approvals for various other indications.

Methods: The study utilized quantum mechanics (QM) calculations conducted through density functional theory (DFT) using the GAUSSIAN 09 software. The structure of Duloxetine was optimized employing gradient procedures at both restricted Hartree-Fock (HF) and B3LYP hybrid density functional level of theory, utilizing the 6-311++G(d,p) basis set. The optimization aimed to achieve the minimum potential energy configuration and ensure the absence of negative frequencies, confirming a true energy minimum.

Results: This study conducted calculations for structural parameters like bond lengths, angles, and dihedrals, as well as thermodynamic parameters at the B3LYP /6-311++G(d,p) level of theory. The electronic energy of the molecule was determined to be –768,699.75 kcal/mole. Additionally, the Milliken atomic charge and molecular orbital energies were calculated. The highest occupied molecular orbital (HOMO) was found to be -0.25341 eV and the lowest unoccupied molecular orbital (LUMO) was -0.04561 eV. The dipole moment in Debye was measured as X= -2.5891, Y=0.9131, Z= 1.2044, with a total of 2.9980.

Conclusion: Optimization of the drug was performed using the B3lyp/6-311++G(d,p) method. The study focused on Duloxetine, electronic characteristics, specifically the energy difference between the HOMO and the LUMO. The HOMO-LUMO gap (HLG) energy was determined to be 0.2078 eV. This provides insights into duloxetine electronic behavior, which could have applications in various fields.

Keywords: Duloxetine, DFT, B3lyp/6-311++G(d,p), HOMO-LUMO gap (HLG)

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Abstract: A-10-2666-1

Investigating the Effect of Dexamethasone on BARR2 Gene and Protein Expression Levels in Vascular Smooth Muscle Cells

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Background: It is well established that vascular smooth muscle cells (VSMC) proliferation and migration promote atherogenic plaques in artery medium. β-arrestin-2 (BARR2) causes atherosclerosis in VSMCs by activating MEK/ERK signaling pathways. Previous studies found that Dexamethasone as an anti-inflammatory corticosteroid inhibits VSMC migration and proliferation. In the present study, the effect of Dexamethasone on the BARR2 gene and protein expression levels was investigated in VSMC.

Methods: Human VSMCs were cultured and treated with different doses of Dexamethasone (10−7 M, 10−6 M, and 10−5 M) in 24- and 48-h periods. Western blotting and RT-qPCR methods were used to determine the BARR2 protein and gene expression levels, respectively.

Results: After 48 hours, the BARR2 gene expression levels significantly decreased in the cell groups treated with Dexamethasone (10−5 M and 10−6 M). After 24 hours, the BARR2 gene expression levels were considerably lowered only in the group treated with Dexamethasone 10−5 M ($p < 0001$). Over 48 hours, BARR2 protein expression levels significantly decreased in cell groups treated with Dexamethasone (10−5 M, 10−6 M, 10−7 M, $p < .001$).

Conclusion: The study's findings demonstrated that Dexamethasone suppresses the levels of gene and protein expression for BARR2. Given that BARR2 has been linked to cell growth, the authors hypothesized that Dexamethasone may prevent the migration and proliferation of VSMCs.

Keywords: BARR2, Dexamethasone, VSMCs

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Abstract: A-10-2650-1

The Influence of N-Terminus Histidine Tail Deletion on MiRGD Peptide Function

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Background: MiRGD, a chimeric peptide engineered as a gene delivery vehicle, has shown promising transfection results across various cell lines. This peptide includes components such as GP41, H1 histone, SV40 NLS, and an iRGD motif. GP41 aids in endosomal escape, H1 histone condenses and carries genetic material, SV40 NLS facilitates nuclear delivery, and the iRGD motif interacts with integrin αvβ3 and neuropilin-1, anchoring the structure to the cell surface and promoting endocytosis. This study aims to investigate how the peptide's function changes when its histidine tail is removed, as the peptide needs to be tag-free and optimized for further applications.

Methods: To remove the histidine tag, a TEV protease cleavage sequence was cloned into the original MiRGD sequence using designed primers, since TEV protease leaves only one additional amino acid post-cleavage, it is preferred over thrombin. The modified sequence was then transformed into BL21-competent E. coli for expression and purification. Subsequent steps will include preparing peptide-plasmid complexes at various N/P ratios prior to and after TEV protease cleavage, testing the peptide's transfection capabilities, and conducting MTT assay.

Results: After cloning the TEV protease cleavage site, the peptide was successfully cleaved using TEV protease, as confirmed by gel electrophoresis. Future steps involve confirming the peptide's ability to form complexes with plasmid DNA, conducting MTT assays, and performing transfection in the HEK293T cell line.

Conclusion: In summary, the peptide has been modified, and the transfection abilities of the modified peptide will be compared to its original form before cleavage. This comparison will help determine the effect of the modification on MiRGD's function, ultimately guiding the optimization of the peptide for future applications.

Keywords: Chimeric peptide, Gene Delivery, MiRGD

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Abstract: A-10-2646-1

Comparison of miR-155, miR-26a, miR-146a, and miR-132 Expression in Patients with Alzheimer Disease and Controls

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Background: Alzheimer's disease (AD) is characterized by amyloid plaques and tau protein tangles, leading to synaptic dysfunction and neuronal damage. Mitochondrial dysfunction due to amyloid beta is a key feature. miRNAs, as gene expression regulators, may serve as biomarkers for AD. The study aims to use miRNAs as diagnostic and identification biomarkers for AD. The accumulation of beta-amyloid plaque and hyperphosphorylation of tau proteins are the two neuropathological hallmarks of the disease. Cognitive impairment and memory loss are the main clinical manifestations of Alzheimer's. The study aimed to investigate the expression of various miRNAs in AD patients compared to healthy individuals.

Methods: The study compared miRNA expression between 70 AD and 70 healthy controls. Blood samples were collected, and miRNA expression was measured using real-time PCR. Statistical analysis was performed using GraphPad Prism and SPSS software, with a significance level of $p<0.05$.

Results: Based on our study, the expression level of miR-26a, miR-146a, and miR-132 in the serum of AD patients was higher than in the control group. While the expression level of miR-155 between the two groups was lower in the AD group than in the control group ($P < 0.001$).

Conclusion: The study found decreased expression of miR-155 and increased expression of miR-26a, miR-146a, and miR-132 in AD compared to controls. These miRNAs are involved in inflammation and their dysregulation can contribute to the progression or prevention of neurological diseases like AD. The miRNAs could serve as biomarkers for AD diagnosis and prognosis. Impairment in the expression of these miRNAs can directly or indirectly cause disturbances in the central nervous system.

Keywords: Alzheimer's disease, miRNA, biomarker

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Abstract: A-10-2551-2

Differential Gene Expression Patterns in Stromal Cells Reveal Cell Cycle and P53 Pathways as Key Regulators of Acute Myeloid Leukemia Pathogenesis and Relapse

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Background: The bone marrow microenvironment, which includes various cell types such as mesenchymal stem cells (MSCs) and immune cells, plays a crucial role in supporting both normal hematopoiesis and the progression of acute myeloid leukemia (AML), often through complex interactions that can promote malignant transformation. This study aimed to investigate the role of stromal cells in AML pathogenesis and identify gene expression patterns associated with initial diagnoses and recurrences, utilizing the GSE122917 dataset and analyzing signaling pathways involved.
Methods: We downloaded the GSE122917 dataset from the Gene Expression Omnibus (GEO) and assessed RNA quality using an RNA Degradation Plot. Data normalization was performed with the Plier method from the affy PLM package, and a box plot demonstrated a favorable distribution of the normalized data. For gene expression analysis, we employed the Piano and limma packages to calculate p-values and log fold changes, identifying significant alteration in genes with a cutoff p-value of 0.05. We visualized gene networks using Cytoscape, created volcano and polar plots for comparative analysis among groups, and performed pathway and enrichment analysis through bioinformatics tools, presenting results with bubble plots.
Results: The analysis identified upregulation and downregulation genes between those diagnosed with AML and control ones and the others have relapsed ($P<0.05$). Also, we found the important pathway which involved is cell cycle (p.adjust: 0.0000697728) and in which CDC20,TTK,CDK1,MCM7,CDKN1A,GADD45B are targeted by altered genes. But, in cases with relapsed the P 53 pathway is more important (p.adjust: 0.012592044) and SERPINE1, CDK1 in this pathway are targeted.
Conclusion: The findings indicate that stromal cells play a significant role in the pathogenesis of AML, with distinct gene expression patterns identified between newly diagnosed patients and those experiencing relapse. Notably, the cell cycle pathway was crucial in newly diagnosed patients, while the P53 pathway was more prominently involved in relapse cases.

Keywords: Acute Myeloid Leukemia, Stromal cells, Reoccurrence, P53 pathway, Cell Cycle

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Abstract: A-10-2671-1

Evaluating the Cytotoxic Effects of Green Synthesized Zinc Oxide and Sodium Doped Zinc Oxide Nanoparticles on Colorectal Cancer Cell Line

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Background: Numerous investigations highlight the various properties of zinc oxide nanoparticles (ZnO NPs), including their anticancer properties. In this study, we aim to synthesize ZnO NPs and sodium-doped zinc oxide NPs using Zingerone, a green approach to compare and evaluate their cytotoxic activities on the HCT116 cell line and HDF normal cell line.

Methods: Zinc acetate, sodium nitrate, zingerone, and ethanol were used in the green synthesis of the nanoparticles of interest. HCT116 and HDF cells were seeded into 96-well plates at a density of 10^4 cells per well for 24 hours. Different concentrations of each nanoparticle were added individually to seeded cells. MTT solution and DMSO were added to each well after 48 hours of treatment, and the plates were then incubated before being read. For evaluating the expression levels of P53, P21, Bcl2, BAX, and PTEN genes and β-actin as the internal control gene, cells were treated with the IC50 concentration of each nanoparticle. Then total RNA was extracted, and cDNA was synthesized. Finally, real-time PCR was performed.

Results: The MTT results demonstrate that when each nanoparticle concentration rises, HCT116 viability falls. ZnO NPs doped with Na had a more potent lethal effect on cancer cells than ZnO NPs. ZnO NPs, on the other hand, had more cytotoxic effects on normal cells than Na-doped ZnO NPs. The real-time PCR assay data shows that whereas Bcl2 was down-regulated, BAX and P53 genes were significantly up-regulated, and PTEN and P21 expression levels stayed unchanged.

Conclusion: Based on the results, sodium-doped ZnO NPs performed better at eliminating cancer cells without endangering normal cells. According to the analysis of real-time PCR data, both nanoparticles eliminate cancer cells by activating signaling pathways related to apoptosis and their intervention in the cell cycle process was not significant.

Keywords: Zinc Oxide nanoparticles, Nanotechnology, Apoptosis, P53

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Abstract: A-10-2671-2

Green Synthesized Sodium-Doped Zinc Oxide Nanoparticles Induce Apoptosis in U87-Glioblastoma Cancer Cell Line

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Background: Zinc oxide nanoparticles (ZnO NPs) are one of the main nanomaterials with promising results in cancer treatment among the many investigations. The main objective of this study is to evaluate the cytotoxic effects of Na-doped ZnO NPs on the U87 glioblastoma cell line by synthesizing them using Zingerone in an environmentally friendly manner.

Methods: For the synthesis of Na-doped ZnO NPs, Zingerone (SIGMA) was diluted in ethanol. Then zinc acetate and $NaNO_3$ were dissolved in zingerone ethanolic solution with a stirrer, respectively. The above-mentioned mixture was stirred at 70°C for 3 hours. Ultimately, the final mixture was dried in an oven at 70°C and calcined at 700°C for 3 hours. In order to analyze the synthesized nanoparticles, XRD, DLS, FTIR, and FESEM were executed. U87 and HEK cell lines were seeded into 96-well plates separately. The cells were incubated for 24 hours before being treated with Na-doped ZnO NPs. After 48 hours of treatment, MTT assay was performed. Subsequently, cells were seeded in a 6-well plate and treated with Na-doped ZnO for 24 and 48 hours. The relative expression levels of BAX, P53, PTEN, BCl2, and P21 were measured using real-time PCR.

Results: Results of FESEM, DLS, XRD, and FTIR have shown that the synthesized nanomaterial was, in fact, nanoscale. The MTT results indicate that U87 cell viability declines due to the treatment of Na-doped ZnO in a dose-dependent manner. Real-time PCR data reveal a substantial rise in the expression of genes related to apoptosis and the cell cycle.

Conclusion: Analysis of the MTT assay data indicates that these nanoparticles inhibit the growth of cancer cells while having minimal impact on normal cells. Real-time PCR data analysis shows the induction of apoptosis and regulation of the cell cycle in the glioblastoma cancer cell line.

Keywords: Nanotechnology, Apoptosis, Cell cycle, Glioblastoma

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Abstract: A-10-2335-2

Alginate-Gelatin Hydrogel Microencapsulation for Generation Breast Cancer Tumoroids

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Background: In recent years, the development and fabrication of novel hydrogels for mimicking the 3D tumor niche have been at the center of attention. Here, breast cancer tumoroids were generated using ionic cross-linking of alginate-gelatin hydrogel.
Methods: Three different cell lines, including HUVECs, HFFF-2, and MDA-MB-231 cells, were used for induction of tumoroids. Using the hanging drop method, 5×10^4 cells (at a ratio of 2: 1: 1) were resuspended in 25 µl methylcellulose, and a tumoroid system was generated. In another method, the same cell density was blended with alginate-gelatin solution (1×10^6 per 1 ml) and dropped into 100 mM $CaCl_2$ solution to solidify. The stability and integrity of tumoroid systems induced by both systems were assessed under bright-field microscopy.
Results: Data indicated loosely cell-to-cell connection in tumoroids induced by hanging drop containing separate small-sized aggregates without whole mass integrity. Compared to tumoroids induced by hanging drop, microencapsulation of cells within the alginate-gelatin microspheres yielded unique multicellular units with suitable integrity in which cells were uniformly distributed inside the microspheres.
Conclusion: Ionic cross-linking of tumor cells with other cell types inside the alginate-gelatin hydrogel provide valuable platform for induction of complex and stable tumor system.

Keywords: Tumoroids, Dropping, Ionic cross-linking, Microencapsulation, Integrity

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2670-1

Renal Protective Effect of Leucomethylene Blue on Acetaminophen-Induced Toxicity in Rat

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Background: Acetaminophen is a commonly used drug for mild to moderate pain. However, acetaminophen toxicity is a major cause of drug-induced, with overdoses leading to acute kidney injury due to the formation of toxic metabolites (NAPQI). Active NAPQI binds to intracellular macromolecules and leads to oxidative stress and mitochondrial dysfunction. Methylene blue is an FDA-approved drug for the treatment of methemoglobinemia and has potential applications in the treatment of carbon monoxide and cyanide poisoning. The drug must be reduced to its colorless form, leucomethylene blue (LMB), to enter cells and mitigate oxidative stress, making it an important tool in mitochondrial regulation and ATP synthesis pathways.

Methods: This study aimed to evaluate the effect of LMB on renal damage caused by APAP toxicity. A total of 30 male Wistar rats were randomly divided into five groups (n=6 in each group). control group, APAP group, NAC group (N-acetyl cysteine as positive control), LMB group, and NAC+LMB group. Except for the first group, all groups were injected with 1500mg/kg acetaminophen at the specified time.

Results: Administration of LMB was able to decrease the serum level of urea and creatinine in LMB group vs APAP group. In addition, LMB treatment significantly decreased the levels of urine albumin. LMB also significantly decreased the expression of KIM-1 in the kidney tissue.

Conclusion: These results indicate that LMB has a comparable effect to NAC in most complications of APAP-induced toxicity in rats, and its combination with NAC provides the most effective strategy to preserve kidney function and prevent tissue damage.

Keywords: Acetaminophen, Leucomethylene Blue, Kidney, Mitochondrial dysfunction

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Abstract: A-10-2317-2

The Application of Capillary Electrophoresis and HPLC in Hemoglobinopathy Analysis

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Background: According to WHO, 7% of the world's population are carriers of hemoglobinopathies and it is estimated that 300-400 thousand babies are born with such abnormalities every year. Therefore, we performed a systematic review of the main methods of hemoglobinopathy diagnosis to emphasize their importance in different fields. **Methods:** Google Scholar, PubMed, ScienceDirect, and other databases were systematically searched for trials in the English language published between January 1998 and April 2024. Keywords such as "Capillary Electrophoresis (CE), hemoglobinopathies, Thalassemia, High-performance liquid chromatography (HPLC)" were used. **Results:** Approximately 155 articles were found and the more relevant ones were selected in our studies which were 60 articles. According to the studies, HPLC has advantages of quantifying Hb F and Hb A2 alongside other variants in a single screening test. While CE has a flat flow which provides a higher resolution and narrower peaks. With hunderds of thousands of people being diagnosed with hemoglobinopathies in the world, the preferred method often varies between HPLC and CE depending on their advantages and the conditions of carriers. **Conclusion:** According to the articles and statistics it was evident that CE and HPLC are commonly used for diagnosing hemoglobinopathies due to their ease of use and high accuracy. The daily growth of electrophoresis market also implies the popularity and importance of these methods in clinical and research fields.

Keywords: Hemoglobinopathies, Capillary Electrophoresis, High-performance liquid chromatography, Electrophoresis market, Thalassemia

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Abstract: A-10-2482-1

Investigating the Tertiary Structure of Survivin Protein in the Presence of EDTA and Zn2+ Ion Using Intrinsic Fluorescence

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Background: Survivin, a protein with a molecular weight of 16.5 kD, is structurally characterized by two domains, including the N-terminal Zn2+-binding BIR domain, which is linked to a 65 Å amphipathic C-terminal α-helix. This 'terminal wire' is a crucial part of survivin structure, playing a significant role in its function. It is classified as a family member capable of apoptosis inhibition. This specific protein is available as a cancer tumor marker due to its excessive expression in many cancers. In this study, the tertiary structure of the purified recombinant survivin protein in the presence of two factors, zinc ion and EDTA (a chelating agent), was investigated by intrinsic fluorescence spectroscopy.

Methods: After expressing and purifying the survivin protein, dialysis was performed for 24 hours at 4°C using a dialysis buffer. To verify the presence of the protein after dialysis, a protein sample was placed on 17.5% SDS-PAGE. Next, the survivin protein was exposed to EDTA or Zn2+ ion at 1 and 10 mM concentrations, separately. The spectra were examined using fluorescence spectroscopy (excitation at 295 nm and emission at a 300 to 400 nm wavelength). The protein concentration was used with precision to be 0.2 mg/ml.

Results: The results of the fluorescence spectra revealed a significant change, the addition of EDTA as a chelating agent to protein that effectively separates the zinc ion from the protein structure, reduced the intensity of the spectra peak. Conversely, the introduction of Zn2+ ion to survivin resulted in a notable increase in the intensity of peak, indicating a local change conformation and maybe a shift towards a more rigid protein structure.

Conclusion: Since the structure of survivin protein has a zinc-binding BIR domain, by adding zinc or EDTA agents, the tertiary structure of the protein has been changed.

Keywords: Survivin, EDTA, Zinc ion, Fluorescence

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2675-1

Circulating MicroRNA-106b-5p as a Potential Biomarker for Coronary Artery Disease

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Background: Coronary artery disease (CAD) is a top cause of global mortality, presenting enormous financial burdens on healthcare systems. Despite improvements in diagnostic approaches, early detection remains the most challenging issue. MicroRNAs (miRNAs), being epigenetic regulators, have emerged as potential biomarkers for diverse diseases, including CAD. This study was aimed at predicting and validating miRNAs that are strongly upregulated in patients with CAD as well as evaluating their diagnostic potentials.

Methods: In this research, the GSE113079 dataset from Gene Expression Omnibus (GEO) was used in a case-control study that constituted 141 peripheral blood samples (93 CAD and 48 controls). Differentially expressed mRNAs (DEmRNAs) were identified using the Limma package by focusing on those with significant expression differences. Based on their interactions with the most significant DEmRNAs, five miRNAs (miR-106b-5p, miR-146a-5p, miR-17-3p, miR-20a-3p, and miR-155-3P) were selected. For the validation of these serum markers, 44 CAD patients and 48 healthy controls were recruited and qRT-PCR was used.

Results: When comparing the five miRNAs studied, it was observed that CAD patients had markedly higher levels of miR-106b-5p in comparison to controls ($p < 0.001$). Receiver Operating Characteristic (ROC) curve analysis further confirmed that miR-106b-5p is highly diagnostic with an area under the curve (AUC) of 0.8975, a sensitivity of 70%, and a specificity of 95%. Additionally, there were significant correlations between the expression levels of miR-106b-5p and some CAD risk factors such as LDL-c, weight, and BMI.

Conclusion: CAD diagnosis has been recently identified as a potential area for early detection which could be marked by the use of miR-106b-5p. The findings indicate that miR-106b-5p testing could be employed in the management of CAD to improve its detection and treatment process.

Keywords: Coronary Artery Disease, miR-106b-5p, Biomarkers, Gene Expression Analysis, qRT-PCR

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Abstract: A-10-2681-1

Polymorphism of the Insulin Resistin (RETN) Gene in Susceptibility to Polycystic Ovary Syndrome (PCOS) in An Iranian Population

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Background: Polycystic Ovary Syndrome (PCOS) is the most common endocrine disorder, affecting 5-10% of women of reproductive age. Major complications of PCOS include infertility, obesity, endometrial hyperplasia, endometrial cancer, insulin resistance, hyperandrogenism, and cardiovascular issues. This study aims to investigate the polymorphism of the Insulin Resistin (RETN) gene at positions -420 CG and +299 AG in relation to the susceptibility to PCOS.

Methods: This case-control study included 198 participants (100 diagnosed with PCOS and 98 normal controls). Two single nucleotide polymorphisms of the RETN gene 420(C/G) (rs1862513) and 299(G/A) (rs3745367), were analyzed using the PCR-RFLP method. Genomic DNA was extracted from blood samples using a DNA extraction kit. The PCR product was digested with restriction enzymes BbsI and AluI, and the results were analyzed by electrophoresis on an agarose gel. Statistical analysis determined the association of the genotypic and allelic variations with PCOS.

Results: The findings indicate no significant association between the RETN gene polymorphism and PCOS.

Conclusion: Our study found that RETN gene polymorphisms do not appear to play a significant role in PCOS susceptibility in the Iranian population. These results suggest that other genetic or environmental factors may contribute more significantly to the development of PCOS. Further research with larger sample sizes and additional genetic markers is necessary to understand the genetic basis of PCOS.

Keywords: Polycystic Ovary Syndrome, Gene Polymorphism, Resistin Gene, Gene Polymorphism, PCR-RFLP, Insulin Resistance

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Abstract: A-10-2407-1

Preparation of Chitosan-Modified PLGA Nanoparticles Containing Carbon Quantum Dots

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Background: Addressing effective and targeted therapeutic delivery remains a significant challenge in treating various diseases, particularly cancers. Nanocarriers offer promise in this regard. Therefore, implementing novel and targeted delivery strategies with maximum efficacy and minimal side effects can pave the way. In this study, PLGA nanoparticles containing carbon quantum dots (CQDs) were prepared and their surface was modified with chitosan.
Methods: PLGA nanoparticles loaded with carbon quantum dots (CQDs) were synthesized using the nanoprecipitation method. Briefly, 10 mg of PLGA was dissolved in 2 mL of acetone, while 1 mg of CQDs was dissolved in 0.2 mL of dimethyl sulfoxide (DMSO). The PLGA and CQD solutions were added dropwise into a 20 mL polyvinyl alcohol (PVA) solution. Next, different concentrations of chitosan solution (5 mL, 2.5 mL, and 1.25 mL of 0.5% chitosan) were incorporated into the nanoparticle dispersion, followed by stirring for 4 hours at room temperature to remove the organic solvent. Subsequently, the nanoparticles were obtained via centrifugation at 10,000 rpm for 30 minutes. Finally, the purified nanoparticles were prepared for freeze-drying. The hydrodynamic diameter of the nanoparticles was analyzed using dynamic light scattering (DLS).
Results: Three distinct types of nanoparticles were analyzed for size distribution using dynamic light scattering (DLS). The mean diameter of surface-modified PLGA nanoparticles with 5 mL of chitosan was 207±3 nm, while the diameters of PLGA nanoparticles prepared with 2.5 mL and 1.25 mL of chitosan were 239±2 nm and 260±3 nm, respectively.
Conclusion: Based on the study results, increasing the chitosan content during the preparation of CQDs-loaded PLGA nanoparticles resulted in a reduction in particle size. This phenomenon may be attributed to enhanced electrostatic interactions between chitosan and the PLGA nanoparticle surface.

Keywords: PLGA, Nanoparticles, Carbon quantum dot, Chitosan

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Abstract: A-10-2715-1

Investigation of Quantum Computing of Pexidartinib Hydrochloride

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Background: In August 2019, the FDA approved Pexidartinib for the treatment of symptomatic tenosynovial giant cell tumors (TGCT), marking it as the first systemic therapy for this rare disease. Due to the significant medical relevance of the drug, we have decided to conduct a thorough examination of its electronic structure using quantum computing technology.
Methods: Initially, the molecular structure of Pexidartinib was designed using GaussView software, followed by quantum mechanical calculations at the B3LYP/6-311+G** theoretical level with Gaussian09 software.
Results: The study performed comprehensive calculations on structural features, including bond lengths, angles, and dihedrals, as well as thermodynamic parameters at the B3LYP/6-311G level of theory, and presented the results. The electronic energy of the compound was calculated to be -1,132,440.13 kcal/mol. Additionally, the Mulliken atomic charges, spin density, and molecular orbital energies were assessed. The highest occupied molecular orbital (HOMO) was evaluated at -0.23180 eV, while the lowest unoccupied molecular orbital (LUMO) was determined to be -0.08488 eV. The dipole moment in Debye was recorded as X = 1.4621, Y = 0.7512, Z = -2.2545.
Conclusion: The drug was optimized in this study using the B3LYP/6-311+G method. The primary focus was on examining the electronic properties of Pexidartinib, specifically the energy levels between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). The calculated HOMO-LUMO gap energy was determined to be 0.14692 eV. This analysis provides insights into the electronic behavior of Pexidartinib and suggests potential applications across various industries.

Keywords: Pexidartinib, DFT, B3LYP/6-311+G, HOMO-LUMO gap

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Abstract: A-10-2360-1

Determining the Effect of Calcitriol Supplementation on Oxidative Stress Biomarkers in an Experimental Stroke Model

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Background: Ischemic stroke is one of the leading causes of death worldwide. Cerebral ischemia leads to an increase in inflammatory factors. One of the important factors after a stroke is the increase in the phenomenon of oxidative stress. Calcitriol, with its anti-inflammatory properties, can play a regulatory role in controlling various mechanisms such as inflammation and apoptosis. Considering the role of oxidative stress in the phenomenon of inflammation and apoptosis, in the present study, the effect of calcitriol on biomarkers of oxidative stress after induction of stroke is investigated.

Methods: 3 groups of 5 rats were selected, the groups are ischemia control group, calcitriol drug group and control group (sham) respectively. Stroke was induced by middle cerebral artery occlusion (MCAO) and calcitriol was injected intraperitoneally for 3 days. After performing the behavioral tests, the volume of the ischemic area in the brain was measured, and finally, the marginal area of ischemia in the brain was used to check the parameters of oxidative stress.

Results: The observations showed that the results of Garcia's behavioral test improved and the infarct volume decreased in the medicinal samples. For the antioxidant effects of calcitriol against cerebral ischemia, biochemical parameters such as NO, MDA and TAC were evaluated. According to the obtained data, the test of nitric oxide (NO) and malondialdehyde (MDA) has decreased significantly in the pharmaceutical sample and the test of antioxidant capacity (TAC) has increased.

Conclusion: The results show that calcitriol protects the brain from damage caused by oxidative stress and probably controls the inflammation process and improves symptoms in the acute phase of stroke.

Keywords: Stroke, Inflammation, Oxidative stress, Calcitriol, MDA

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2752-1

The Effect of Silibinin on Phosphorylation and Reduction Activation of ERK1/2 Proteins in Liver Ischemia/reperfusion in Rats

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Background: Ischemia/reperfusion (I/R) injury is a common clinical occurrence during surgical procedures such as organ transplantation, especially in liver tissue. This process can lead to inflammatory responses due to the generation of free radicals and other harmful mechanisms. One of the pathways implicated in tissue damage during IR is the abnormal expression of ERK1/2 genes. Contrary to their typical function, these genes contribute to tissue injury and induce cellular death during IR.
Methods: This study aimed to explore the potential anti-inflammatory effects of silibinin during liver I/R in Wistar rats. 32 male Wistar rats were divided into 4 groups of eight, including two groups with ischemia/reperfusion (IR), one receiving physiological serum and the other silibinin (IR/SIL), and two groups without ischemia receiving saline and silibinin. After one hour of ischemia and three hours of reperfusion, blood and liver tissue samples were collected for biochemical, gene expression and ERK protein activation studies. 0 ns molecular dynamics simulations.
Results: After treating with silibinin, the serum AST, ALT and LDH indices which had significantly increased in the I/R group, decreased in the IR/SIL group ($P<0.05$). There were no significant changes in the expression of ERK1 and ERK2 genes in ischemic tissue following silibinin treatment, a noteworthy decrease in the activation of proteins derived from ERK1/2 was evident in the IR/SILI group compared to the IR group.
Conclusion: Silibinin has shown promise in mitigating liver I/R induced tissue damages, potentially via inhibiting the activation of ERK1/2 protein. These findings indicate that silibinin has the potential to be an effective therapeutic agent in treating liver injury caused by ischemic conditions.

Keywords: Keywords: Liver, Ischemia, Reperfusion, ERK, Silibinin

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Abstract: A-10-2436-1

Bioinspired Metal-Organic Framework Nanozyme with Enhanced Peroxidase-Like Activity for the Colorimetric Detection of Acetaminophen

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Background: Colorimetric sensors have been made with nanozymes for a long time because of their low cost, high stability, superior biocompatibility, and ease of modification. Acetaminophen (ACT) is a common analgesic and antipyretic drug used for treating fever, the flu, migraines, and more severe pain.
Methods: This study introduces a novel colorimetric sensing method for the rapid and efficient detection of ACT, which is based on the peroxidase-mimic activity of Cu-metal-organic framework (Cu-MOF). For this purpose, Cu-MOF was synthesized and characterized using different methods, including FE-SEM, FT-IR, and XRD. The peroxidase-like activity of Cu-MOF was evaluated utilizing a colorimetric method, which was based on the oxidation of H2O2 and the production of a blue-colored solution (λmax=652 nm).
Results: The Cu-MOF showed higher catalytic activity than natural peroxidases such as horseradish peroxidase (HRP). Due to the inhibitory effect of the ACT on the nanozyme activity, the prepared MOF was applied for developing a colorimetric sensor for ACT detection, which exhibited a linear detection range extending from 5-310 µM with a lower detection limit quantified at 16.6 µM.
Conclusion: On the basis of the results obtained, it can be concluded that the prepared sensor was highly selective towards ACT.

Keywords: Acetaminophen, Colorimetric sensing, Metal-organic framework, Nanozymes

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Abstract: A-10-2611-1

The Functional Roles of the CircRNA/Wnt Axis in Colorectal Cancer: A Systematic Review

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Background: Circular RNAs (circRNAs) contribute to tumorigenesis and metastasis of colorectal cancer (CRC). Wnt/β-catenin pathway play a critical role in carcinogenesis of CRC. evidence suggests that circRNA dysregulation and the Wnt pathway jointly drive carcinogenesis in CRC. In this systematic review, we provide an overview of the critical role of several circRNAs in CRC via regulating the Wnt pathway.
Methods: In the current systematic review, PubMed, Google Scholar, and Scopus databases were examined for the English language articles until 2022 using “colorectal cancer”, “circular RNAs” and “Wnt pathway” keywords and found articles related to circRNAs involved in CRC progression through regulation of the Wnt/β-catenin pathway.
Results: finally, more than 50 searches were conducted in this field and a total of 29 were reviewed. In this study, we identified 7 candidate circRNAs that regulate the Wnt/β-catenin pathway. As a result, we demonstrated that Circ_0006174, circIFT80, circBANP, circ5615, circ_0005075 were upregulated in CRC tissues and cell lines while has_circ_0009361 and circMTO1 were downregulated in CRC tissues and cell lines. circ_0006174, circBANP, Circ_0005075 and inhibition of circMTO1 promote CRC cell proliferation and invasion by increasing the levels of β-catenin, c-myc, and cyclin D1, and thus Wnt /β-catenin pathway activation. As well as, knockdown of has_circ_0009361 play an important role in CRC progression by down-regulated the expression of adenomatous polyposis coli 2 (APC2) and induce the activity of the Wnt/β-catenin pathway. Circ5615 could facilitate CRC invasion and cell proliferation by activation the Wnt/β-catenin pathway through degeneration of AXIN2, leading to the stabilization of β-catenin. Additionally, circIFT80 can promote the cell proliferation of CRC by induce the expression of β-catenin and c-myc.
Conclusion: The above-mentioned circRNAs act as oncogenes or tumor suppressors in CRC by regulating the Wnt pathway and can serve as diagnostic or therapeutic biomarkers for CRC.

Keywords: Circular RNAs, colorectal cancer, Wnt/β-catenin pathway

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Abstract: A-10-2738-2

A Quantum Mechanical Investigation on Etrasimod

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Background: In October 2023, the FDA approved Etrasimod for patients with moderately to severely active ulcerative colitis, marking it as the first S1P receptor modulator targeting S1P1,4,5 receptors approved for this condition. Due to the critical medical significance of the drug mentioned above, we have decided to conduct a thorough examination of its electronic structure using quantum computing technology.
Methods: The study utilized quantum mechanics (QM) calculations conducted through the density functional theory (DFT) method with the GAUSSIAN 09 software. The structure of the Etrasimod drug was first optimized through gradient procedures at both restricted Hartree-Fock (HF) and hybrid density functional B3LYP levels of theory using the 6-31G basis set. Examination of the results revealed that the optimized structure achieved in this research was situated at the minimum point on the potential energy surface, displaying no negative modes.
Results: This study conducted calculations for structural parameters like bond lengths, angles, and dihedrals, as well as thermodynamic parameters at the B3LYP/6-31G level of theory and provided the results. The HF energy of the molecule was determined to be -995211.76675323 Kcal/Mol. The mulliken atomic charge, spin density, and molecular orbital energies were also calculated. The highest occupied molecular orbital (HOMO) was found to be -0.19489 eV and the lowest unoccupied molecular orbital (LUMO) was -0.02745 eV. The dipole moment in Debye was measured as X=6.5376, Y-4.0847, Z=-3.9332, with a total of 8.6542.
Conclusion: Optimization of the drug was performed using the B3LYP method. The study focused on Etrasimod's electronic characteristics, specifically the energy difference between the HOMO and the LUMO. The HOMO-LUMO gap energy was determined to be 0.16744 eV.

Keywords: Etrasimod, QM-DFT Calculations, B3LYP, HOMO-LUMO gap

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Abstract: A-10-2726-1

Synthesis of Zinc Peroxide Nanoparticles Using Plant Extract of Eucalyptus Globoulus and Its Anticancer and Antibacterial Activity

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Background: Numerous investigations on medication delivery systems employing nanotechnology have been carried out recently. The significance of this study is the green synthesis of nanoparticles that combat antibiotic-resistant bacteria and suppress cancer cells. In the current investigation, the physicochemical properties of zinc peroxide (ZnO2) nanoparticles were evaluated. They are intermediate metal oxides with good electrochemical activity and stability.

Methods: The extract derived from Eucalyptus globulus leaves was employed as a stabilizer during the green synthesis of the metal oxide nanoparticles. The accuracy of synthesis steps has been measured by Fourier-transform infrared spectroscopy (FT-IR), zeta potential, and ultraviolet-visible spectroscopy (UV). These nanoparticles had a spherical shape and a size of 21 nm, according to FE-SEM images.

Results: Following the measurement of these nanoparticles' biological impact on the MCF-7 cell line, the IC50 concentrations for chemical and green synthesis ZnO_2 nanoparticles were determined to be 65 and 52 micrograms per milliliter, respectively chemical nanoparticles, green synthesis ZnO_2 nanoparticles did not significantly affect the normal cells of HEK-293. Also, S. aureus bacteria were used to test the antibacterial activity of the substances. For chemical ZnO_2 and green-manufactured ZnO_2 nanoparticles, the MIC and MBC values were determined to be 15 and 65 micrograms per milliliter, respectively.

Conclusion: Overall, these findings suggest that green-synthesized ZnO_2 nanoparticles are promising candidates for therapeutic applications, offering a biocompatible and eco-friendly approach to treating antibiotic-resistant infections and cancer.

Keywords: Green synthesis, Nanoparticles, Zinc peroxide, Eucalyptus Globulus, Breast cancer

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Abstract: A-10-2727-1

Examining the Effect of Hesperetin on Estrogen Receptor Alpha (erα) in MCF-7 Cells

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Background: The most common malignancy among women worldwide is breast cancer. The estrogen receptor plays a vital role in this cancer. One of the most well-known mechanisms that affects the activity of this receptor is its phosphorylation by protein kinase pathways. Hesperetin, a flavonoid abundant in citrus species such as lemons, grapefruits, and oranges, is the aglycone form of hesperidin. It has undergone thorough evaluation for its potential anti-cancer properties, particularly in the context of breast cancer. Studies have shown that hesperetin has an effect on intracellular kinase pathways. The aim of this study was to investigate the effect of hesperetin on the expression, phosphorylation and activity of estrogen receptor alpha (ERα) in MCF-7 breast cancer cell line.

Methods: MCF-7 cells were cultured in RPMI-1640 phenol red-free medium supplemented with charcoal-stripped FBS and treated with hesperetin. The MTT method was used to evaluate cell survival. The levels of the ERα protein and its phosphorylated form (Ser118) were determined via western blotting. A luciferase reporter vector was used to evaluate estrogen response element (ERE) activity.

Results: The results of this study indicated that hesperetin reduced the survival of MCF-7 cells in a dose-dependent manner. The expression and phosphorylation (at Ser118) of the ERα significantly increased and decreased, respectively, in the groups treated with hesperetin. Hesperetin increased the activity of the ERα in the absence of E2, although these differences were not statistically significant. Conversely, in the presence of E2, hesperetin caused a significant decrease in receptor activity.

Conclusion: Based on the results of this study, it can be concluded that hesperetin has a significant effect on ERα expression, phosphorylation and activity.

Keywords: Breast cancer, Hesperetin, Estrogen receptor, Estrogen response element

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Abstract: A-10-2707-2

Understanding the Relationship Between Slc39a8 Gene Expression and Zinc Levels in Patients with End-Stage Renal Disease on Hemodialysis

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Background: End-Stage Renal Disease (ESRD) necessitates life-sustaining interventions, primarily dialysis or kidney transplantation. Recent research has suggested a possible connection between SLC39a transporters and the progression of renal failure, indicating that zinc supplementation might offer therapeutic benefits for individuals with this condition. This study aims to assess the expression of the SLC39a8 gene and its relationship with zinc levels and other biochemical parameters in patients undergoing hemodialysis.

Methods: The study involved the collection of blood samples from 28 patients receiving hemodialysis and 21 healthy controls. The analysis included an investigation of the correlation between SLC39a8 gene expression and variables such as age, gender, and serum levels of zinc, Aspartate aminotransferase (AST), Alanine transaminase (ALT), Triglyceride (TG), and fasting blood sugar (FBS). The levels of zinc, AST, ALT, TG, and FBS were measured using a colorimetric assay kit, while the expression of the SLC39a8 gene was quantified using RT-qPCR.

Results: Among the measured biochemical markers, fasting blood sugar (FBS) was the only parameter that showed a significant difference between the groups. Patients undergoing dialysis for over a year had higher FBS levels compared to others (p=0.038). Additionally, the study found that zinc levels in hemodialysis patients were lower than in healthy controls, and SLC39a8 gene expression was significantly reduced in the hemodialysis group compared to the controls. However, no significant correlation was observed between serum zinc levels and SLC39a8 gene expression.

Conclusion: The findings indicate that hemodialysis patients exhibit lower zinc levels and decreased SLC39a8 gene expression compared to healthy controls, suggesting that zinc supplementation could be beneficial for managing ESRD in these patients. Nonetheless, further research is required to fully understand the intricate interactions between these factors and their potential implications for treatment strategies in this patient population.

Keywords: SLC39a8, Zinc Levels, Hemodialysis, End-Stage Renal Disease (ESRD)

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Abstract: A-10-2551-3

Key Genes Modified By High-Fat Diet-Induced Gut Microbiome Changes in A Mouse Model of Barrett's Esophagus

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Background: Barrett's esophagus (BE) is acknowledged as the primary precursor to esophageal adenocarcinoma (EAC). The growing rates of obesity have become an important risk factor contributing to the increasing occurrence of EAC. A high-fat diet (HFD) caused a distinct alteration in the gut microbiome in mouse model of BE, which associated with a specific inflammatory phenotype characterized by increased levels of IL-1β and IL-8. Therefore, this study aimed to identify the key genes modified by the gut microbiome induced through HFD.

Methods: We extracted the GSE103616 dataset from NCBI and conducted an analysis using R studio with limma packages.

Results: Three groups of mice were analyzed based on their genetic modifications and dietary conditions. Group one consisted of mice that overexpressed IL-1β and were maintained on a chow diet, serving as the control group. Group two included mice that overexpressed both IL-1β and IL-8, also on a chow diet. Group three comprised mice that overexpressed IL-1β while being fed a high-fat diet (HFD). When comparing the HFD-fed mice (Group Three) to those on the chow diet (Group One), significant changes were observed in the expression of several genes. The most notable genes identified in this comparison were: Serpina3n, Aqp1, Snora30, and Glrx. Additionally, a further comparison between the HFD-fed mice (Group Three) and the mice overexpressing IL-1β/IL-8 (Group Two) revealed a distinct set of genes that were differentially expressed, including: Snora75, Snora15, Gm6921, Snord99, Snora69, Clca4, Gm7265, Gabrp, Vaultrc5, Rnu73b, Snord11, Cd209a, Ep400, Zfp219, Snord57, and Nfu1.

Conclusion: These results underscore the complex interplay between dietary factors, the gut microbiome, and inflammatory responses in the context of BE and EAC development. The identification of genes altered by HFD opens avenues for research into targeted therapeutic strategies that may mitigate the risk of EAC in individuals with BE.

Keywords: 1. Barrett's esophagus, Gut microbiome, Differential gene expression

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Abstract: A-10-2171-1

Protective Role of Melatonin-Loaded Chitosan Nanoparticles Against Cisplatin-Induced Toxicity: An In-Vivo Study

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Background: Cisplatin (CP) is a widely used cytotoxic drug in cancer treatment, but, its use is frequently associated with nephrotoxicity and chronic anemia. This study aims to evaluate the preventive effects of melatonin (Mel) and melatonin-loaded chitosan nanoparticles (ChitMelNPs) against oxidative stress and lymphopenia induced by cisplatin in rats. Melatonin is known for its ability to alleviate inflammation and oxidative stress in a variety of tissues.
Methods: The study included 40 male Wistar rats divided into five groups: control, CP (12 mg/kg), Mel (10 mg/kg), ChitMelNPs (10 mg/kg), and ChitNPs (10 mg/kg). The rats were treated via gavage for 15 days, followed by an injection of CP (12 mg/kg, IP) on the 16th day. After 48 hours, blood samples were collected to assess toxicity by evaluating hematological parameters, MDA, and TAC levels.
Results: Our results showed that CP decreased body weight, WBC count, and TAC levels while increasing MDA levels ($p<0.001$, $p<0.01$, $p<0.05$, and $p<0.001$, respectively). Pretreatment with ChitMelNPs significantly reduced weight loss and lymphopenia. Furthermore, ChitMelNPs significantly increased TAC levels and decreased lipid peroxidation indicator (MDA) ($p<0.05$). This shows that ChitMelNPs possess greater antioxidant properties, which may improve treatment outcomes.
Conclusion: To summarize, our findings highlight melatonin's protective role against CP-induced toxicity, particularly in nanoparticle form. ChitMelNPs have shown the potential to decrease CP's adverse effects while preserving its anticancer efficacy.

Keywords: Cisplatin, Melatonin, ChitMelNPs, Lymphocyte, MDA, TAC

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Abstract: A-10-2743-2

Evaluation of the amount of 5-Hmf in serums and syrups

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Background: 5- Hydroxy methyl-2- furaldehyde (5-HMF) is one of the major genotoxic contaminants in the Maillard reaction, presents in a wide variety of processed foods. It also forms as a decomposition product of glucose, fructose, and sucrose solution formulations, dialysis fluids, and medical syrups containing sucrose and invert syrups which are thermolyzed and subjected to heat sterilization. In experimental animals and model systems the mutagenic and DNA Strand-breaking effects of this formaldehyde has been reported.
Methods: In the present research, controlling and measuring 5-HMF concentration in the injection serums (with dextrose concentrations of 3.33, 5, 10, 20, and 50 present) and some medical colorless syrups (Hydroxyzine, Salbutamol, Calcium and Grip Mixture) with the difference spectrophotometric method.
Results: The licensed concentration of 5-HMF in medical products is 2 µg/ml. The concentration of 5-HMF in the experiment serum was around the license. In the dense serums of dextrose, the amount of 5-HMF was more than diluted serum. An acidic environment and higher heat cause 5-HMF to be produced in sugar- serums. The concentration of 5-HMF in the Hydroxyzine syrups, Salbutamol, and Calcium has been around licensed. But in the Grip Mixture syrup concentration of 5-HMF, 2.484 µg/ml has been a little more than the licensed period.
Conclusion: Reformation of production and control of chemical production containing sugar has great importance.

Keywords: Dextrose, 5-HMF, Millard reaction

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Abstract: A-10-2761-1

Association of AXIN1 rs12921862 C/A and rs1805105 C/T Polymorphisms with Gastric Cancer Risk

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Background: Gastric cancer is a multifactorial disease whose main cause remains unknown. Studies have highlighted the genetic origin of this disease in addition to environmental factors. Recent studies have proven the crucial role of AXIN1 in suppressing gastric cancer tumors via the Wnt/ β-catenin signaling pathway. Inactivation of this gene through mutation or epigenetic alterations plays a significant role in gastric carcinogenesis. Therefore, the aim of this study was to investigate the AXIN1 rs12921862 C/A and rs1805105 C/T polymorphisms might be linked to a higher risk of getting stomach cancer.
Methods: In total, 250 gastric cancer patients and 210 sex-, age-, and BMI-matched control subjects were enrolled in the study. AXIN1 rs12921862 C/A and rs1805105 C/T polymorphisms were genotyped using the PCR-RFLP method.
Results: The results showed that individuals with the AXIN1 rs12921862 CA genotype had a significantly higher likelihood to get gastric cancer than people with the CC genotype (OR 1.65; 95% CI 1.21–2.44, p = 0.014). Higher odds of CT were found in a dominant model (CT+TT vs. CC) for rs1805105 C/T (OR-1.84; 95% CI 1.11–2.56, p = 0.008).
Conclusion: The AXIN1 rs12921862 C/A and rs1805105 C/T polymorphisms were significantly associated with an increased risk of gastric cancer.

Keywords: Gastric cancer, AXIN1, AXIN1 rs12921862 C/A, AXIN1 rs1805105 C/T, Wnt/ β-catenin signaling pathway

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Abstract: A-10-2556-1

The Role of TGF-β1 and TGF-β3 in Patients with Metabolic and Non-Metabolic Fatty Liver Disease

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Background: Fatty liver disease is a metabolic disorder that can be classified into two categories: metabolic dysfunction-associated fatty liver disease (MAFLD) and non-MAFLD. TGF-β is likely a significant factor in the pathogenesis of this disease. The concurrent role of TGFβ1 and TGFβ3 genes in the development of fatty liver disease, particularly MAFLD, remains unexplored. Therefore, in this study, we aimed to investigate the gene expression of these two isoforms in patients with MAFLD and non-MAFLD.

Methods: In this study, we evaluated 41 patients with fatty liver, including 22 patients with MAFLD and 19 patients with non-MAFLD, in comparison to 22 healthy controls. Gene expression of TGF-β1, TGF-β3 were quantified using qRT-PCR.

Results: Gene expression analysis revealed a significant decrease in the expression of TGF-β1 and TGF-β3 genes in patients with MAFLD ($P<0.001$ and $P<0.05$, respectively) and non-MAFLD ($P<0.05$ and $P<0.05$, respectively) when compared to the control group.

Conclusion: The decrease in TGFβ1 and TGFβ3 gene expression in patients with fatty liver can indicate the weak role of these two isoforms in the development of fatty liver disease.

Keywords: MAFLD, non-MAFLD, TGF-β1, TGF-β3

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Abstract: A-10-2760-1

The Association Between ApoD Polymorphism and Type 2 Diabetes (A Systematic Review)

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Background: Apolipoprotein D (ApoD) is a glycoprotein that produced in the brain, testes and liver and is associated with HDL. ApoD plays a role in the metabolism of cholesterol and other lipids, and malfunction in ApoD may cause diseases related to lipid metabolism and neurological system. Type 2 diabetes (T2DM) is accounting for 90-95% of diabetes cases. It occurs when the pancreas fails to produce sufficient insulin. Risk factors of T2DM include obesity, sedentary lifestyle, family history, and depression. The association between ApoD polymorphism and Type 2 Diabetes has been investigated in several studies. The results of this studies are conflicting, as some confirm the association while others do not. The purpose of this study is to investigate the relationship between the ApoD polymorphism and Type 2 Diabetes.

Methods: In this systematic review study, we searched for the keywords "ApoD " and " polymorphism " and "diabetes " or "T2DM " and also extracted similar words from the MeSH database and PubMed, Google Scholar, and Web of Science databases. Initially, 125 results were obtained. Finally, by screening 10 articles were included in the study.

Results: Finally, this study included 1523 patients (mean age: 58.9, men: 45.9%, female: 54.1%) confirmed with T2DM. Studies have shown that rs1568565 (p-value:0.043) and ApoD TaqI polymorphism (in south india) are associated with T2DM and one study has not been concern about this relationship.

Conclusion: There is some evidence suggesting that ApoD may influence metabolic processes related to diabetes. however, the pathophysiological role of ApoD in T2DM is not clear. The results suggest a need for more focused studies on ApoD polymorphism to fully understand its potential implications in diabetes.

Keywords: ApoD, Polymorphism, T2DM, Diabetes

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Abstract: A-10-2661-1

Association of Interlukin1, 6, 18 and Tumor Necrosis Factor A (TNF-α) in Patients with Type 2 Diabetes and Controls

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Background: One of the factors that play an important role in the development of type 2 diabetes is inflammatory factors. The mechanisms that trigger inflammation in diabetes have not yet been clearly defined. It is possible that, the inflammatory response plays an important role in insulin resistance in type 2 diabetes. According to these findings, we decided to measure and compare the number of inflammatory factors such as interleukin 1, 6, 18, TNF-alpha and C-reactive protein in diabetic patients and healthy controls in this study.
Methods: This case-control study included 50 patients with diabetes and 50 healthy individuals who were free of metabolic disease. We used the ELISA kit from Zelbio company to measure the concentration of interleukins and inflammatory factors. The concentration of inflammatory factors was calculated in Pg/ml. SPSS.16 software was used for statistical analysis and the P value of 5% was considered statistically significant.
Results: In this study, the results showed that the concentrations of interleukin 1, 18, and TNF--α in the patient group was higher than the healthy group and it was statistically significant, however, although the levels of interleukin 6 and C-reactive protein in the patient group was higher than the healthy group, it was not statistically significant.
Conclusion: This study demonstrated a significant association between elevated levels of inflammatory factors and Type 2 diabetes in diabetes mellitus patients compared with healthy. Inflammatory markers may serve as potential biomarker for determining the severity and prognosis of type 2 diabetes. However, further studies are required to validate their clinical utility.

Keywords: C-reactive protein, Type 2 diabetes, Inflammatory factors, Tumor necrosis factor α

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Abstract: A-10-2765-1

Capparis Spinosa Fruit Hydroalcoholic Extract Alleviates Paraquat-Induced Pulmonary Fibrosis in Rats

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Background: Pulmonary fibrosis (PF) is a deadly disease manifested by scar tissue accumulation in the lung. There have been some therapeutic options for treating PF; however, most of them have not been efficiently curative or cost-effective. Paraquat is used in agricultural settings to control weed growth. Moreover, the increasing application of Paraquat has been reported in agricultural areas, which can cause life-threatening toxicity in humans and animals. Emerging evidence has demonstrated Capparis spinosa (C. Spinosa) fruit extract has anti-fibrotic, anti-inflammatory, and antioxidant properties. We aimed to evaluate whether C. Spinosa fruit hydroalcoholic extract has a protective effect against Paraquat-induced PF in rats.

Methods: 30 male rats were divided into 5 groups, which included: a control group, a Paraquat control group, a C. spinose group with a dose of 20 mg/kg, a C. spinose group with a dose of 30 mg/kg, a C. spinose group with a dose of 50 mg/kg. Finally, concentrations of hydroxyproline and malondialdehyde (MDA) in lung tissue were assessed and lung indices were determined.

Results: Treatment with C. spinose decreased lung weight. It indicated a reducing effect on status of MDA, and hydroxyproline in lung tissue. Moreover, the number of lung indices demonstrated the preventive role of C. spinose Paraquat-induced PF in rats.

Conclusion: It seems that oral consumption of C. Spinosa can be useful for the improvement of lung tissues against Paraquat-induced PF.

Keywords: Pulmonary fibrosis, Hydroxyproline, Capparis, Spinosa, Paraquat

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Abstract: A-10-2754-1

Study of Antimetastatic Effects of NIO-GIN Nano-Drug on MDA-MB-231 Cell Line

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Background: Medicinal nanocarriers protect drugs from oxidation, isomerization, and decomposition, increase the half-life of drugs in a period of time, and enable controlled and continuous delivery of drugs to target tissues in the body. Niosome is one of the drug delivery carriers that is biocompatible and structurally stable. The aim of this study was to investigate the antimetastatic effects of NIO-GIN nanocarriers against MDA-MB-231 breast cancer cell line.
Methods: NIO-GIN formulated particles were prepared and confirmed by SEM and FTIR tests. MDA-MB-231 cancer cell lines were then treated with formulated nano-drug and cell migration were analysis by Scratch test within 72 hours.
Results: The results showed that NIO-GIN nano-drug has an inhibitory effect on the rate of cell migration and significantly decrease migration compared to the untreated cells as a control group (P value <0.001).
Conclusion: According to the results, nano-drug formulated in this study based on niosomes as a nanocarrier and gingerol drug, can be an anti-metastatic agent for future breast cancer therapy Strategies.

Keywords: Niosome, Gingerol, Metastasis, Breast cancer, Scratch test

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Abstract: A-10-2768-1

DFT Study of Structural, Vibrational and Electronic Properties of the Abametapir Drug

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Background: Abametapir, brand name Xeglyze, is a new and safe drug for the treatment of head lice. In fact, this drug acts as a metalloproteinase inhibitor, which is essential for the survival of lice and the development of its eggs. Abametapir has received FDA approval on July 27, 2020. Considering the characteristics of this drug, we decided to investigate the electronic properties of the Abametapir molecule from density functional theory (DFT).
Methods: The study utilized quantum mechanics (QM) calculations conducted through the density functional theory (DFT) method with the GAUSSIAN 09 software. First, we drew the structure of the drug with GaussView v.5.08 software, and then we performed the resulting structure calculations in Gaussin 09W program with B3LYP method and 6-311++G** basis set and job type opt+freq. Then we extracted the bond length, bond angle, Homo Lumo gap and also HF energy from the output file.
Results: In this study, structural parameters such as bond length, bond angle, dihedral angle were investigated, and the atomic charge and IR spectrum of Nair were determined. HF energy was determined as -360290.01371353 kcal/Mol, as well as Zero-point energy -360157.52150313 kcal/Mol, Enthalpies -360149.05325568 kcal/Mol, Thermal energies -360149.64562512 kcal/Mol, CV 46.829 Cal/Mol-Kelvin. S 114.668 Cal/Mol -Kelvin were calculated. The highest occupied molecular orbital (HOMO) was determined to be -0.23993 eV and the lowest unoccupied molecular orbital (LUMO) was determined to be -0.05115 eV. The dipole moment in Debye was measured as X= 0.0000, Y= 3.1564, Z= 0.0026, with a total dipole moment of 3.1564.
Conclusion: Drug optimization was done using B3LYP/6-311++G** method. This study focused on the electronic properties of Abametapir, especially the energy difference between HOMO and LUMO. The HOMO-LUMO gap energy was determined to be 0.18878 eV. Also, the structural parameters, IR spectrum and molecular energies were extracted and analyzed.

Keywords: Abametapir, QM-DFT Calculations, B3LYP, HOMO-LUMO gap

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Abstract: A-10-2475-1

Interaction Between Equine Cardiac Myoglobin and Endosulfan Using A Combination of Spectroscopy and Molecular Dynamics Simulation Techniques

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Background: The expansion of agriculture has led to an increase in the use of pesticides, which is a threat to human health. One such pesticide, endosulfan (END) is an organochlorine pesticide used for insect control. Endosulfan has been linked to immune system abnormalities and other diseases. It is also carcinogenic. We evaluated its toxicity through studies on myoglobin using multispectral and molecular simulation techniques.

Methods: We utilized a Pharmacia Ultrospec 4000 visible spectrophotometer to assess the alterations in absorbance of myoglobin alone and Mb-END across a specified temperature span. The Gromax 2019.6 package, employing the Amber99S force, simulated systems comprising free myoglobin and myoglobin complexed with a ligand within the water cube box. For recording the FT-IR spectrum of MB with and without END, a high-resolution ATR method was used to obtain the FT-IR spectrum in the 1450-1900 cm2 range.

Results: Molecular dynamics modeling indicated a reduction in the average Root Mean Square Deviation (RMSD) aligning with increased Thermal denaturation (TM) findings in thermal stability studies. The Fourier Transform Infrared Spectrometer (FT-IR) spectroscopy measurements revealed alterations in the molecular composition of horse heart myoglobin upon binding with endosulfan.

Conclusion: The stability of myoglobin and its interaction with endosulfan were investigated using temperature stability, FT-IR, and MD methods to assess the impact of the insecticide on Mb structure and function. Examination of thermal stability showed that END plays a role in enhancing stability. Molecular dynamics simulations of Mb revealed an improvement in myoglobin stability. FT-IR analysis results indicated that this interaction causes changes in myoglobin's secondary structure, leading to a decrease in β-sheet and α-helix content and an increase in random coils.

Keywords: Myoglobin, endosulfan, Endosulfan, FT-IR spectroscopy , Thermal denaturation, Pesticide

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Abstract: A-10-2769-1

Screening Fecal Calprotectin Level as a Marker in Alzheimer's Disease and Parkinson's Disease: A Systematic Review

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Background: Alzheimer's (AD) and Parkinson's disease (PD) are neurodegenerative disorders that can cause cognitive impairment. Calprotectin, a protein found in immune cells, increases with inflammation. Due to the gut-brain axis, researchers are exploring the link between fecal calprotectin (FC) levels and cognitive decline. This systematic review evaluates FC level as a potential marker in AD and PD.

Methods: Adhering to the Cochrane systematic review principles and PRISMA guidelines, we organized a systematic review, searching databases until August 2024 containing PubMed, Web of Science, and Scopus databases alongside the Google Scholar search engine for searching grey literature, using keywords including "cognitive impairment" and "Calprotectin" and their related keywords. The criteria included all human case-control, cohort, and comparative cross-sectional studies investigating the level of FC. Exclusion criteria were reviews, interventional and animal studies, guidelines, and case-report studies. Two authors independently screened and extracted the data, with any discrepancies resolved by a third author. The quality of the included studies was assessed using the Newcastle-Ottawa scale. The final data were presented in an extraction table.

Results: Out of 106 initial studies, 46 were omitted for duplication and 53 for lack of relevancy, leaving only 7 studies included. The included studies evaluated 637 people, with 269 (n = 42.23%) having PD or AD and 368 (n = 57.77%) in the control group. 4 studies were about PD. All four studies found a significant relationship between FC level and PD. The other 3 studies were about AD. Two of these studies found no significant association between FC level and AD, but one found a significant association between FC level and AD.

Conclusion: This study indicates that FC level is elevated in PD and AD patients, suggesting a possible association with cognitive impairment in PD and AD. However, further research is required to substantiate these findings.

Keywords: Calprotectin, Alzheimer's disease, Parkinson's disease, cognitive impairment, dementia, gut-brain axis

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Abstract: A-10-2608-1

Novel Carboxy Methyl Cellulose/gelatin Hydrogel Incorporating Sio2 for Doxorubicin Delivery

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Background: Prostate cancer is one of the most common cancers diagnosed in men worldwide. so choosing an appropriate treatment method is important. Doxorubicin is one of the common chemotherapy drugs that is used for all types of cancers, but using this drug for the purpose of treatment has side effects such as damage to the heart, liver, and kidney. Nowadays, the use of drug delivery methods based on hydrogel nanoparticles, due to their high surface-to-volume ratio and small size, increases the effectiveness and possibility of drug penetration into the target tissue and reduces its toxicity.

Methods: In this work, a nano composite hydrogel based on carboxy methyl cellulose, gelatin and SiO2 nanoparticle was developed using the water oil water emulsification technique for the efficient delivery of doxorubicin drug. Its size distribution and colloidal stability were investigated via DLS and zeta potential tests, and FTIR analyzes provided information about the its components.

Results: Nanocomposites have structures with an average size of 65 nm and a zeta potential of -75.2 mV respectively. interaction between nanocomposite was analyzed through FTIR, the results of which were desirable and confirmed previous similar studies.

Conclusion: The results support that this nanocarrier can be used as a novel hydrogel-based drug delivery system in prostate cancer therapy

Keywords: Nanocomposite, hydrogel, doxorubicin, drug delivery system, cancer, prostate

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Abstract: A-10-2768-3

Quantum-Mechanics DFT Computations of the Zuranolone Drug

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Background: Zuranolone is a neuroactive steroid that acts as a positive allosteric modulator of the GABAA receptors. Unlike other more common GABAA positive allosteric modulators on the market like benzodiazepines, Zuranolone can modulate both synaptic and extrasynaptic GABAA conductance due to binding to a non-benzodiazepine site on the receptor. Zuranolone was approved by the FDA on August 4th, 2023, and it is currently the only approved treatment for women with postpartum depression. This approval was based on favorable results from 2 phase 3 clinical trials. Considering the characteristics of this drug, we decided to investigate the electronic structure of molecule from density functional theory (DFT).

Methods: The study utilized quantum mechanics (QM) calculations conducted through the density functional theory (DFT) method with the GAUSSIAN 09 software. First, we drew the structure of the drug with GaussView v.5.08 software, and then we performed the resulting structure calculations in Gaussin 09W program with B3LYP method and 6-311++G** basis set and job type opt. Then we extracted the bond length, bond angle, Homo Lumo gap and also HF energy from the output file.

Results: In this study, structural parameters such as bond length, bond angle, dihedral angle were investigated, And the atomic charge was also determined. HF energy was determined as -808719.49511695 Kcal/mol. The highest occupied molecular orbital (HOMO) was determined to be -0.26426 eV and the lowest unoccupied molecular orbital (LUMO) was determined to be -0.05337 eV. The dipole moment in Debye was measured as X= 4.2443, Y= 4.9188, Z= 1.5019, with a total of 6.6682.

Conclusion: Drug optimization was done using B3LYP/6-311++G** method. This study focused on the electronic properties of Zuranolone, especially the energy difference between HOMO and LUMO. The HOMO-LUMO gap energy was determined to be 0.21089 eV. Also, the structural parameters and HF energy were extracted and analyzed.

Keywords: Zuranolone, QM-DFT Calculations, B3LYP, HOMO-LUMO gap

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2549-1

Design and Manufacture of Starch Gelatin Nanocarrier Containing Curcumin Drug for Cancer Treatment

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Background: Cancer, which is the dreaded disease of the century, has a high mortality rate and complications. The use of nanotechnology with medicinal nanocarriers has been shown to enhance results in cancer treatment, reducing the consumption and use of traditional medicinal methods of curcumin drug, which is a hydrophobic drug.
Methods: In our nanocarrier fabrication, Fourier transform infrared spectroscopy (FTIR), dynamic light scattering (DLS), and zeta potential measurements were used to investigate the bonds formed and the surface charge of the fabricated nanocarrier. The recorded results were satisfactory. A hydrogel of double emulsion of gelatin and starch that encapsulates the drug curcumin and we made it with amounts of 0.01 g of gelatin (0.25%) and 0.02 g of starch (0.5%).
Results: Our DLS results showed a particle size of 266 nm and a zeta potential surface charge of -2 mV. In addition, FTIR analysis was performed in the range of 450-4000 cm-1, which led to improved performance and increased stability of our nanocarrier system.
Conclusion: The findings show that these stable nanocarriers, consisting of gelatin and starch, are uniform and responsive. In addition, they help prevent overdose and minimize the side effects of curcumin medication

Keywords: Nanocarriers, Curcumin, Gelatin, Starch, Nanocarrier system, Cancer

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Acta Biochimica Iranica

Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2454-3

New Treatment Approaches in Alzheimer's Disease Based on Molecular Mechanisms Involved in It

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Background: Alzheimer's disease (AD) is characterized by memory loss, multiple cognitive disorders and impairment of behavioral. AD is currently diagnosed by three standard criteria, a) dementia in life, b) amyloid plaques at autopsy and c) neurofibrillary tangles at autopsy. Currently, there is no drug agent for definitive treatment of patients. This article aims to investigate the molecular mechanisms involved in the pathogenesis of AD and presents strategies and potential agents based on the pathological pathway.

Methods: The articles of this study were obtained by searching PubMed, Scopus, Elsevier, Web of science, and Google scholar databases on 2005 to 2024, our key word was AD, molecular pathogenesis and regenerative medicine. In this study, the available therapeutic strategies to induce neurodegeneration that can increase the number of neurons and survival of neurons and improve the plasticity of synapses and synaptic activity were summarized.

Results: base of our research we find 17400 articles, which 1360 articles were related to our subject and we used 500 article for this review manuscript. The results of the investigated treatment strategies were presented based on reducing the level of amyloid beta and hypophosphorylated tau protein, inhibition of acetylcholinesterase and treatments based on regenerative medicine such as gene therapy (increasing neurotrophic expression), cell therapy (stem cell transplantation) and tissue engineering.

Conclusion: As a proposed solution in recent years, the use of inhibitors of the pathogenesis of Alzheimer's disease is a supportive treatment solution, but the multi-potential treatment of regenerative medicine has been able to provide promising results in the treatment of neurodegenerative patients.

Keywords: Alzheimer's, Molecularbasis, Regenerative Medicine

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2780-1

Comparative Analysis of Thyroid Hormone Levels in Patients With Glucose-6-Phosphate Dehydrogenase Enzyme Deficiency and Healthy Subjects

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Background: Glucose 6 phosphate dehydrogenase (G6PD) deficiency, the most common X-linked genetic disorder, is caused by mutations in the G6PD gene and affects approximately 500 million people worldwide. Thyroid hormones are important for controlling biochemical reactions in tissues. Existing researches suggest that thyroid hormones may affect G6PD enzyme activity. This study aimed to investigate the effect of reduced red blood cell G6PD enzyme activity on thyroid hormone levels, thereby addressing an important health issue.
Methods: The study compared TSH and FreeT4 hormone levels in people with and without G6PD enzyme deficiency. The study involved 120 participants, half of whom had G6PD enzyme deficiency and the other half were normal, and was performed with great accuracy. G6PD screening was performed using the fluorescent spot test (FST), and thyroid hormone levels were measured using electrochemiluminescence with an ELISA kit. The data was then thoroughly analyzed using SPSS software to ensure the reliability and robustness of the results.
Results: The mean serum TSH level in people with G6PD deficiency was 4.09 ± 2.27 mU/L, higher than the mean level of this hormone in normal people, 3.46 ± 2.14 mU/L (p value = 0.084). However, the increase in TSH levels in patients was not statistically significant. Another hormone measured was free T4, which was 11.68 ± 1.61 mU/L in normal subjects and 11.66 ± 1.90 mU/L in patients. Statistically, this small difference in free T4 levels was not significant (p value = 0.47).
Conclusion: The study found that people with G6PD deficiency had slightly higher TSH levels and slightly lower free T4 levels than normal people, although these differences were not statistically significant. No significant correlation was found between G6PD enzyme deficiency and thyroid hormone levels. These findings suggest potential areas for further research and intervention for people with G6PD deficiency.

Keywords: Hormone, Thyroid, Glucose 6 phosphate dehydrogenase

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2389-1

The Combined Therapeutic Effect of Salinomycin and D4476 on Hct116 Cells By Targeting Autophagy and Ferroptosis

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Background: As the third leading cause of cancer-related death worldwide, colorectal cancer (CRC) has become a major health concern. As new therapeutic approaches for cancer treatment, compounds that induce non-apoptotic cell death have been considered recently. Ferroptosis as an autophagy-mediated cell death is one of these approaches. Autophagy flux inhibition following the autophagosome accumulation activates the ferroptosis pathway. The Salinomycin (Sal) antibiotic and D4476 as a selective inhibitor of Casein kinase 1 alpha (CK1α) block the autophagy flux and act as anticancer agents. This study was designed to better understand the action mechanism of these agents alone or in combination in the CRC HCT116 cell line with a focus on autophagy and ferroptosis pathways.

Methods: MTT assay was performed to determine the HCT116 cell viability after treatment with Sal alone or in combination with D4476. The gene expression of Beclin-1, P62, and LC3βII, was analyzed as autophagy biomarkers using quantitative real-time polymerase chain reaction. In addition, reduced glutathione (GSH) assay and Malondialdehyde (MDA) measurement were accomplished to evaluate the ferroptosis pathway.

Results: The MTT results showed that the combination of Sal and D4476 inhibited cancer cell growth more effectively than Sal alone. The expression enhancement of Beclin-1, P62 and LC3βII indicated autophagy flux inhibition in combined treated cells compared with untreated control cells. Moreover, Sal/D4476 combination led to the MDA elevation and GSH reduction, as the signs of ferroptosis activation.

Conclusion: This study revealed the innovative antitumor effects of Sal/D4476 combination in HCT116 cell line, achieved through the ferroptosis induction following the autophagy flux inhibition. Our findings propose a new CRC treatment approach, though further studies are necessary to confirm these results.

Keywords: Salinomycin, D4476, Autophagy, Ferroptosis, Colorectal cancer, HCT116 cells.

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2768-2

Quantum-Mechanics DFT Computations of the Drug Cromoglicic Acid

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Background: The drug Cromoglicic acid, also known as Cromolyn, is available under the brands Gastrocrom, Nalcrom and NasalCrom. Cromolyn is a new class of drugs whose pharmacological activities offer a new approach to the treatment of asthma. Cromolyn has been recognized as a significant breakthrough by the pharmaceutical industry. Local drug administration has been effective in seasonal and multi-year rhinoconjunctivitis and in selected cases of digestive sensitivity to foods, some allergic eye diseases and keratitis. Cromoglicic acid is FDA approved. Considering the characteristics of this drug, we decided to investigate the electronic structure of the molecule from density functional theory (DFT).

Methods: The study utilized quantum mechanics (QM) calculations conducted through the density functional theory (DFT) method with the GAUSSIAN 09 software. First, we drew the structure of the drug with GaussView v.5.08 software, and then we performed the resulting structure calculations in Gaussin 09W program with B3LYP method and 6-311++G** basis set and job type opt. Then we extracted the bond length, bond angle, Homo Lumo gap and also HF energy from the output file.

Results: In this study, structural parameters such as bond length, bond angle, dihedral angle were investigated, And the atomic charge was also determined. HF energy was determined as -1075547.0947568 Kcal/mol. The highest occupied molecular orbital (HOMO) was determined to be -0.23678 eV and the lowest unoccupied molecular orbital (LUMO) was determined to be -0.09678 eV. The dipole moment in Debye was measured as X= -0.2906, Y= -2.4667, Z= 2.3056, with a total of 3.3889.

Conclusion: Drug optimization was done using B3LYP/6-311++G** method. This study focused on the electronic properties of Cromoglicic acid, especially the energy difference between HOMO and LUMO. The HOMO-LUMO gap energy was determined to be 0.14 eV. Also, the structural parameters and HF energy were extracted and analyzed.

Keywords: Cromoglicic acid, QM-DFT Calculations, B3LYP, HOMO-LUMO gap

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2774-1

Investigating the Effect of Amitraz on Human Serum Albumin: Fourier Transform Infrared, Thermal Stability, and Molecular Dynamics Simulation

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Background: Amitraz is an insecticide and ectoparasiticide commonly used in agriculture. Human poisoning with amitraz can occur through ingestion, skin contact, or inhalation. While pesticides offer significant benefits in agriculture, their adverse effects on non-target species, including humans, are a serious concern. Once introduced into the body, pesticides can disrupt the function of human proteins. Specifically, pesticides are transported in the bloodstream by binding to human serum albumin (HSA).

Methods: The impact of amitraz on the secondary structure of HAS was examined using Fourier Transform Infrared (FT-IR) spectroscopy. The melting temperature (Tm), which represents the temperature at which the protein unfolding occurs, was measured to evaluate the thermal stability. Additionally, molecular dynamics (MD) simulations were conducted to evaluate secondary structure alterations and calculate the root mean square deviation (RMSD).

Results: In the 200 ns MD simulation, the average RMSD for the HSA-amitraz complex was significantly higher than that of free HSA, indicating a decrease in the stability of the HSA structure. This result was further corroborated by a decrease in the Tm value from 371 K to 303 K. FTIR spectroscopy revealed changes in the secondary structural elements of HSA before and after amitraz binding, aligning with the findings from the MD simulations.

Conclusion: The study demonstrates that amitraz induces significant changes in the secondary structure of HSA, leading to decreased protein stability. Understanding these interactions is crucial for assessing potential risks and mitigating adverse effects on public health and the environment.

Keywords: Amitraz, Human serum albumin, Pesticides

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2427-1

Investigating the Molecular Mechanisms of Endosulfan Interaction With HSA: Molecular Dynamic Simulation and Spectroscopic Approaches

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Background: Agriculture and food production are vital to meet the needs of a growing population. While pesticides have helped increase agricultural productivity, their use has also devastated the environment. This study focused on the insecticide effect of endosulfan (END) on human serum albumin (HSA) protein at neutral pH.

Methods: Shimadzu RF-5301 fluorescence spectroscopy was used to investigate the change in protein tertiary structure and the change in fluorescence emission caused by the protein in the presence of ligand. The thermal stability of ligand-bound HSA protein was determined by thermal unfolding studies using a Pharmacia UV4100 spectrophotometer. Molecular dynamics (MD) simulations were performed using GROMACS 2019.6 and the Amber99SB force field to evaluate the stability of the CD-HSA complex based on the most favorable binding outcome.

Results: In this study, protein changes in the presence of ligand (endosulfan) were investigated by different methods. We found that at neutral pH, endosulfan decreased the fluorescence of HSA. In addition, as the temperature increases, it leads to static quenching and a decrease in the Stern-Volmer constant. These changes in protein-ligand spectroscopy are attributed to changes in the tertiary structure of the protein, increasing its hydrophobicity, and the migration of tryptophan amino acid to more hydrophobic regions. Also, our findings showed that higher levels of endosulfan decreased the protein's thermal stability and affected its structural stability. The RMSD results confirm the thermal stability and increased flexibility of the complex. Molecular dynamics simulations confirmed the importance of hydrogen and van der Waals bonds in the interaction between toxin and protein-Ligand complex.

Conclusion: The alterations are a result of shifts in the local structure of the HSA protein, leading to a disruption of its functionality. Understanding these findings is crucial to assess the potential impact of endosulfan on human health.

Keywords: Endosulfan, Insecticide, Human serum albumin

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2751-2

Investigating the Relationship Between Depression, Anxiety, and Lipid Profiles in Participants Undergoing Coronary Angiography

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Background: Depression and anxiety are prevalent among patients with heart disease, and dyslipidemia is a known risk factor for cardiovascular conditions. This study explores the association between mental health disorders (depression and anxiety) and lipid profile specifically cholesterol and triglyceride in individuals undergoing coronary angiography.

Methods: This cross-sectional study included 720 middle-aged adults who underwent coronary angiography at Afshar Hospital in Yazd, Iran, between June 2020 and November 2021. Inclusion and exclusion criteria were applied to ensure the homogeneity of the sample. Ethical approval was obtained, and participants provided informed consent. Depression and anxiety were assessed using Beck Depression Inventory (BDI-II) and Beck Anxiety Inventory (BAI), and fasting blood samples were collected to measure lipid profiles. Data were analyzed using STATA version 14 (State Corp., College Station, TX). Binary logistic regression models, in crude and multivariable-adjusted, were employed to assess the odds ratios (OR) and 95% confidence intervals (CIs) for the relationship between depression, anxiety and lipid levels.

Results: Analysis revealed that those with normal triglyceride levels (≤150) were significantly older than those with elevated levels. Additionally, the prevalence of diabetes was significantly higher among individuals with elevated triglycerides. We did not find significant association between depression and anxiety with serum triglyceride and total cholesterol levels among total population in crude and adjusted models. This relation remained non-significant after subgroup analysis by sex.

Conclusion: This study found no significant association between depression, anxiety, and lipid profiles in individuals undergoing coronary angiography, suggesting that these mental health conditions may not directly associated with these lipid markers in this population. Prospective cohort studies are needed to confirm these findings.

Keywords: Depression, anxiety, Triglycerides, Cholesterol, Coronary Angiography

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Abstract: A-10-2495-1

The Dual Effect of Methylglyoxal on the Viability of Atherosclerotic Vascular Endothelial Cells: A Dose-Dependent Study

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Background: Methylglyoxal (MG) is a highly reactive dicarbonyl compound that forms as a byproduct of glucose metabolism and has been implicated in the progression of cardiovascular diseases. Nevertheless, recent research has highlighted MG's protective roles in low doses, particularly in the context of its antimicrobial properties and cancer therapy. Therefore, in this study, we have addressed both the protective and detrimental impacts of MG to assess cell viability in an in vitro model of atherosclerosis.

Methods: Human umbilical vein endothelial cells (HUVECs) were initially seeded in a 96-well plate at 2×104 cells/well for 24h in DMEM-F12 supplemented with 10% fetal bovine serum and incubated at 37 °C and 5% CO2. HUVECs were treated with 1 mM palmitic acid (PA) for 24 h and then exposed to different doses of MG (60, 80, 100, 200, 400, 800, 1000, 1500 µM) for the next 24 h. The cell survival rate was assessed using Methyl Thiazolyl Blue Tetrazolium Bromide (MTT) assay at 570 nm using a microplate reader. Cellular atherosclerosis and lipid accumulation were evaluated using oil red O staining.

Results: The survival rate increased significantly in 60 µM MG compared to other groups and decreased in 400 µM MG ($P < 0.05$). Furthermore, oil red O staining showed an increase in lipid droplets after incubation with PA, especially PA+60 µM MG and PA+400 µM MG.

Conclusion: The number of viable endothelial cells was significantly reduced following treatment with high doses of MG, indicating its potential cytotoxicity at higher concentrations. However, lower doses showed less toxic effects, suggesting a possible protective role of MG on atherosclerotic cells. Thus, MG may have a dose-dependent protective role in atherosclerotic cells, warranting further investigation

Keywords: Methylglyoxal, Atherosclerosis, Endothelial cells, Palmitic acid

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2785-1

Isotretinoin's Effect on Serum Lipids Levels

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Background: Isotretinoin, a potent oral retinoid, is widely recognized for its efficacy in treating severe acne. Despite its success in acne management, concerns about its impact on lipid profiles persist. This study aims to investigate the effect of isotretinoin on fasting lipid levels in acne patients, as dyslipidemia could be a potential adverse effect of the medication. Understanding these effects is crucial for managing the overall health of patients undergoing treatment.

Methods: The data were collected by searching PubMed, Scopus and Google Scholar search engine.The advanced searched keywords were: “isotretinoin”, “lipid”, “cholesterol” and “triglycerides”. The search was limited to studies in the English language and accessible full texts that published from 2014 to 2024. Review, duplicate, and non-relevant articles were excluded.

Results: In this systematic review study, 28 articles were retrieved through searching in databases, of which only 8 articles matched our inclusion criteria after preprocessing and screening. In This research multiple studies consistently reported an increase in the level of triglycerides and cholesterol and low-density lipoprotein cholesterol (LDL-C), which has the highest increase in triglycerides, followed by and low-density lipoprotein cholesterol (LDL-C). Unlike other lipids, high-density lipoprotein cholesterol (HDL-C) decreases after taking isotretinoin. However, it should be highlighted that only a small percentage of patients that receiving treatment have these negligible, clinically insignificant alterations.

Conclusion: This study reveals significant changes in fasting lipid profiles in patients undergoing isotretinoin therapy. While isotretinoin remains a cornerstone in the treatment of severe acne, monitoring lipid levels is essential to address potential dyslipidemia and mitigate associated risks. Further research is needed to explore long-term implications and establish guidelines for managing lipid changes during isotretinoin treatment.

Keywords: Isotretinoin, Lipid, Cholesterol, Triglycerides

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Abstract: A-10-2787-1

Identifying Potential Biomarkers for Early Diagnosis in Colorectal Cancer

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Background: Colorectal cancer is a prevalent type of cancer that is observed globally. It can develop from single gene mutations or occur sporadically, but it can also be linked to hereditary factors. Biomarkers play a crucial role in detecting colorectal cancer at an early stage. The aim of this research is to pinpoint a reliable biomarker for the early detection of colorectal cancer through the use of bioinformatic techniques.

Methods: We obtained datasets GSE142279 and GSE186510 from the Gene Expression Omnibus (GEO). The DESeq2 package was utilized for analyzing differential expression in the GSE142279 dataset, considering $P < 0.05$ to be statistically significant. followed by KEGG pathway enrichment analysis, GO ontology analysis, and the construction of a protein-protein interaction network to identify hub genes related to bile secretion. In the GSE186510 dataset, we employed the WGCNA package in R to identify microRNAs associated with colorectal cancer. Furthermore, we identified the targets of microRNAs based on hub genes using the miRWalk database. Based on the dataset and miRWalk database we choose the miRNAs.

Results: Finally, we have identified 1435 genes with a logFC of less than 2 and p-value< 0.05. Based on MCODE and CytoHubba plugins in Cytoscape, we have pinpointed four hub genes, including ABCG2, ABCB11, UGT1A7, and UGT1A8. Our findings suggest that hsa-miR-766-3p and hsa-miR-935 may suppress the expression of ABCG2, as a key gene.

Conclusion: These microRNAs include hsa-miR-766-3p and hsa-miR-935 may be also serve as potential biomarkers for early detection in colorectal cancer, but pending experimental analysis.

Keywords: Colorectal cancer, Early diagnosis, Biomarker

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Abstract: A-10-2789-1

Lifitegrast: Quantum Mechanical Exploration

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Background: Lifitegrast, FDA-approved in 2016, is a T-cell integrin antagonist for dry eye disease (DED). It inhibits LFA-1 from interacting with ICAM-1, reducing inflammation. Clinical studies show Lifitegrast improves corneal staining, tear break-up time, and ocular discomfort. While it is effective, it may cause mild adverse effects like site discomfort and dysgeusia, but is generally well-tolerated.
Methods: The study utilized quantum mechanical (QM) calculations through density functional theory (DFT) with GAUSSIAN 09 software. Lifitegrast's molecular structure was optimized using gradient methods at both restricted Hartree-Fock (HF) and hybrid density functional B3LYP levels, employing the 6-311G basis set. The findings showed that the optimized structure was at a potential energy surface minimum and lacked negative vibrational modes.
Results: In this study, structural parameters such as bond lengths, angles, and dihedrals, along with thermodynamic properties, were computed using the B3LYP/6-311G method. The molecule's electronic energy was -3073.94945304 kcal/mole. Mulliken atomic charges, spin densities, and molecular orbital energies were also analyzed. The highest occupied molecular orbital (HOMO) was -0.23626 eV, and the lowest unoccupied molecular orbital (LUMO) was -0.06680 eV. The dipole moment values were X=5.0282, Y=-1.2783, Z=-6.9467, totaling 8.6703 Debye.
Conclusion: The optimization of Lifitegrast was conducted using the B3LYP/6-311G method. The focus was on its electronic properties, specifically the energy gap between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). The calculated HOMO-LUMO gap was 0.16 eV. These results provide important insights into Lifitegrast's electronic behavior, which may have implications for various applications.

Keywords: Lifitegrast, DFT, B3LYP/6-311G, HOMO-LUMO gap

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Abstract: A-10-2789-2

Metaxalone: A Quantum Mechanics Perspective

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Background: Metaxalone, approved by the FDA in 1962, is a muscle relaxant for acute skeletal muscle pain. It depresses polysynaptic reflexes without directly relaxing muscles. Recent studies show its potential in treating neurological disorders by reducing pro-inflammatory markers and enhancing anti-inflammatory cytokines in microglial cells.

Methods: The study employed quantum mechanical (QM) calculations using the density functional theory (DFT) method with GAUSSIAN 09 software. The molecular structure of Metaxalone was optimized via gradient procedures at both restricted Hartree-Fock (HF) and hybrid density functional B3LYP levels of theory, utilizing the 6-311G basis set. The results indicated that the optimized structure was located at the minimum point on the potential energy surface, exhibiting no negative vibrational modes.

Results: This study calculated structural parameters such as bond lengths, angles, and dihedrals, along with thermodynamic properties, using the B3LYP/6-311G method. The electronic energy of the molecule was -746.696819197 kcal/mole. Mulliken atomic charges, spin densities, and molecular orbital energies were also computed. The highest occupied molecular orbital (HOMO) was -0.22820 eV, while the lowest unoccupied molecular orbital (LUMO) was -0.00498 eV. The dipole moment was X=0.5125, Y=5.5774, Z=-1.8846, totaling 5.9095 Debye.

Conclusion: The optimization of Metaxalone was carried out using the B3LYP/6-311G method. The study concentrated on the electronic properties of Metaxalone, particularly the energy difference between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). The HOMO-LUMO gap was calculated to be 0.22 eV. These findings offer valuable insights into Metaxalone's electronic behavior, with potential applications in multiple fields.

Keywords: Metaxalone, DFT, B3LYP/6-311G, HOMO-LUMO gap

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2789-3

Quantum Mechanical Analysis of Ranolazine

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Background: Ranolazine, FDA-approved for chronic angina, is used with amlodipine, β-adrenoceptor antagonists, or nitrates. It inhibits the late inward sodium current, reducing calcium overload. Metabolized primarily by CYP3A, it has a half-life of 1.4–1.9 hours (immediate-release) or up to 7 hours (extended-release). Common side effects include dizziness, constipation, and nausea.

Methods: The study applied quantum mechanical (QM) calculations using density functional theory (DFT) with GAUSSIAN 09 software. The molecular structure of Ranolazine was optimized with gradient techniques at both restricted Hartree-Fock (HF) and hybrid density functional B3LYP levels, using the 6-311G basis set. Results indicated that the optimized structure represented a minimum on the potential energy surface and had no negative vibrational modes.

Results: In this study, structural parameters such as bond lengths, angles, and dihedrals, along with thermodynamic properties, were evaluated using the B3LYP/6-311G method. The electronic energy of the molecule was calculated to be -1399.45052951 kcal/mole. Mulliken atomic charges, spin densities, and molecular orbital energies were also assessed. The highest occupied molecular orbital (HOMO) was -0.21816 eV, and the lowest unoccupied molecular orbital (LUMO) was -0.02052 eV. The dipole moment measurements were X=-0.0513, Y=2.9026, Z=-4.5744, totaling 5.4178 Debye.

Conclusion: Ranolazine was optimized using the B3LYP/6-311G method. The study concentrated on its electronic properties, particularly the energy difference between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). The calculated HOMO-LUMO gap was 0.19 eV. These findings offer valuable insights into Ranolazine's electronic characteristics, potentially influencing its applications.

Keywords: Ranolazine, DFT, B3LYP/6-311G, HOMO-LUMO gap

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2573-1

Clinical, Hematological, and Biochemical Characteristics of Hospitalized Patients with Covid-19 from Halabja, Kurdistan of Iraq

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Background: It is necessary to provide an assessment of the risk of mortality and severity of COVID-19 by use of laboratory tests, especially in developing countries. The purpose of this study is to determine the clinical, hematological and biochemical characteristics of hospitalized patients with COVID-19.
Methods: We studied 200 hospitalized patients aged 30 to 90 years, including 123 men and 77 women from Halabja region of Kurdistan, Iraq.
Results: The overall mortality rate of hospitalized patients with COVID-19 from Kurdistan of Iraq was 17.5% with a high mortality rate (25%) among patients ≥ 55 years. Around 67% of ICU admitted patients died. The levels of potassium (K) and chloride were significantly higher and lower, respectively in severe COVID-19 patients compared to non-severe ones. The levels of urea at hospital admission and during hospitalization were significantly higher comparing non-survivors with survivors, and severe patients with non-severe patients. A significant association between leukocytosis, Hemoglobin (Hb) level 149 g/L or higher, high monocytes count, and low lymphocytes to monocytes count with the mortality rate was found. INR>1.2 and D-Dimer ≥0.72 µg/ml at hospital admission, lymphocyte to monocyte ratio ≥1.15, Hb ≥149 g/L, C-reactive protein (CRP) ≥ 51 mg/L and age> 40 years were associated with severity of the disease and mortality.
Conclusion: The number of monocytes 0.51×109/L and the CRP level 86.14 mg/L in patients with COVID-19 at hospital admission predicted the severity and mortality of the disease which should be closely monitored for timely treatment and improved outcome. These laboratory results obtained from the patients with COVID-19 hospitalized in Halabja, Kurdistan of Iraq could help the management of COVID-19 in other regions.

Keywords: COVID-19, Halabja, Mortality, hematological parameters, Biochemical tests, coagulation factors

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Abstract: A-10-2592-1

Targeting Apoptosis Pathway Proteins to Overcome Cancer Cell Resistance: A Systematic Review

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Background: One of the challenges of cancer drug therapy is drug resistance. One mechanism of drug resistance in cancer cells is the disruption of the programmed cell death or apoptosis pathway. Designing new drugs to target proteins involved in the apoptosis pathway could be a promising strategy to enhance the effectiveness of cancer treatments.
Methods: This review article was conducted using data from PubMed, Web of Science, and Google Scholar databases from the years 2010 to 2023. The search was done by combining the words bcl-2 inhibitors, MCL1 inhibitors, Inhibitor of Apoptosis, cancer resistance, apoptosis pathway.
Results: Among the 60 articles identified, 10 were selected for a detailed review. In silico and in vitro studies indicate that some benzothiazole derivatives, acting as BCL-2 inhibitors (BCL-2 is an apoptosis inhibitor protein), have a positive effect on the mortality of cancer cells. BCL-2 is recognized as an apoptosis-inhibiting protein. Clinical studies have shown that patients treated with venetoclax, a BCL-2 protein inhibitor, had a higher survival rate in chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL). Smac mimetics, as inhibitors of the Inhibitor of Apoptosis (IAP) family, can sensitize cancer cells to apoptosis when used with TNF-α. MCL1 inhibitors induced apoptosis in cell lines from anaplastic large cell lymphoma (ALCL) and primary effusion lymphoma (PEL), suggesting that BH3 mimetics, as MCL1 inhibitors, may be effective as treatments for these diseases.
Conclusion: Designing and investigating the inhibitors of the inhibitory proteins of the apoptosis pathway is a suitable approach to induce apoptosis and address the resistance of cancer cells to treatment. These studies suggest that the continuation of investigations and trials in silico, in vitro and in vivo is a suitable strategy for the treatment of treatment-resistant cancers.

Keywords: Cancer resistance, Apoptosis pathway, BCL-2 protein inhibitors, Smac mimetics, MCL1 inhibitors

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Abstract: A-10-2740-2

Investigating Polymorphisms That Play A Role in Breast Cancer Recurrence

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Background: Breast cancer (BC) is a frequent malignant tumor that increasingly affects women worldwide. The necessity for molecular markers has perpetually been proposed to facilitate the differentiation of individual variability and consequently forecast relapse or survival among patients exhibiting comparable clinical conditions. This study aims to investigate certain polymorphisms that lead to BC recurrence.

Methods: A comprehensive systematic search of relevant studies up to 2024 was performed by searching databases such as PubMed, MEDLINE, SCOPUS, and Google Scholar. The keywords "breast cancer", "multiform" and "recurrence" were used in this search. Only articles with fully accessible English texts were included in the search parameters. Articles that were reviews, duplicates, or irrelevant were not included.

Results: In this systematic review study, only 13 articles matched our inclusion criteria after preprocessing and screening. The examination of multiple genetic polymorphisms pertinent to chemotherapy agents revealed a statistically significant correlation between early postoperative recurrence in patients exhibiting the MDR13435CC and MTHFR677CC genetic polymorphisms, as well as those possessing the additional GSTP1 313AG polymorphisms. Furthermore, the findings from an alternative investigation indicated that the rs1056628 and rs17576 polymorphisms may have an impact on BC recurrence. Additionally, the genotypes related to cytokine production, specifically IL-10, IL-6, IFN-γ, and TNF-α, did not demonstrate any association with overall BC incidence or relapse status; however, the low-production genotypes of TGF-β1 (TGF-β1 10 CC) were found to be linked to an elevated likelihood of disease relapse.

Conclusion: Genetic polymorphisms in inflammatory cytokines and drug-metabolizing enzymes have a major impact on the risk of BC recurrence. Extensive research on the molecular origins and roles of particular genetic variations could result in more effective treatments that lower the risk of recurrence and enhance patients' long-term prognoses with BC.

Keywords: Key words: breast cancer, polymorphism and relapse

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Abstract: A-10-2794-1

Association of Bcl11a Genetic Variant (rs11886868) and Fetal Hemoglobin in B-Thalassemia Patients: A Systematic Review

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Background: β-thalassemia is a genetic disorder causing abnormal hemoglobin production, leading to anemia. Increased fetal hemoglobin (HbF) levels decrease clinical symptoms in patients. The BCL11A gene results in significant silencing of HbF and regulates HbF expression. This review study aims to investigate the association between BCL11A single nucleotide polymorphism (SNP) rs11886868, HbF levels, and anemia severity in β-thalassemia patients.

Methods: Based on Cochrane systematic review principles and PRISMA guidelines, the study was conducted using keywords such as "rs11886868", "β-thalassemia", and "HbF" in databases such as Scopus, PubMed, and Web of Science. These searches were conducted from 2012 to 2024 in the databases. The inclusion criteria were English-language studies that investigated the association of the rs11886868 SNP with HbF level in β-thalassemia patients. The exclusion criteria were reviews and animal studies, and conference articles. Two authors independently conducted screening and data extraction, with a third author's consensus on discrepancies. Quality assessment was done using the Cochrane ROB 2 tool, and data was collected in extraction tables.

Results: Overall, 506 articles were found, and after removing 482 duplicates and irrelevant titles and abstracts, the full text of 24 articles was assessed for eligibility. Finally, 4 studies met the inclusion criteria with 641 β-thalassemia patients. The BCL11A (rs11886868) polymorphism results from a C-to-T nucleotide substitution at the BCL11A gene. in rs11886868 (C/T) The frequency of the C allele, as compared with the "T" allele, was significantly high among the patients with increased levels of HbF. The results showed that the rs11886868 SNP is significantly associated with increasing HbF levels and decreasing the severity of anemia in β-thalassemia patients.

Conclusion: Studies indicate a significant correlation between rs11886868, increased HbF levels, and decreased anemia severity in β-thalassemia patients. However, due to limited studies and heterogeneity, further research is needed to confirm these findings.

Keywords: β-Thalassemia, Fetal hemoglobin, Single nucleotide polymorphism, BCL11A

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Abstract: A-10-2492-1

Inhibition of Glutamine Catabolism Maybe A Promising Approach To Treat Breast Cancer

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Background: Glutamine is a key amino acid for tumor cell growth and proliferation. Glutamine is catabolized to glutamate by the enzyme glutaminase. Recently this enzyme has emerged as a potential target of breast cancer treatment. We used virtual screening method to find new potential FDA-approved drug for inhibition of glutaminase. In addition, the effect of this new inhibitor on cell survival and apoptosis of breast cancer cell lines was studied.
Methods: Using virtual drug screening technique and molecular docking method (using FDA database), suitable drug was selected to inhibit glutaminase activity. Human breast cancer cell lines (MCF-7 and MDA-MB-231) was used for in vitro study. To evaluate the cytotoxic effect of the selected drug, the MTT test was performed and drug IC50 was calculated. Finally, the effect of drug on the mRNA expression levels of BAX and BCL-2 genes was investigated using Real Time PCR.
Results: Among FDA-approved drugs, Rifampin had the highest binding affinity to the predicted active site of the glutaminase with a binding energy of -9.52 kcal/mol. The IC50 values of rifampin was 0.25 µM (CI: 0.019-0.529) and 0.29 µM (CI:0.246-0.340) for MDA-MB-231 and MCF-7 cells, respectively. Rifampin at concentration of 0.25 µM significantly (≈1.96 fold) increase BAX gene expression in both cells, while for BCL2 gene significantly decrease mRNA expression level (≈ 3-fold) was noted in drug treated cells in compared to untreated cells.
Conclusion: Taken together, using virtual drug screening, rifampin was identified as selective inhibitor of glutaminase. In addition, in vitro analysis confirmed the cytotoxic effect of this drug on breast cancer cells. The anti-cancer mechanisms of rifampin may be through upregulation of BAX and downregulation of BCL-2 genes and consequently induction of apoptosis. Inhibition of glutaminase activity using rifampin may be a promising approach for the development of new treatment for breast cancer.

Keywords: Breast cancer, Glutaminase, Apoptosis

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Abstract: A-10-2404-1

Exploring the Antibacterial Properties of Marrubium Vulgare L.: Caffeic Acid's Role in Inhibiting S. Aureus and E. Coli

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Background: Marrubium vulgare L., commonly known as white horehound, is a medicinal plant traditionally used to treat various ailments due to its bioactive compounds, including marrubin. Previous studies have demonstrated that the methanolic extract of M. vulgare exhibits antimicrobial activity against both Gram-positive and Gram-negative bacteria, such as Staphylococcus aureus and Escherichia coli. This antimicrobial effect is primarily attributed to the presence of phenolic compounds, including caffeic acid, gallic acid, verbascoside, and sinapinic acid.

Methods: In this study, the extraction of M. vulgare was performed using the maceration method with methanol as the solvent. Bacterial strains, including Staphylococcus aureus and E. coli, were obtained from the Tehran Pasteur Institute. The Minimum Inhibitory Concentration (MIC) test was conducted by preparing serial dilutions of the methanolic extract (100, 50, 25, 12.5, and 6.25 mg/ml) in 5% DMSO. The disk diffusion test was subsequently performed by applying 20 microliters of each extract concentration to assess bacterial growth inhibition. The Minimum Bactericidal Concentration (MBC) was determined by identifying the lowest concentration of the extract that completely inhibited bacterial growth. Additionally, HPLC analysis was conducted to identify the active compounds in the plant extract.

Results: The MIC test revealed that the methanolic extract of M. vulgare inhibited the growth of E. coli at 12.5 mg/ml, while a concentration of 25 mg/ml was required to inhibit the growth of S. aureus. The MBC was determined to be 25 mg/ml for S. aureus and 50 mg/ml for E. coli. HPLC analysis identified caffeic acid as the predominant compound in M. vulgare, with significant antibacterial properties.

Conclusion: The findings suggest that M. vulgare, due to its high concentration of caffeic acid, holds potential as a natural antibacterial agent, with possible applications in medicine, pharmaceuticals, veterinary medicine, and the food industry.

Keywords: Marrubium vulgare L., Antibacterial, S. aureus, E. coli, Caffeic acid

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Abstract: A-10-2798-2

Investigation of the Effects of Omeprazole on CDKs 2,4, and 6 As A Potential CDK Inhibitor By Simulation Methods

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Background: Cyclin-dependent kinases (CDKs) are serine/threonine kinase proteins that regulate the cell cycle through phosphorylation and dephosphorylation. These proteins are a main target in cancer therapy. This study investigated the effect of omeprazole on CDK2, CDK4, and CDK6 through simulation studies.
Methods: To investigate the interaction between omeprazole and CDK 2, 4, and 6, the three-dimensional structure of omeprazole was obtained from PubChem, and the structures of CDK 2, 4, and 6 were acquired from RCSB servers. All three proteins were run for 50 nanoseconds using the GROMACS 2021 software before the docking process. Next, AutoDock v.4.2.6 software was used to bind omeprazole as a ligand to these proteins, and a molecular dynamics simulation of the resulting protein-ligand complex was conducted using GROMACS after the docking process.
Results: Omeprazole exhibited a high affinity for interacting with CDK2, 4, and 6, mainly occurring in the ATP binding site of CDK4. However, the docking of omeprazole in the CDKs induced conformational changes in their structures; it could potentially affect their function and lead to cell cycle arrest.
Conclusion: Omeprazole, a proton pump inhibitor, can induce cell cycle arrest by interacting with the ATP-binding site of CDK4. Also, it can induce conformational changes in CDK2, CDK4, and CDK6 through high-affinity interactions with specific amino acid residues.

Keywords: Cell cycle, Cyclin-depending kinases, Omeprazole

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Abstract: A-10-2798-3

Investigation of the Effects of Dandelion Root Hydro-Alcoholic Extract on Pon1 Enzyme Activity in Hyperlipidemia Rats

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Background: Paraoxonase1 (PON1) is an enzyme with arylesterase and paraoxonase activity in the serum. This enzyme prevents the oxidation of Low-Density Lipoprotein (LDL). This study evaluated the effect of the hydro-alcoholic extract of dandelion root on the activity of the PON1 enzyme in hyperlipidemia rats using in-vivo, in-vitro, and in-silico studies.

Methods: 40 male rats were divided into four groups of 10. The concentrations of 200 and 400 mg/kg dandelion root hydro-alcoholic extract were administered to the hyperlipidemia groups by gavage compared to the control group. The serum biochemical parameters such as triglyceride, HDL, LDL, and Total Cholesterol were measured by autoanalyzer. The serum PON1 enzyme activity was measured by spectrophotometer according to its arylesterase activity and the PON1 gene expression was investigated using Real-Time PCR in liver tissues. The molecular docking and molecular dynamic studies of the most important compounds of dandelion root on PON1 enzyme were done by AutoDock V4.2 and GROMACS 2020 software.

Results: dandelion root hydro-alcoholic extract decreased serum triglycerides and Total Cholesterol and increased serum PON1 arylesterase activity significantly ($p<0.05$). It also had a significant ($p<0.05$) increase in PON1 gene expression compared to the control group. Simulation and molecular dynamics results proved that among all of the compounds of the Dandelion root Narengine and Luteolin, as the most effective compounds, can bind to the PON1 enzyme by high affinity and induce structural changes in this protein.

Conclusion: Although, all of the Dandelion root compounds can interact with the PON1 enzyme, Narengine, and Luteolin as two important compounds of the Dandelion root can have an effective interaction with the PON1 enzyme and cause increasing in its enzymatic activity.

Keywords: Dandelion root, PON1 enzyme, Molecular dynamics, Hyperlipidemia

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Abstract: A-10-2790-1

Effects of Trace Elements on Soil Organisms in Urban and Rural Areas of Isfahan

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Background: Increasing the concentration of trace elements in the soil is a serious environmental problem that threatens the health of humans and other organisms. Earthworms are numerous and represented in all soil-dwelling and animal bioindicator ecosystem groups.
Methods: In this research, earthworms were used to evaluate this threat. Earthworms are widely used as biological indicators of pollution in soil ecosystems. The accumulation of heavy metals in earthworm samples was measured using atomic absorption spectroscopy. In this study, a total of four species of earthworms were identified.
Results: The low number of earthworms in the urban ecosystems of Isfahan was determined due to the presence of amounts of lead, cadmium, arsenic and mercury. The number and species diversity of earthworms are different in urban and rural habitats, indicating that increased heavy metal content significantly affects earthworms. Earthworms can absorb heavy metals from contaminated soils that mimic the function of key body elements and cause disease. Therefore, one of the main factors determining the physical and chemical condition of the soil is the number and species composition of earthworms.
Conclusion: These data can be used to monitor and evaluate soil pollution near various industries.

Keywords: Earthworms, Trace elements, Lead, Cadmium, Mercury

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Abstract: A-10-2369-2

How Fibulins Change in Gastric Cancer: A Systematic Review

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Background: Gastric cancer (GC) is one of the widespread gastrointestinal tumors in the worldwide, with mortality rates among the highest. In the world, we face more than one million newly diagnosed stomach cancer patients every year. Various factors closely associated with formation of GC. One of these factors is the change in the level of components of the extracellular matrix in the microenvironment of the stomach tumor. Fibulins are one of the secreted glycoproteins of extracellular matrix, which are known as matrix organizers. The purpose of this study is to investigate the changes in fibulins in gastric tumor tissue compared to control samples.
Methods: The search was performed on June 21, 2024, according to the PRISMA statement. Scopus, PubMed, and Web of Science databases were searched for articles that examined FBLN gene family and protein expression in patients with gastric cancer and gastric cancer cell lines. A total of 43 articles were collected, and after eliminating duplicates, 28 articles remained. After removing review articles and articles related to other and unrelated cancers, eight articles were selected following our inclusion and exclusion criteria.
Results: A total of 853 esophageal cancer tumor samples and AGS, Kato III, MKN28, MKN45, SNU1, SNU16, NCI-N87, MGC-803, BGC-83, SGC-7901, SGC-790, and HGC27 gastric cancer cell lines were analyzed in these eight articles.
Conclusion: Examining the results published in these eight studies shows that the expression of fibulin one and two in GC samples is reduced compared to the control. The role of fibulin one and two in inducing apoptosis and controlling cell growth shows that these two can be introduced as stomach tumor suppressors. Fibulin-5 is increased in gastric cancer samples compared to Kernel. The results of the studies show that fibulin 5 is one of the transcription factors expressed in gastric tumors under hypoxic conditions.

Keywords: Gastric cancer, Fibulin1, Fibulin2, Fibulin5

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Abstract: A-10-2546-2

REM Sleep Duration Is Correlated with Serum Levels of Pro-Inflammatory Cytokines Interleukin-12 and Interferon Gamma in People with Chronic Insomnia Disorder

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Background: An increasing field of studies suggest that cytokines can play an important role in chronic insomnia disorder; however, the underlying mechanisms are still unknown. So, the present study aims to evaluate the relationship between serum levels of IL-12 and IFN-γ and parameters of sleep quality in subjects with chronic insomnia disorder (CID).
Methods: Blood samples were collected from 24 subjects diagnosed with CID based on Pittsburgh Sleep Quality Index (PSQI) and full-night video-polysomnography (V-PSG) and 24 healthy volunteers based on PSQI. The serum levels of IL-12 and IFN-γ was evaluated using enzyme-linked immunosorbent assay (ELISA). Statistical analyses were performed by the SPSS®, version 26.0.
Results: We found the increased serum levels of pro-inflammatory cytokines including IL-12 and IFN-γ in CID group compared to control group. Moreover, the rapid eye movement (REM) sleep duration was found to be correlated with IL-12 and IFN-γ concentrations in serums from CID group.
Conclusion: These data add to the evidence that the high levels of circulating pro-inflammatory cytokines IL-12 and IFN-γ are important in CID pathogenesis.

Keywords: Chronic insomnia, Cytokines, Interferon gamma, Interleukin-12, REM sleep

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Abstract: A-10-2625-1

Synthesis of A Novel Hydrogel Nanocarrier Made of Pva-Alginate-Sio2 for Sustained Delivery of Curcumin

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Background: Breast cancer is the most common cancer worldwide. Intriguingly due to variety of breast cancer types, drug resistance and metastasis increase in most patients after treatment. Curcumin can be used as an anti-cancer drug due to its anti-tumor properties. Exquisitely its solubility and effectiveness can be increased by nanocarriers. In this present research, a curcumin-loaded PVA-Alginate-Sio2 nanocarrier was fabricated by means of water/oil/water emulsification method. We are optimistic that with the help of this process, we will be able to open wildly useful treatment methods for cancer.

Methods: The nanocarrier was made by combining PVA-Alginate-Sio2 together. The ingredients were thoroughly dissolved in an ultrasonic bath. Curcumin was dissolved in Methanol and incorporated into the nanocarrier material as the drug. The final product was then prepared with tween, oil, and water. DLS was used to measure the size and zeta potential of nanocarrier particles from cloudy and transparent layers that had formed. We obtained entrapment efficiency (EE%) based on standard curve and following formula:

Results: The DLS results of Curcumin- loaded nanoparticles were 211.9 nm and -83.5 mV. Additionally, the EE% was estimated to be 80%.

Conclusion: PVA-Alg-Sio2 have great potential for biomedical applications such as drug delivery. Utilizing PVA-Alginate-Sio2 in the structure of a nanocarrier is a novel and effective method of drug delivery due to the increased synergistic effect. Moreover, the use of the water/oil/water emulsification enhances the nanocarrier steadiness and maintain its size.

Keywords: Curcumin, Nanocarrier, PVA, Alginate, Sio2, Hydrogel

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Abstract: A-10-2511-1

Bioinformatic Investigation of lncRNA Pvt1 Expression in Healthy and Cancerous Colorectal Cells and Design SiRNA Against Pvt1

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Background: PVT1 is a lncRNA that has been identified as playing a critical role in various cancers. By interacting with other molecular pathways and chromatin remodeling, PVT1 is linked to the control of gene expression. It promotes tumor development, metastasis, and resistance to apoptosis by acting as an oncogene.
Methods: Initially, we found lncRNA PVT1 following broad investigation on many genes and variables linked to colorectal cancer. We next looked at its expression levels in both healthy and malignant cells using the TCGA and NCBI databases. Proceeding to the following stage, the sequence of PVT1 was first acquired from LNCipedia. The complementary and reverse strands of the retrieved sequence were produced with the aid of Bioinformatics.org. Then, to help with the fragment design, the obtained sequence was uploaded to the OligoWalk website. Ultimately, the optimal siRNA was chosen.
Results: Analysis of TCGA data revealed that this ncRNA (UUAACAAUUUUA) exhibited upregulation specifically in colorectal cancer cells, while its expression did not significantly increase in healthy cells. At 37.3°C, the siRNA shows significant thermodynamic stability with a total energy of -5.4 kcal/mol. This 12-nucleotide siRNA fragment has been carefully designed to guarantee sequence specificity and may be effectively delivered into target cells using either lipid nanoparticles. An analysis of this siRNA design's effectiveness by experts results in a probability of 1.87316e-05, which represents the possibility of successful gene silencing.
Conclusion: The successful design of specific siRNA against PVT1 presents a promising strategy for targeted cancer therapy. Further research and clinical trials are necessary to validate the therapeutic potential of PVT1 siRNA in cancer treatment. This advancement in the field of gene therapy could lead to the development of innovative treatments for colorectal and other cancers where PVT1 plays a critical role.

Keywords: siRNA, lncRNA PVT1, Colorectal cancer, Gene therapy

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Abstract: A-10-2602-3

The Role of CAR-Nk Cells in Cancer Immunotherapy

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Background: Chimeric antigen receptor (CAR) natural killer (NK) cell immunotherapy is a revolutionary approach to cancer treatment, shifting from conventional therapy to individualized cellular engineering that precisely targets malignancy. Building on the success of CAR-engineered T cells, the adoptive transfer of CAR-NK cells offers a promising alternative. NK cells possess inherent killing abilities and do not carry the risk of cytokine release syndrome (CRS) or graft-versus-host disease (GvHD).
Methods: Associated databases, including Scopus, PubMed, and Google Scholar, were systematically searched for English-language trials examining the role of CAR-NK cells in cancer immunotherapy using relevant keywords such as "chimeric antigen receptor," "natural killer cell," and "cancer."
Results: Recent research has highlighted the benefits of CAR-NK cells in cancer immunotherapy. A total of 43 trials met the inclusion criteria. CAR-NK cells offer improved safety features, allowing for both autologous and allogeneic use. Their "off-the-shelf" applicability and ability to mediate cancer cell death through multifaceted pathways are additional advantages compared to other immunotherapy methods. CAR-NK cells can be genetically modified to enhance proliferation, survival, and tumor infiltration capabilities. They can penetrate solid tumors at higher levels than normal, breaking through the suppressive barrier of the tumor microenvironment to increase antitumor activity. Recent trials have demonstrated promising results, highlighting their clinical potential and significant efficacy in reducing tumor burden without the severe toxicities typical of CAR-T therapies.
Conclusion: CAR-NK cells have transformed the landscape of cancer immunotherapy. With advancements in genetic engineering, these cells offer greater versatility and safety compared to traditional cancer therapies, promising a future where cancer treatment is universal and potentially curative.

Keywords: Chimeric antigen receptor, Natural killer cell, Immunotherapy, Cancer

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Abstract: A-10-2312-1

Effect of miR-27 and miR-27 A on Initiation and Progression of Breast Cancer

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Background: Breast cancer remains a significant health concern within society, accounting for 15.5% of all newly diagnosed cancer cases among females. MicroRNAs (miRNAs) play pivotal roles in tumor biology, including polymorphisms, tumorigenesis, cellular proliferation, and apoptosis. This study aimed to investigate the relationship between miR-27, miR-27a, and breast cancer.
Methods: A comprehensive literature search was conducted in PubMed, Web of Science, Scopus, and RNAcentral databases up to April 2024. Thirty-one articles were qualified and included in this systematic review.
Results: Detailed investigations of microRNAs have shown that overexpression of miR-27 is associated with malignancy. Research indicates that the expression level of miR-27 in cancerous breast tissue is remarkably high, leading to increased growth, inhibition of apoptosis, and reduced mobility of breast cancer cells. The variant allele G of rs895819 within pre-miR-27a is associated with breast cancer. Cell culture and animal experiments support this speculation, showing that down-regulation of miR-27 expression can suppress cell proliferation and slow tumor growth. Additionally, the G/A polymorphism in the miR-27a gene (rs11671784) has been associated with decreased miR-27a expression and reduced cancer risk. Some research has revealed that miR-27 could target and down-regulate TMEM170B to inhibit the Wnt/β-catenin pathway, suppressing breast cancer proliferation.
Conclusion: Our systematic study identified miR-27 as a carcinogenic factor in breast cells. Furthermore, miR-27a exhibits an inhibitory effect on cell proliferation and could be considered a therapeutic target to prevent cancer progression.

Keywords: Breast cancer, miR-27, miR-27 a, Carcinogenic, Tumor suppressor

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Abstract: A-10-2517-1

The Occurrence of Anemia Resulting from Ferritin and TIBC Deficiency Among Women Patients Referred to Imam Khomeini Hospital in Someh Sara

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Background: Iron deficiency anemia is one of the most common types of anemia. Diagnosing and tracking this condition typically requires various measurements of iron, ferritin, and total iron-binding capacity (TIBC) through blood tests. The purpose of this research is to assess the prevalence of anemia attributed to iron deficiency by analyzing and correlating the serum levels of iron, ferritin, and TIBC in anemic patients referred to Emma Khomeini Someh Sara Hospital.
Methods: This comparative research involved a cohort of 40 women aged between 20 and 40 years, all diagnosed with anemia (hemoglobin levels below 11.7) and exhibiting similar periodontal health. Measurements of iron, ferritin, and total iron-binding capacity (TIBC) were conducted utilizing a biochemical autoanalyzer. The obtained data were analyzed using SPSS version 24 software.
Results: The study's findings indicated a significant disparity in the concentrations of iron, ferritin, and total iron-binding capacity (TIBC), with a P-value of 0.001.
Conclusion: The prevalence of anemia attributed to iron deficiency or disruptions in iron absorption and storage among women in Someh Sara City is greater than that associated with other conditions contributing to anemia within this research population

Keywords: Iron Deficiency, Iron, Ferritin, Anemia, TIBC

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Abstract: A-10-2808-1

Expression and Clinicopathological Significance of PPAR-γ in Human Gastric Cancer

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Background: Peroxisome proliferator-activated receptor-gamma (PPAR-γ) is a nuclear receptor protein that plays a crucial role in lipid metabolism, facilitating adipogenesis and fatty acid storage. Recent studies have highlighted the association between metabolic disorders, including lipid metabolism, and cancer cells. This study aimed to evaluate PPAR-γ expression and its prognostic significance in patients with gastric cancer (GC).
Methods: Twenty-five pairs of fresh GC and adjacent non-cancerous tissue samples were used to assess the expression levels of the investigated genes using real-time polymerase chain reaction.
Results: PPAR-γ expression was significantly increased in GC tissues compared to adjacent normal tissues. Additionally, its expression was negatively associated with tumor size. Analysis of the Kaplan-Meier data set showed a strong correlation between PPAR-γ expression and good survival in GC patients.
Conclusion: The increased expression of PPAR-γ may confirm its role in regulating lipid metabolism in cancer cells. The negative association with tumor size and increased survival suggests that PPAR-γ could serve as a promising prognostic biomarker for predicting outcomes in GC patients. However, further studies are needed to confirm the significance of these findings.

Keywords: Keywords: PPAR gamma, gastric cancer, survival

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Abstract: A-10-2603-2

The Study of microRNAs in the Diagnosis of Viral Hepatitis: A Systematic Review

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Background: This study reviews the role of microRNAs (miRNAs) in diagnosing viral hepatitis, particularly hepatitis B and C. MicroRNAs are emerging as novel biomarkers for viral hepatitis.
Methods: Data were extracted from PubMed, SpringerLink, ScienceDirect, Wiley Online Library, and the WHO database, covering publications up to 2023. The search used the keywords "microRNA" and "hepatitis," focusing on articles investigating microRNAs in viral hepatitis diagnosis. Of the 100 initially screened articles, 60 met the inclusion criteria.
Results: MicroRNA-122, specific to the liver, binds to two conserved sites in the internal ribosome entry site, essential for hepatitis C virus replication and RNA stabilization. Pathways like phosphatidyl 4-kinase IIIα and cholesterol biosynthesis are also involved in virus replication. MicroRNA-21, linked to inflammatory and immune processes, is upregulated in hepatitis B and C patients. MicroRNA-199a, a diagnostic marker for hepatitis B and C, shows decreased expression inversely related to viral load in the blood. miR-155, an oncogenic miRNA, regulates the antiviral immune response in peripheral blood mononuclear cells, with levels correlating with HCV infection. It reduces C/EBPβ expression and upregulates β-catenin, increasing cell proliferation and tumorigenesis. Chronic HCV patients exhibit elevated plasma IP-10 levels, correlating with liver inflammation. miRNAs such as miRNA-196, miRNA-1, miRNA-296, miRNA-351, and miRNA-448 act as negative regulators of HCV replication in the Huh-7 cell line.
Conclusion: This review highlights miRNAs as crucial biomarkers for diagnosing and prognosing viral hepatitis. MicroRNA-122 and miRNA-21 are validated markers, while miRNA-155 plays a significant role in tumorigenesis and inflammation. Other miRNAs serve as negative regulators of viral replication, suggesting potential for new diagnostic and therapeutic approaches.

Keywords: Liver, Infection, microRNA, Oncogenic

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Abstract: A-10-2744-1

lncRNA Pkmyt1ar Promotes Glioblastoma Multiforme Growth by Downregulating miR-485-5p: Evidence from Tumor Vs. Normal Tissue Expression Analysis

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Background: Glioblastoma multiforme (GBM) is the most common, aggressive, and malignant primary brain tumor, with a poor prognosis and an average survival time of 12 to 15 months. MicroRNA-485-5p (miR-485-5p) has been implicated in the progression of various human cancers, including GBM. Recent studies highlight the potential role of miR-485-5p in suppressing GBM tumor growth through its interactions with long non-coding RNAs (lncRNAs). This study aims to investigate the relationship between lncRNA PKMYT1AR and miR-485-5p in GBM patients, shedding light on their potential roles in GBM tumorigenesis.
Methods: Fifty tumor tissue samples and fifty adjacent normal tissue samples were collected from GBM patients at Erfan Hospital in Tehran, Iran. The diagnosis of GBM was confirmed through MRI. RNA was extracted from the tissue samples, and the gene expression levels of lncRNA PKMYT1AR and miR-485-5p were evaluated using real-time PCR.
Results: We observed a significant increase in the expression of lncRNA PKMYT1AR in GBM tissue compared to the control group. Additionally, there was a pronounced reduction in the expression of miR-485-5p in tumor tissue relative to normal tissues.
Conclusion: This study highlights the distinct expression patterns of lncRNA PKMYT1AR and miR-485-5p in GBM tissue, suggesting that lncRNA PKMYT1AR may promote tumor growth by targeting and downregulating miR-485-5p.

Keywords: Glioblastoma multiform, lncRNA PKMYT1AR, miR-485-5p, Real Time PCR

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Abstract: A-10-2347-3

Dual Roles of miR-206 in Breast Cancer Pathogenesis: A Review of Current Evidence and Opportunities for Future Studies

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Background: Breast cancer (BC) is a major public health problem affecting women worldwide. Growing evidence has highlighted the role of miR-206 in BC pathogenesis. Changes in its expression have diagnostic and prognostic potential as they are associated with clinicopathological parameters, including lymph node metastasis, overall survival, tumor size, metastatic stage, resistance to chemotherapy, and recurrence. This study aimed to summarize, assess, and discuss the most recent understanding of miR-206 functions in BC.
Methods: This study was conducted to identify the role of miR-206 in the pathogenesis of breast cancer according to the Guidelines for Review Articles (PRISMA). We searched five international databases, including PubMed, Embase, Web of Science, Google Scholar, and Scopus, for publications between January 2000 and May 30, 2024.
Results: Following our search strategy, a total of 2948 articles were retrieved from PubMed, Scopus, Embase, and Web of Science. After removing duplicates, screening abstracts, and titles, 2500 studies were removed. Additionally, by reading the full text, another 408 articles were removed, resulting in 40 final studies for this review. The results report is descriptive. Two-thirds of the articles showed a decrease in the expression of miR-206 in breast cancer samples, indicating its tumor suppressor role.
Conclusion: We addressed the diagnostic and prognostic value of miR-206 and its potential for the development of new therapeutic strategies.

Keywords: miRNA-206, Breast cancer, Oncogene, Tumor suppressor, Upstream regulator, Prognosis

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Abstract: A-10-2314-1

miRNA-Based Diagnosis of Non-Small Cell Lung Cancer Using miR-21 and Let-7

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Background: Cancer is a significant public health issue, affecting all demographics. In 2020, there were 19.3 million cases and 10 million deaths, with projections exceeding 30 million cases by 2040. Lung cancer (LC) is the second most common cancer, with non-small cell lung cancer (NSCLC) accounting for over 80% of cases. High mortality rates are attributed to recurrence, chemotherapy resistance, and late diagnosis. Early detection through biomarkers such as miR-21 and let-7 may improve survival rates and provide more effective diagnostic tools.
Methods: We conducted a literature search in PubMed, Google Scholar, and ScienceDirect from February 25, 2010, to June 3, 2024, using keywords such as let-7, miR-21, LC, NSCLC, and diagnosis. Our review included 21 eligible studies.
Results: Recent studies have identified miR-21 as an oncogene in NSCLC and let-7 as a tumor suppressor. miR-21 expression was significantly higher in LC patients compared to healthy individuals, while let-7 levels were slightly elevated. These findings suggest that both miRNAs are useful for LC diagnosis, and their combined use may enhance the efficacy of diagnostic biomarkers.
Conclusion: LC is one of the most common cancers, with NSCLC being the most prevalent form. Despite improvements in environmental factors, such as reduced smoking rates, LC progression continues due to genetic abnormalities. Increased expression of miR-21 has been observed in several malignancies, including breast cancer, NSCLC, head and neck cancers, melanoma, and glioblastoma, confirming its oncogenic role. miR-21 functions by reducing the expression of signaling suppressors (PTEN) and (SOCS1/6), thereby disrupting apoptosis mechanisms and promoting the growth and proliferation of NSCLC cells. Conversely, reduced let-7 expression in NSCLC increases the oncogenic genes RAS and HMGA2, accelerating tumor growth and metastasis. Therefore, the simultaneous evaluation of miR-21 and let-7 can aid in improving diagnosis, prognosis, and prediction for LC.

Keywords: let-7, mir-21, Lung Cancer, NSCLC, Diagnosis

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Abstract: A-10-2814-1

Investigating the Mechanisms of Mitogen-Activated Protein Kinase Kinase 4 (MKK4) Inhibition as A Novel Therapeutic Approach in Liver Regeneration: A Systematic Review

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Background: Diminished hepatocyte regeneration is a characteristic of acute and chronic liver diseases, resulting in the inability to maintain or restore a sufficient functional liver mass. Therapies to restore hepatocytes are lacking, making liver transplantation the only curative option for end-stage liver disease. Mitogen-activated protein kinase kinase 4 (MKK4) is involved in transmitting extracellular signals to the nucleus, regulating various cellular responses such as cell growth, proliferation, apoptosis, and response to stress stimuli. Inhibition of MKK4 has recently been identified as a potential therapy to enhance liver regeneration. The purpose of this study is to investigate the potential mechanisms of liver regeneration through MKK4 inhibition.

Methods: Following PRISMA guidelines, a systematic search was conducted in PubMed, Scopus, Wolf, and Google Scholar for gray literature using keywords such as "Mitogen-Activated Protein Kinase Kinase 4," "regeneration," and "hepatocyte, liver." All experimental studies investigating the impact of MKK4 on liver regeneration were included, while studies that did not produce decisive or conclusive results were excluded. Data were extracted and checked by three authors. The quality of included studies was assessed using the Systematic Review Centre for Laboratory Animal Experimentation (SYRCLE) Risk of Bias tool for animal studies and ROB 2 for human studies, and information was organized into an extraction table.

Results: Initially, 112 articles were identified, and after excluding 27 duplicates and 77 irrelevant articles, 8 articles were included in the study. These studies induced liver regeneration using various strategies for MKK4 inhibition with significant results, including investigation through genetic intervention and phosphorylation and activation of transcription factors (N=2), injection of MKK4 inhibitors (HRX215, PLX4032, 1H-pyrazolo[3,4-b]) and assessment of liver regeneration (N=6).

Conclusion: Investigating MKK4 in liver regeneration has opened avenues for therapeutic interventions to increase liver regeneration and prevent liver failure.

Keywords: mitogen-activated protein kinase kinase 4, Mkk4, liver regeneration, hepatocyte, Regeneration.

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Abstract: A-10-2441-1

Analysis of RN7SK Expression Level in Glioblastoma Tissues and Its Correlation with Apoptotic, Cell Cycle, and Important Cancer Genes

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Background: Glioblastoma multiforme (GBM) remains a formidable therapeutic challenge globally despite recent advancements in medical and clinical management. Emerging evidence highlights the crucial role of long non-coding RNAs (lncRNAs) and their aberrant expression in various cancers, including glioblastoma. Studies have demonstrated the dysregulation of lncRNAs, such as RN7SK, in several cancers. RN7SK is a non-coding RNA protected by a specific protein complex that regulates transcription elongation in the cell cycle and chromatin remodeling by interacting with P-TEFb and HMGA1, respectively.
Methods: This study quantified the expression level of RN7SK in seven snap-frozen GBM tissues and ten non-cancerous tissues using RT-qPCR. The correlation between RN7SK expression and its protein partners, along with key cancer genes involved in apoptosis, cell cycle, and EMT, was also analyzed.
Results: We observed a significant downregulation of RN7SK in GBM tissues compared to normal brain tissue. While HMGA1 expression was elevated in GBM patients, the increase was not statistically significant. Additionally, changes in the expression of apoptotic genes, cell cycle regulatory genes, and EMT-associated genes were not significantly different from the control group. Correlation analyses revealed a positive correlation between RN7SK downregulation and the upregulation of HMGA1 and HEXIM1, two protein partners of RN7SK complexes.
Conclusion: The expression of RN7SK is significantly decreased in GBM tumor tissue compared to normal brain tissue. Although a positive correlation was observed between RN7SK downregulation and the upregulation of HMGA1 and HEXIM1, further validation with a larger sample size is warranted.

Keywords: RN7SK, Protein Partners, HMGA1, Glioblastoma Multiforme, RT-qPCR, LncRNA, Gene Expression

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Abstract: A-10-2281-1

Increased of miR-7 and Its Correlation with Sirtuin1 in Non-Alcoholic Fatty Liver Disease

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Background: Identifying the molecular mechanisms underlying non-alcoholic fatty liver disease (NAFLD) is crucial for developing diagnostic and therapeutic strategies. This study investigated the potential role of microRNA-7 (miR-7) in NAFLD detection and pathogenesis.
Methods: Thirty NAFLD patients (aged 22-60) and 15 healthy controls were enrolled. miR-7 levels and SIRT1 gene expression were measured in peripheral blood mononuclear cells (PBMCs) using real-time PCR. MicroRNA extraction from PBMC samples was followed by cDNA synthesis. Real-time PCR was performed using SYBR Green, and delta Ct was calculated using the formula: Ct (reference gene) - Ct (target gene). U6 served as the reference gene.
Results: miR-7 expression was significantly higher in NAFLD patients compared to the control group. A significant negative correlation was observed between miR-7 and SIRT1 levels, with SIRT1 being lower in NAFLD subjects.
Conclusion: Increased miR-7 expression in NAFLD patients may be associated with decreased SIRT1 levels. Targeting SIRT1 signaling through miR-7 upregulation could be considered a potential therapeutic strategy for NAFLD.

Keywords: miR-7, non-alcoholic fatty liver disease, SIRT1

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Abstract: A-10-2330-1

Assess the Effect of E6 and E7 Proteins of HPV on Increasing Il-10 As an Immune Suppressor Cytokine By Downregulating" Hsa-miR-194-5p microRNA"

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Background: Human papillomavirus (HPV) is a widespread sexually transmitted infection. Persistent infection with high-risk HPV types, like 16 and 18, significantly elevates the risk of cancers in the genital tract and oropharynx. While most individuals clear HPV infections through immune responses, around 2% develop into cancer. MicroRNAs (miRNAs) are non-coding RNAs that regulate gene expression and hold promise as diagnostic and therapeutic targets for various diseases.
Methods: A comprehensive literature search using the PubMed database was conducted between 2006 and 2024. Keywords included: "HPV," "cervical cancer," "human papillomavirus," "oropharyngeal cancer," and "microRNA." The search yielded 422 articles, of which 28 were chosen for analysis focusing on HPV infection's impact on human miRNA expression.
Results: The analysis identified the most dysregulated miRNAs in HPV and cancers as hsa-mir-07-5p, hsa-mir-1246, miR-377, and hsa-mir-194-5p. Notably, hsa-miR-194-5p was significantly downregulated in HPV-positive patients with both cervical and oropharyngeal cancers. Further investigation using the RNAcentral web server (https://rnacentral.org/) revealed that hsa-miR-194-5p negatively regulates the expression of IL-10, a crucial immune regulatory cytokine. According to the STRING web server (https://string-db.org/), IL-10 is a major immune regulatory cytokine with potent anti-inflammatory functions that act on various immune system cells. Consequently, it suppresses the immune system. This aligns with previous findings that HPV's E6/E7 proteins can increase IL-10 levels.
Conclusion: The link between IL-10 and hsa-mir-194-5p could be a potential approach to controlling HPV infection and inhibiting cancer progression. Targeting this regulatory pathway might offer a promising therapeutic strategy. Further research is necessary to validate its effectiveness in clinical settings.

Keywords: HPV, cervical cancer, Human papillomavirus, oropharyngeal cancer, microRNA

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Abstract: A-10-2820-1

Linking DNA Health to Fertility Outcomes in Unexplained Male Infertility

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Background: While normal sperm parameters are essential, they do not guarantee fertility. Factors such as genetics, hormonal imbalances, and conditions like varicocele can influence male reproductive health. Research suggests a link between sperm DNA integrity, particularly as assessed by the DNA fragmentation index (DFI), and fertility outcomes, especially in IVF. External factors, including aging and environmental toxins, as well as nutrients like vitamins A, D, and E, can also affect sperm quality.
Methods: This retrospective cross-sectional study analyzed 1,992 normozoospermic men with unexplained infertility, following WHO 2010 criteria. Conducted at the Andrology Laboratory of Shahid Sadouqhi University from March 2020 to October 2022, it focused on men aged 20 to 70 with no significant medical history that could impact semen quality. Semen samples were evaluated for sperm motility, concentration, and morphology. DNA damage was assessed using the chromatin dispersion method to calculate DFI, and chromatin condensation was assessed via CMA3 staining to evaluate protamine levels.
Results: Higher DFI levels were associated with lower sperm concentration, normal morphology, and decreased motility. Increased DFI correlated with a higher proportion of immotile and non-progressive sperm. CMA3 staining revealed uncondensed DNA associated with higher DFI. Older age groups exhibited elevated DFI levels, indicating a greater risk of DNA damage.
Conclusion: The research emphasizes the importance of DNA health, particularly DFI, in evaluating sperm quality in normozoospermic men with unexplained infertility. The findings demonstrate a strong negative correlation between DFI (comprising DFI and high DNA staining) and fertility, suggesting that DFI may be a more reliable indicator than age.

Keywords: DNA Fragmentation, Sperm, Male Infertility.

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Abstract: A-10-2718-2

The Effect of Vitamin D on the Cell Cycle of Cancer Cells: A Systematic Review

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Background: The incidence and mortality rates of cancer are increasing, prompting scientists to focus on both prevention and treatment. Beyond its classical effects, the active form of vitamin D, calcitriol, has been shown to have diverse impacts on various types of cancer. Recent studies have highlighted the link between vitamin D deficiency and cancer cell proliferation caused by disruptions in the cell cycle. This systematic review examines the effects of vitamin D on the cell cycle of different cancer cells.
Methods: A comprehensive literature search was conducted using the Springer, PubMed, Direct Science, and Google Scholar databases from 2002 to 2024. The search terms "vitamin D," "cell cycle," "cancer," and "proliferation" were employed. After initial screening, full texts of relevant publications were assessed, and articles meeting the inclusion criteria were selected.
Results: Fifty-three articles pertaining to the research topic were reviewed and included in this study. Vitamin D regulates the cell cycle in the G0 and G1 phases by acting on P21 and P27, inhibiting C-MYC gene expression, and suppressing D and E cyclins. These effects suggest that vitamin D may be beneficial in the prevention and treatment of cancers.
Conclusion: Further research on the antiproliferative mechanisms of vitamin D, the processes governing the cell cycle, and the identification of appropriate vitamin D analogs for in vivo use could contribute to the development of vitamin D-based strategies for cancer prevention and treatment.

Keywords: vitamin D, Cycle Cell, Cancer, Proliferation

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Abstract: A-10-2827-1

Genotypic and Phenotypic Spectrum of Pontocerebellar Hypoplasia Type 3: Novel Variants in PCLO and Literature Review

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Background: The objective of this study was to identify genetic variants in Iranian patients with pontocerebellar hypoplasia type 3 (PCH3). Pathogenic variants in PCLO, the gene encoding Piccolo Presynaptic Cytomatrix Protein, result in PCH3. Previous studies suggested that loss of PCLO may lead to synaptic dysfunction and apoptosis, resulting in neuronal loss. Common symptoms of PCH3 include seizures, intellectual disability, developmental delay, ataxia, microcephaly, and cerebellar hypoplasia. It is a rare autosomal recessive disease previously reported in only four patients from Oman.
Methods: This study aimed to describe five additional PCH3 patients from three unrelated families. Whole-exome sequencing identified three novel variants, which were confirmed by Sanger sequencing.
Results: This study expanded our understanding of the genotypic and phenotypic spectrum of PCH3. A literature review summarized all known PCH3 variants. Almost all patients exhibited mild to severe motor development deficiencies. Microcephaly was a common feature, while toe walking was a novel finding. One patient presented with moyamoya and ischemia, features not previously associated with PCH3. PCH3 is a clinically heterogeneous disorder with significant phenotypic variability.
Conclusion: The identified variants in the PCLO gene are predicted to reduce Piccolo stability. This study adds to the growing body of knowledge about PCH3, highlighting the need for further research to fully delineate its phenotypic features and improve patient management.

Keywords: PCLO, Piccolo, Pontocerebellar hypoplasia type 3, whole-exome sequencing, Variant

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Abstract: A-10-2830-1

Photodynamic Therapy Inhibits Migration of Ovarian Cancer Cells

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Background: Ovarian cancer (OC) is the third most prevalent cancer in women and has the highest mortality rate among gynecologic malignancies. Photodynamic therapy (PDT) is an advanced cancer treatment approach that involves three components: a photosensitizer, light, and oxygen. Its unique characteristics, such as specific targeting, minimal invasiveness, reduced systemic side effects, and synergy with other treatments, make it promising for various malignancies.
Methods: This study administered PDT to OC cells. Cells were cultured and incubated for 24 hours with zinc phthalocyanine, a photosensitizing compound. After another 24-hour incubation, cells were subjected to laser irradiation at 675 nm, which zinc phthalocyanine specifically absorbs. The cytotoxic effects of PDT on OC cells were evaluated using the methylthiazole tetrazolium (MTT) assay, measuring optical density (OD) at 570 nm with an ELISA reader to determine the IC-50 dose. To assess the migration mechanism, real-time PCR was performed on MMP3 and MMP9 genes. Total RNA was extracted from the cells following photodynamic treatment, and mRNA was converted to cDNA. The relative levels of gene expression were calculated using the 2-ΔΔCt method.
Results: PDT on OC significantly decreased MMP3 and MMP9 gene expression compared to the control group, with a more pronounced decrease in MMP9.
Conclusion: These data suggest that PDT inhibits the migration properties of OC cells. Consequently, PDT may be considered a non-invasive and effective therapeutic option for OC.

Keywords: Photodynamic therapy, ovarian cancer, migration genes, MMP3, MMP9.

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2732-1

Synthesis and Characterization of A Novel Biopolymeric Hydrogel

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Background: Hydrogels derived from natural polysaccharides are valuable materials today due to their biocompatibility, biodegradability, and ability to mimic the extracellular matrix of tissues, making them ideal for medical applications.
Methods: This research focused on synthesizing and characterizing a hydrogel composed of polyvinyl alcohol (PVA), gum Arabic (GA), acrylic acid (AA), and glycidyl methacrylate (GMA) as a crosslinker. The influence of the AA monomer ratio on swelling properties was evaluated under various pH and salt conditions. Hydrogel morphologies were analyzed using Fourier-transform infrared spectroscopy (FTIR) and scanning electron microscopy (SEM).
Results: SEM analysis revealed a homogeneous surface morphology primarily influenced by monomer concentration. FTIR analysis confirmed the presence of the constituent components and significant intermolecular interactions. The hydrogel exhibited a water absorption capacity of 141 g/g in deionized water. This capacity increased with rising pH levels but decreased gradually in various electrolyte solutions due to reduced osmotic pressure. The concentration of AA significantly improved water absorption.
Conclusion: The synthesized hydrogel demonstrates potential for biomedical applications.

Keywords: Hydrogel, Biopolymers, Gum Arabic, Polyvinyl alcohol

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Abstract: A-10-2737-1

Analyzing the Blood Urea Nitrogen to Creatinine Ratio in Diabetic Patients in Comparison to A Control Group at Golestan Hospital in Ahvaz

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Background: Type 2 diabetes mellitus (T2DM) is a medical condition characterized by elevated blood glucose levels, insulin deficiency, and insulin resistance. Notable complications of T2DM include renal failure, which can lead to changes in blood urea nitrogen (BUN) and creatinine levels. This study compared the BUN/Cr ratio in individuals with diabetes to a control group.

Methods: Between 2023 and 2024, 83 diabetic patients and 151 healthy individuals were enrolled. Clinical information was collected and analyzed, including fasting blood sugar, HbA1c, BUN, creatinine, and other relevant data.

Results: The study included 143 females and 91 males with a mean age of 50.6 ± 3 years. Diabetic patients had a significantly higher mean BUN/Cr ratio (16.61 ± 5.33) compared to the control group (14.43 ± 3.88) (P-value = 0.001).

Conclusion: The findings of this research demonstrate a significant elevation in the BUN/Cr ratio among individuals with diabetes compared to the control group. This increase is likely associated with the complications of diabetes, including advanced-stage kidney failure.

Keywords: T2DM, Blood Urea Nitrogen, Creatinine

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Abstract: A-10-2821-1

The Therapeutic Potential of Niosome-Loaded with Hesperidin in Change of Oxidative Stress Parameters in Depression Model Rats

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Background: Major depressive disorder is a severe condition often associated with oxidative stress. Hesperidin, a potent antioxidant, has been investigated in nanoparticle formulations for potential short-term treatment options. This study aimed to examine the effects of niosome-encapsulated hesperidin on glutathione peroxidase (GPX) and superoxide dismutase (SOD) levels in the blood serum of depressed rats.
Methods: Thirty-six adult male rats were divided into six groups: a control group, a depressed group induced by reserpine (0.5 mg/kg for 14 days), a treatment group with hesperidin (res0.5 mg/kg for 14 days, hes20 mg/kg for 14 days), a hesperidin group (hes20 mg/kg for 14 days), a niosome hesperidin treatment group (res0.5 mg/kg for 14 days, niohes20 mg/kg for 7 days), and a niosome hesperidin group (niohes20 mg/kg for 7 days). After 24 hours of the final injection, blood samples were collected, centrifuged, and analyzed for GPX and SOD levels using spectrophotometric methods. Data were analyzed using one-way ANOVA.
Results: The study found a significant increase in GPX levels in the blood serum of the niosome hesperidin treatment group compared to the depressed group ($p < 0.01$). Additionally, SOD levels were significantly higher in the hesperidin and niosome hesperidin treatment groups compared to the depressed group ($p < 0.05$ and $p < 0.01$, respectively).
Conclusion: Niosome-encapsulated hesperidin demonstrated the potential to elevate GPX and SOD levels in the blood serum of depressed rats, suggesting its potential as a therapeutic agent for depression in Wistar rats.

Keywords: Nanoparticle, Niosome-hesperidin, Oxidative stress, depression, Glutathione peroxidase, superoxide dismutase

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2832-1

Effects of Irreversible Electroporation on Death of Triple Negative Breast Cancer Cells Under In Vitro Condition

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Background: Triple-negative breast cancer (TNBC) is a challenging subtype of breast cancer. Irreversible electroporation (IRE), a non-thermal method that uses high-voltage, low-energy electrical pulses to kill cells, has gained significant attention in recent years for its potential in cancer treatment. IRE offers the advantage of preserving the extracellular matrix, making it a promising approach for clinical studies.
Methods: The MDA-MB-231 cell line was selected as a TNBC model. Two experimental groups and two control groups were established. Cell survival rates were assessed using the trypan blue staining (TBS) method in both control and experimental groups. Experimental groups were subjected to in vitro electroporation to determine optimal pulse parameters for destroying cancer cells without causing thermal damage.
Results: After applying electrical pulses to the experimental groups, cell survival rates ranged from 19% to 58%, significantly lower than the control groups (89-94%). By analyzing these results, appropriate pulse parameters were identified to effectively destroy MDA-MB-231 cancer cells.
Conclusion: IRE demonstrated the ability to destroy a significant portion of MDA-MB-231 cancer cells without causing thermal damage. This study highlights the potential of IRE as a promising treatment option for TNBC and other cancers.

Keywords: Irreversible electroporation, MDA-MB-231 cell line, Triple-negative breast cancer

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2816-1

Effect of A PPARα Agonist on Osteogenic Differentiation of Human Mesenchymal Stem Cells

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Background: All peroxisome proliferator-activated receptors (PPARs) are expressed in bone cells. PPARs are nuclear transcription factors that regulate the expression of various genes. Fibrates, PPARα agonists, have been shown to stimulate osteoblastic differentiation and matrix mineralization in osteogenic progenitor cells by increasing BMP2 expression. This study examined the differential effects of the PPARα agonist clofibrate on adipose-derived human mesenchymal stem cells (AdMSCs) in vitro.
Methods: AdMSCs were cultured in bone differentiation culture medium with or without clofibrate. On days 7 and 14, differentiation markers were assessed using Von Kossa staining and tests for catalase and superoxide dismutase activity. Additionally, the expression levels of Runx2, type 1 collagen, osteonectin, and alkaline phosphatase genes were measured using real-time PCR.
Results: Von Kossa staining revealed increased calcium deposition in samples treated with clofibrate compared to controls. Catalase and superoxide dismutase activity also increased significantly. A significant upregulation of specific bone differentiation genes was observed. On day 7, all genes (Runx2, type 1 collagen, osteonectin, alkaline phosphatase) showed increased expression (P.Value ≤ 0.001). On day 14, Runx2, type 1 collagen, and osteonectin continued to show significant upregulation (P.Value ≤ 0.001).
Conclusion: The results of imaging, enzymatic activity testing, and real-time PCR demonstrate that clofibrate stimulated differentiation in AdMSCs.

Keywords: PPARs, Bone Differentiation, AdMSCs, Clofibrate

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2784-1

M2e-Hsp70 Chimeric Protein as An Influenza Vaccine Candidate

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Background: The influenza virus causes annual epidemics and thousands of deaths worldwide. It spreads through respiratory droplets and contact with contaminated surfaces, causing respiratory tract damage. Effective and universal vaccines are needed to prevent its spread. There is a need to develop vaccines against the influenza virus that provide broader and longer-lasting immunity. Transitioning from the embryonated egg system to biotechnology-based vaccine production is essential. Recombinant protein vaccines offer a promising approach for seasonal influenza vaccines.

Methods: This study produced the recombinant influenza virus M2e protein in Escherichia coli bacteria and purified it for use in an influenza vaccine. The 4xM2e.HSP70 gene fragment was expressed in the E. coli strain M-15 using the IPTG inducer. Expression was optimized, and the protein was extracted using urea and purified with a Ni-NTA affinity chromatography column. The production efficiency was approximately 165 µg/ml protein, indicating efficient recombinant protein production.

Results: The study successfully expressed the recombinant protein 4xM2e.HSP70c in the prokaryotic expression system, E. coli strain (M15), in a short time. After extraction and purification, the presence of the recombinant protein was confirmed using SDS-PAGE and western blot analysis.

Conclusion: The study suggests investigating the expression of the desired gene construct in other hosts and evaluating its function and immunogenicity alone, with an adjuvant, or with other protective proteins of the influenza virus.

Keywords: Influenza A virus, M2e, HSP70, Protein expression, E. coli

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2781-1

Investigating Changes in CatSper Gene Expression and TDI Index in Testis Tissue after Treatment with Niosome Hesperidin in Depressed Rats

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Background: Depression is a mental disorder that can affect the sperm cation channel (CatSper), essential for sperm hyperactivity and male fertility. Hesperidin, a potential antidepressant, is often delivered in nanoparticle formulations. This study aimed to investigate the effects of niosome-encapsulated hesperidin on CatSper gene expression and tubular diameter index (TDI) changes in depressed rats.
Methods: Thirty-six adult male rats were divided into six groups: a control group, a depressed group induced by reserpine (0.5 mg/kg for 14 days), a hesperidin group (hes20 mg/kg for 14 days), a depressed group treated with hesperidin (res0.5 mg/kg for 14 days followed by hes20 mg/kg for 14 days), a niosome hesperidin treatment group (res0.5 mg/kg for 14 days followed by niohes20 mg/kg for 7 days), and a niosome hesperidin group (niohes20 mg/kg for 7 days). Animals were sacrificed, and CatSper gene expression and TDI were analyzed using PCR and microscopic methods.
Results: CatSper gene expression was significantly higher in the control group and niosome hesperidin groups compared to the depressed group ($p < 0.05$ and $p < 0.01$, respectively). Additionally, testicular TDI was significantly higher in the control group and hesperidin groups compared to the depressed group ($p < 0.001$). In the depressed group, TDI was significantly decreased in the hesperidin and niosome hesperidin groups compared to the control group ($p < 0.001$ and $p < 0.05$, respectively). Furthermore, hesperidin treatment significantly decreased TDI in the niosome hesperidin group compared to the hesperidin group ($p < 0.01$).
Conclusion: Niosome-encapsulated hesperidin appears to positively affect CatSper gene expression and the TDI indicator in depressed rats, suggesting its potential benefits for male fertility.

Keywords: depression, hesperidin, CatSper, TDI, testis

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Abstract: A-10-2416-1

Cloning, Expression, and Purification of Recombinant Human Ferritin in E. Coli

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Background: Ferritin is a protein composed of two subunits (H and L) that play a crucial role in iron storage and homeostasis. Ferritin light chain (FTL) is a biomarker for diseases such as hyperferritinemia with cataracts, neurodegeneration with brain iron accumulation (NBIA), and others. Therefore, measuring FTL levels is valuable.
Methods: This study aimed to express FTL in a bacterial system to create a standard for an ELISA kit to detect human serum FTL levels. The FTL gene with a TEV protease cleavage site was inserted into the pET-28a vector containing the SUMO solubilizing tag. It was then expressed in E. coli BL21(DE3) under various conditions. SUMO-FTL was purified by affinity chromatography, followed by TEV protease cleavage to obtain purified FTL. The purified FTL was standardized for use in a sandwich ELISA kit. Optical density was measured at 450 nm to create a standard curve.
Results: Most of the FTL protein was expressed as inclusion bodies, while SUMO-FTL was successfully expressed in a soluble form under all conditions. The optimal expression condition was 18 hours at 25 °C. The purified FTL was used as a standard in the sandwich ELISA kit, and the standard curve generated was highly correlated with the commercial kit standard curve.
Conclusion: Given the importance of measuring serum ferritin levels, this study successfully produced a standard FTL protein. Compared to previous studies, soluble expression of FTL was achieved efficiently, overcoming the challenges of protein refolding. The produced FTL standard has potential for commercialization in Iran's rapid detection kit industry.

Keywords: Ferritin light chain, SUMO-tag, ELISA, iron storage and homeostasis

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2839-1

Inhibition of Amyloid Fibrils by Flavonoid Compounds: A Docking Study

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Background: Alzheimer's disease (AD) is a devastating neurological disease that places a growing burden on healthcare systems. While the exact etiology of symptoms remains unclear, research suggests that β-amyloid (Aβ) peptides play a significant role. Alzheimer's neuropathology is primarily caused by Aβ peptide aggregation, leading to Aβ plaques, neurodegeneration, neuroinflammation, and ultimately, death. Developing effective treatments for Alzheimer's disease is crucial. Certain flavonoids, like apigenin, genistein, and luteolin, have shown promise in treating AD.
Methods: To investigate the potential of these flavonoids for AD treatment, molecular docking studies were conducted to calculate their binding energy with Aβ peptides. The admetSAR website was used to assess the pharmacokinetic properties of these compounds.
Results: Apigenin demonstrated superior binding affinity to Aβ peptides compared to genistein and luteolin. Additionally, apigenin possesses favorable pharmacokinetic properties, including the ability to cross the blood-brain barrier (BBB), which is essential for treating neuropathic complications, and high intestinal absorption.
Conclusion: Apigenin appears to be a promising candidate for future AD treatment, pending positive results from wet lab experiments.

Keywords: Amyloid fibrils, Flavonoids, Inhibition, Molecular Docking

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2667-1

Identification of A Drug Candidate to Target Pyruvate Kinase M2 in Cancer Cells' Metabolism Using Drug Repurposing and Molecular Docking Methods

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Background: Pyruvate kinase plays a crucial role in regulating cell metabolism. Pyruvate kinase M2 (PKM2) is a widely expressed isoform associated with tumorigenesis. Polydatin, a natural stilbenoid polyphenol and a resveratrol derivative, is an FDA-approved PKM2 inhibitor. However, there is a need for more potent PKM2 inhibitors. Drug repurposing offers a promising approach to accelerate drug discovery by identifying novel clinical uses for existing drugs.
Methods: Using the DrugRep online drug repurposing server, estrogen benzoate was identified as a potential drug candidate. Protein structures were obtained from the RCSB database (PDBID: 3U2Z), and drug structures were acquired from the DrugBank database. Energy minimization was performed, followed by docking using AutoDockTools-1.5.7.
Results: The binding free energies of polydatin and estrogen benzoate to PKM2 were calculated to be -6.05 and -9.54 kcal/mol, respectively. While polydatin had more hydrogen interactions with the protein, it exhibited unfavorable bonding, making it less stable. The amino acids involved in the interaction of both drugs with PKM2 were PHE A28, PHE A561, LEU B888, LUE B562, and TYR A392.
Conclusion: Based on our docking results, estrogen benzoate demonstrated a lower binding free energy and more stable interactions with PKM2 compared to polydatin. This suggests that estrogen benzoate has a higher binding affinity to PKM2 and could be a potential therapeutic target for diseases associated with PKM2 overexpression.

Keywords: Cancer, Docking, Drug repurposing, Pyruvate kinase M2

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2834-1

A Novel Presentation of a Tubb2b Mutation: A Case Report from Northern Iran

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Background: Tubulin mutations are responsible for neuronal migration disorders known as tubulinopathies. These mutations can severely disrupt microtubule function, leading to diverse clinical outcomes. The current understanding of the clinical spectrum of tubulinopathies is primarily based on studies of fetal tissue and early childhood cases. This study aimed to introduce a case with a novel pathogenic variant in the TUBB2B gene affecting neurological abnormality.
Case Presentation: A 7-year-old girl from Sari, north of Iran, with neurological abnormalities was referred to the Fajr medical genetics lab for genetic analysis.
Methods: Whole Exome Sequencing (WES) was applied to detect related pathogenic variants. The WES results showed a heterozygous c.1172G>A variant in the TUBB2B gene.
Results: Segregation analysis using PCR-Sequencing confirmed that the patient was a heterozygous carrier of the c.1172G>A mutation in the TUBB2B gene. Parental testing revealed that the mutation was de novo. In silico analysis categorized the mutation as pathogenic.
Conclusion: This case highlights the utility of novel sequencing technologies in diagnosing neurological abnormalities. The identification of a novel pathogenic variant in the TUBB2B gene contributes to a better understanding of this gene's role in neurological development.

Keywords: TUBB2B gene, Pathogenic Variant, Tubulinopathies

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2805-1

Investigating Oxidative Stress Parameters in the Cerebellum of Depressed Rats During Treatment with Niosome-Loaded Hesperidin

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Background: Oxidative stress can damage nerve cells and contribute to depression. Hesperidin, an antioxidant, has antidepressant effects, and niosomes can be used for its targeted, controlled, and stable delivery. This study aimed to investigate the effects of niosome-encapsulated hesperidin on superoxide dismutase (SOD) and glutathione peroxidase (GPX) levels in the cerebellar tissue of rats with depressive-like behavior.
Methods: Thirty-six rats were divided into six groups: control (saline for 14 days), depressed (reserpine 0.5 mg/kg for 14 days), depressed+hesperidin (reserpine 0.5 mg/kg for 14 days and hesperidin 20 mg/kg for 14 days), hesperidin (hesperidin 20 mg/kg for 14 days), niosome hesperidin (niosome hesperidin 20 mg/kg for 7 days), and depressed+niosome hesperidin (reserpine 0.5 mg/kg for 14 days and niosome hesperidin 20 mg/kg for 7 days). All injections were administered intraperitoneally. Cerebellar tissue was extracted from the rat brain, and SOD and GPX levels were measured using a specialized kit. Data were analyzed using one-way ANOVA.
Results: The level of superoxide dismutase was significantly decreased in the depressed+hesperidin group compared to the depressed+niosome hesperidin group ($p < 0.05$). Glutathione levels were significantly increased in the depressed+niosome hesperidin group compared to the control group ($p < 0.05$). Additionally, GPX levels were significantly increased in the depressed+niosome hesperidin group compared to the hesperidin group ($p < 0.01$).
Conclusion: The study found that niosome-encapsulated hesperidin increased SOD and GPX levels in the cerebellar tissue of depressed rats, suggesting its potential as a therapeutic agent for depression-related oxidative stress.

Keywords: Depression, Oxidative stress, Niosome, Hesperidin

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2842-2

The Effects of Turmeric on Glycemic Index and Lipid Profile in Diabetic Patients: A Systematic Review and Meta-Analysis

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Background: Turmeric, a spice containing the active compound curcumin, has been investigated for its potential health benefits, particularly in managing diabetes. This systematic review and meta-analysis aimed to evaluate the effects of turmeric supplementation on glycemic indexes and lipid profiles in diabetic patients.
Methods: A systematic search was conducted in databases including PubMed, Scopus, and the Cochrane Library for randomized controlled trials (RCTs) published until January 2024. Studies were included if they evaluated the impact of turmeric or curcumin on glycemic control (measured by fasting blood glucose and HbA1c) and lipid profiles (including total cholesterol, LDL, HDL, and triglycerides) in diabetic patients. Data extraction was performed by two independent reviewers, and the quality of included studies was assessed using the Cochrane risk-of-bias tool. Meta-analysis was conducted using random-effects models to calculate standardized mean differences (SMD) and 95% confidence intervals (CIs).
Results: A total of 12 RCTs involving 720 diabetic patients were included in the analysis. Turmeric supplementation significantly reduced fasting blood glucose levels (SMD: -0.85, 95% CI: -1.20 to -0.50, $p < 0.001$) and HbA1c levels (SMD: -0.70, 95% CI: -1.05 to -0.35, $p < 0.001$). Additionally, turmeric was associated with favorable changes in lipid profiles, showing a significant decrease in total cholesterol (SMD: -0.78, 95% CI: -1.10 to -0.46, $p < 0.001$) and triglycerides (SMD: -0.65, 95% CI: -0.95 to -0.35, $p < 0.001$), while HDL levels increased (SMD: 0.55, 95% CI: 0.25 to 0.85, $p < 0.001$).
Conclusion: Turmeric supplementation appears to improve glycemic control and lipid profiles in diabetic patients. These findings suggest that turmeric may serve as a beneficial adjunct in the management of diabetes. Further large-scale studies are needed to confirm these effects and explore the underlying mechanisms.

Keywords: Turmeric, curcumin, glycemic index, lipid profile, diabetes, systematic review, meta-analysis

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2845-1

A Systematic Literature Review of Techniques for Detection of Glucose 6-Phosphate Dehydrogenase Mutations

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Background: Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common hereditary enzymopathy in humans, with an X-linked inheritance pattern. Approximately 7.5% of the world's population are carriers of this deficiency, and 2.9% are affected. While most individuals with G6PD deficiency remain asymptomatic throughout their lives, some may experience clinical manifestations, including a wide range of diseases such as acute hemolytic anemia, atherosclerosis, cardiovascular diseases, neonatal jaundice, kidney failure, and even death.
Methods: A systematic search of databases including Scopus, PubMed, and Google Scholar was conducted for English-language trials published between 1992 and 2024, using relevant keywords such as "G6PD deficiency," "mutation," and "PCR."
Results: Thirty-four of the 109 clinical studies reviewed met the inclusion criteria. The G6PD enzyme has two common isoforms: type B (wild type) and type A (mutant form). To date, 189 mutations have been identified. The Mediterranean type, the A-African type, and the Union and Seattle species are the most common variants worldwide. In Iran, the Mediterranean mutations, Chatham and Cosenza, are the most prevalent. Various diagnostic methods, including molecular techniques like whole genome sequencing and RFLP-PCR, have been used to differentiate between healthy and affected individuals. In Iran, due to the high cost and limited availability of these methods, RFLP-PCR is commonly used, despite its multi-step process and reliance on enzymes. Recently, high-resolution DNA melting curve (HRM) analysis has emerged as a rapid, accessible, and accurate method for detecting polymorphisms and effectively differentiating between homozygous, heterozygous, hemizygous, and healthy individuals.
Conclusion: Given the high global prevalence of G6PD deficiency, especially in Iran, high-resolution techniques like HRM can be considered a convenient and accessible alternative to traditional methods, which are often prohibitive, unavailable, and time-consuming.

Keywords: Glucose 6-phosphate dehydrogenase deficiency, HRM, mutation, G6PD

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2842-3

The Impact of Thyme on Blood Pressure, Glycemic Index, and Anthropometric Profiles in Patients with Metabolic Syndrome: A Systematic Review and Meta-Analysis

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Background: Thyme (Thymus vulgaris) is a widely used culinary herb known for its potential health benefits, particularly in managing metabolic syndrome (MetS). This systematic review and meta-analysis aimed to evaluate the effects of thyme supplementation on blood pressure, glycemic control, and anthropometric profiles in patients with MetS.

Methods: A systematic search was conducted across databases including PubMed, Scopus, and the Cochrane Library for randomized controlled trials (RCTs) published up to April 2024. Studies were included if they evaluated the effects of thyme or its extracts on blood pressure, glycemic control (measured by fasting blood glucose and HbA1c), and anthropometric measurements (such as body mass index and waist circumference) in patients diagnosed with MetS. Data extraction was performed by two independent reviewers, and the quality of the studies was assessed using the Cochrane risk-of-bias tool. Meta-analysis was conducted using random-effects models to calculate standardized mean differences (SMD) and 95% confidence intervals (CIs).

Results: A total of 8 RCTs involving 480 patients with MetS were included in the analysis. Thyme supplementation significantly reduced systolic blood pressure (SBP) and diastolic blood pressure (DBP) with SMDs of -0.70 (95% CI: -1.05 to -0.35, $p < 0.001$) and -0.60 (95% CI: -0.90 to -0.30, $p < 0.001$), respectively. Additionally, thyme was associated with significant improvements in glycemic control, reflected by a reduction in fasting blood glucose levels (SMD: -0.75, 95% CI: -1.10 to -0.40, $p < 0.001$) and HbA1c (SMD: -0.65, 95% CI: -0.95 to -0.35, $p < 0.001$). Improvements in anthropometric measurements, particularly waist circumference, were also observed (SMD: -0.80, 95% CI: -1.10 to -0.50, $p < 0.001$).

Conclusion: Thyme supplementation shows promise in improving blood pressure, glycemic control, and anthropometric profiles in patients with metabolic syndrome. These findings support the potential role of thyme as a complementary therapeutic option in managing MetS.

Keywords: Thyme, metabolic syndrome, blood pressure, glycemic index, anthropometric profile, systematic review, meta-analysis

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Abstract: A-10-2804-2

Thyroid Disease Prevalence in the Male and Female Population of District 12, Tehran

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Background: The thyroid gland produces hormones essential for regulating metabolism, heart rate, and energy levels. Thyroid disorders, such as hypothyroidism and hyperthyroidism, are common, especially in women and older adults. Factors like hormonal changes, aging, and lifestyle can influence thyroid health. This study examines the prevalence of thyroid disorders in a sample population from District 12, Tehran, focusing on the effects of age and gender to better understand and manage thyroid health in this community.

Methods: Samples were collected from men and women aged 20-40 in District 12 of Tehran. After collection, the samples were transferred to a laboratory for ELISA testing. The results were analyzed using the Minitab 17 statistical software. Factors such as age and gender were considered, leading to the following outcomes.

Results: The analysis using Minitab statistical software indicated that gender and age significantly impact the results in District 12 of Tehran. Specifically, women over the age of 30 exhibited more significant hormonal changes. Based on these findings, it is suggested that future studies should also consider the diet and quality of life of these individuals.

Conclusion: The study found that thyroid disorders are more prevalent among women over 30 in District 12 of Tehran, highlighting the significant impact of both age and gender on thyroid function. These findings suggest a need for targeted healthcare interventions, particularly for women in this age group, and recommend further research to explore the influence of diet and lifestyle on thyroid health.

Keywords: ELISA, Hormone, Thyroid, Minitab 17

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Abstract: A-10-2680-2

Investigating the Effect of Treatment with Ghrelin Disease on the Activity of Testicular Antioxidant Enzymes Following Cadmium Damage in Rats

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Background: Cadmium, a potent environmental contaminant, exerts toxic effects on various organs, particularly the testes. The primary mechanism of cadmium-induced testicular damage involves the generation of reactive oxygen species (ROS), leading to oxidative stress. Antioxidant substances, including ghrelin, have been implicated in mitigating such damage by enhancing the antioxidant defense system and inhibiting lipid peroxidation. Ghrelin's antioxidant properties have been demonstrated in rat testes and ovaries, suggesting its potential protective role against cadmium-induced toxicity. This study aimed to investigate the effects of ghrelin hormone treatment on the activity of testicular antioxidant enzymes in rats subjected to cadmium-induced damage, thereby contributing to the understanding of ghrelin's role in protecting against oxidative stress in the testes.

Methods: The study involved 30 adult male rats, divided into three groups: control-saline, cadmium-saline, and cadmium-ghrelin. Cadmium chloride was administered intraperitoneally to induce testicular damage, followed by subcutaneous injections of ghrelin in the cadmium-ghrelin group. Lipid peroxidation was assessed via TBARS concentration, while the activity of antioxidant enzymes (SOD, GPx, CAT) and glutathione levels were measured using established methodologies. Statistical analyses were performed using SPSS to compare enzyme activities and TBARS levels between groups.

Results: Cadmium exposure resulted in a significant decrease in SOD activity and a notable increase in lipid peroxidation, as indicated by elevated TBARS levels. However, the administration of ghrelin to cadmium-exposed rats significantly restored the activity of antioxidant enzymes and reduced lipid peroxidation, with glutathione levels exceeding those in the cadmium-saline group.

Conclusion: Ghrelin treatment effectively counteracted cadmium-induced oxidative stress in the testes by enhancing the activity of antioxidant enzymes and reducing lipid peroxidation. This suggests ghrelin's potential as a therapeutic agent in mitigating testicular damage caused by cadmium.

Keywords: Cadmium Toxicity, Testicular Damage, Oxidative Stress, Ghrelin Hormone, Antioxidant Enzymes, Lipid Peroxidation

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Abstract: A-10-2846-1

Optimization of ZnO Nanoparticle Synthesis Loaded with Anti-cancer Doxorubicin Drug

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Background: Nanotechnology offers an alternative strategy to circumvent systemic toxicity and drug resistance by attaching drugs to nanomaterials with enhanced targeting ability and controlled drug release. ZnO nanoparticles, known for their biocompatibility, high selectivity, enhanced cytotoxicity, and easy synthesis, are promising tools in therapeutic environments. This study explored the use of porous ZnO spherical nanoscale assemblies as a drug release system, hypothesizing that encapsulating the anticancer drug doxorubicin (DOX) within these nanoparticles would enhance its therapeutic efficacy.

Methods: ZnO nanoparticles were prepared using zinc acetate (ZnOA) and zinc nitrate (ZnON) by dissolving them in NaOH or ammonium bicarbonate under various reaction conditions. Doxorubicin (DOX) was loaded into the nanoparticles, and the amount of loaded DOX was determined by measuring fluorescence emission intensity at 560 nm using a standard intensity curve. Additionally, the nanoparticles were coated with polyethyleneimine (PEI) to modify their surface for interaction with amine groups.

Results: The optimal conditions for ZnO nanoparticle synthesis were achieved using zinc acetate in ammonium bicarbonate as a reducing agent at 80°C. The size and charge of the nanoparticles without PEI measured by the DLS device were approximately 50 nm and +26.2 mV, respectively, and the DOX loading efficiency was about 78%. SEM images revealed a spherical and porous structure of the ZnO particles. The prepared nanoparticles were stable with a hexagonal wurtzite structure.

Conclusion: This study successfully prepared ZnO nanoparticles containing doxorubicin. Given the anticancer properties of ZnO nanoparticles, loading with doxorubicin is expected to enhance anticancer activity.

Keywords: Keywords: zinc oxide, nanoparticles, doxorubicin, polyethyleneimine

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Abstract: A-10-2851-1

Investigating the Anticancer Effect of Probiotic Bacteria Lactobacillus Acidophilus and Rhus Coriaria (sumac) Extract on Colon Cancer Cells

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Background: Colon cancer is a leading cause of cancer deaths worldwide. Medicinal plants and probiotics have been explored for their potential therapeutic applications in various diseases. This study aimed to investigate the anticancer effects of aqueous extract of sumac fruit and Lactobacillus acidophilus probiotic bacteria on HT29 colon cancer cells.
Methods: The effects of aqueous extract of sumac fruit and ethyl acetate extract of Lactobacillus acidophilus probiotic bacteria were evaluated individually and in combination on the survival of HT29 cancer cells using the MTT method. Apoptosis induction in HT29 cells after treatment with optimal concentrations of sumac fruit extract and Lactobacillus acidophilus probiotic bacteria was assessed using flow cytometry.
Results: Both sumac fruit extract and Lactobacillus acidophilus bacteria individually caused a significant decrease in the viability of HT29 cells. The combined use of sumac fruit extract and Lactobacillus acidophilus bacteria at a concentration of 250 µg/ml exhibited a synergistic effect, leading to a significant decrease in HT29 cell viability. Additionally, both agents individually and in combination caused a significant increase in apoptosis in HT29 cells, with a more pronounced effect observed when used together.
Conclusion: Aqueous extract of sumac fruit and Lactobacillus acidophilus bacteria individually exhibit anticancer effects and induce apoptosis in colon cancer cells. Their combined use demonstrates a synergistic anticancer effect at lower concentrations. Further studies are warranted to explore the potential of this combination as a biological product for treating colon cancer patients.

Keywords: Rhus-coriaria, colon cancer, Lactobacillus acidophilus probiotic bacteria

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Abstract: A-10-2848-1

Reconstruction of A Metabolic Model for Hyaluronic Acid Production by Streptococcus Zooepidemicus and Its Growth Optimization

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Background: Hyaluronic acid is a linear polymer of repeating units (UDP-GlcUA) and (UDP-GlcNAc). Its properties make it valuable in drug delivery systems, wound healing, cancer treatment, medical aesthetics, dermatology, urology, orthopedics, and soft tissue engineering, leading to its widespread use in the cosmetic and healthcare industries.
Methods: To identify parameters affecting hyaluronic acid production in Streptococcus zooepidemicus, a systems biology approach using genome-scale metabolic networks was employed. This approach computationally defines all enzymatic reactions related to known pathways in a cell, enabling predictions of metabolic reaction flux.
Results: A metabolic model for Streptococcus zooepidemicus (iHM442) was constructed for the first time. This model was analyzed to optimize bacterial growth and hyaluronic acid production. The reconstructed model included 653 reactions, 678 metabolites, and 568 genes. The model's predictions showed good qualitative and quantitative agreement with experimental data. The present model was used to identify parameters involved in hyaluronic acid production and propose strategies for increasing its yield.
Conclusion: Hyaluronic acid is a versatile molecule with numerous applications in various fields. Optimizing product production in a host organism involves various methods, such as modifying culture media compositions and improving bioreactor conditions. Identifying biosynthetic pathways and manipulating them to increase production rates is crucial. Strategies include providing necessary precursors for synthesis, recovering cofactors, and improving substrate consumption for growth.

Keywords: hyaluronic acid, systems biology, Streptococcus equi, metabolic model

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Abstract: A-10-2851-3

Evaluation of Rhus Coriaria Aquse Extract on Fibroblast Cell Survival and Migration Using Scratch Method

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Background: Rhus coriaria is a widely used herbal plant in Iranian traditional medicine as an anti-pain and anti-inflammatory agent for treating various diseases, including skin wounds. Despite its widespread use, there is limited scientific evidence regarding its molecular mechanism. This study aimed to investigate the effects of Rhus coriaria extract on human skin fibroblast cell survival and migration.
Methods: An aqueous extract of Rhus coriaria fruit was prepared, and its safe concentration on fibroblast cells was determined using the MTT method. The effects of different concentrations (200, 400, 600, and 800 µg/ml) of Rhus coriaria extract on cell proliferation were evaluated using the MTT method. The scratch method was used to investigate the effects of Rhus coriaria aqueous extract on fibroblast cell migration after 24 and 48 hours.
Results: Concentrations of 1250 µg/ml or less of the aqueous extract of sumac fruit had no toxic effect on fibroblast cells. Concentrations of 600 and 800 µg/ml significantly increased the viability of fibroblast cells compared to the control group. Concentrations of 400, 600, and 800 µg/ml of sumac extract significantly increased the percentage of fibroblast cell migration and decreased the distance between the scratches of fibroblast cells.
Conclusion: The results demonstrated that Rhus coriaria extract can enhance the wound healing process by increasing fibroblast cell proliferation and migration. This suggests its potential as a suitable medicine for wound treatment.

Keywords: cell migration, sumac extract, fibroblast cells, scratch method

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Abstract: A-10-2782-1

Synthesis of Drug Delivery Nanosystem and Investigation of Its Therapeutic Agent Release Rate

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Background: Cancer treatment is associated with numerous challenges, prompting the development of nanocarriers as drug delivery systems. Fourth-generation polyamidoamine dendrimer, with its active amide amine nodes and empty cavities, is a suitable polymer for nanocarrier synthesis. Polycaprolactone, an aliphatic biopolymer with high biodegradability, can help reduce polyamidoamine toxicity.
Methods: In this study, a therapeutic agent carrier nanosystem was synthesized using polyamidoamine-polycaprolactone and combined with folic acid for targeted delivery to cancer cells. The quality of the synthesized nanosystem was characterized using FTIR and DLS, and the release rate of the therapeutic agent curcumin from the nanosystem was investigated.
Results: The release rate of curcumin from the synthesized nanosystem was reduced by 50% compared to free curcumin at normal pH. Additionally, the release rate of curcumin from the synthetic nanosystem was higher at acidic pH than at normal pH, which is advantageous for targeting cancer cells, as they have an acidic environment.
Conclusion: Cancer treatments often have disadvantages such as affecting the immune system, disrupting normal bodily functions, and indiscriminate drug distribution. Nanosystems in medicine have been effective in mitigating some of these drawbacks.

Keywords: Drug delivery, Nanosystem, Curcumin, Polycaprolacton, Polyamidoamine, Folic acid, Cancer

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Abstract: A-10-2855-1

Investigating the Expression of Mir-21 Which Targets the PTEN Gene from PI3K Signaling Pathway in Clinical Samples of Triple Negative Breast Cancer

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Background: Triple-negative breast cancer (TNBC) is an aggressive form of breast cancer that requires effective treatment methods. Targeted therapy based on microRNAs (miRNAs) is a promising approach. Given the frequent aberrant activation of the PI3K signaling pathway in TNBC patients, this study assessed the expression levels of miR-21 and its target gene, PTEN, in TNBC clinical samples.
Methods: Fifteen TNBC tumor samples and 15 adjacent normal tissue samples were obtained from the tumor bank of Imam Khomeini Hospital, Tehran, Iran. RNA extraction, cDNA synthesis, and quantitative Real-Time PCR analysis were conducted. Relative expression of PTEN and miR-21 was analyzed using REST 2009® software, and gene expression was also evaluated using the UALCAN database. Additionally, ROC curve analysis was performed to assess the diagnostic value of miR-21 in TNBC.
Results: qRT-PCR analysis revealed a significant decrease in PTEN expression in most clinical samples (13 samples) by 4.6-fold and an increase in miR-21 expression by 6.8-fold in 10 samples and a decrease by 8.9-fold in 5 samples compared to normal tissues. These findings were supported by results from the UALCAN database. Furthermore, ROC curve analysis demonstrated the diagnostic potential of miR-21 in TNBC, with an area under the curve of 0.742.
Conclusion: The study suggests that miR-21 could serve as a promising candidate for inhibiting PTEN gene expression, potentially aiding in targeted treatment for TNBC. However, further research in this area is recommended.

Keywords: Triple-negative breast cancer, miR-21, PTEN

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Abstract: A-10-2857-1

Calprotectin as Emerging Biomarker for Multiple Myeloma: A Systematic Review

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Background: Multiple myeloma (MM) is a hematologic cancer characterized by uncontrolled plasma cell proliferation in the bone marrow (BM). Inflammation plays a significant role in the progression and pathogenesis of MM. S100A8 and S100A9 proteins, secreted by granulocytes and monocytes, form a heterodimer called calprotectin (CLP), which has inflammatory properties by activating the NF-κB pathway. Elevated CLP levels are associated with poor prognosis. This study aims to review the relationship between CLP levels and prognosis in MM.

Methods: A systematic review was conducted in the PubMed, Web of Science, and Scopus databases using the keywords "Multiple Myeloma OR Plasma Cell Myeloma OR Kahler Disease" AND "calprotectin OR calgranulin OR S100A8/A9." Human studies investigating the relationship between CLP levels and prognosis in MM patients were included. Meta-analyses, animal studies, clinical trials, case reports, review articles, and non-English articles were excluded.

Results: Out of 86 articles reviewed, 4 were included. Fagerhol assessed neutrophils extracellular traps (NETs) in 16 MM patients and 100 controls. Plasma NETs levels were significantly higher with S100A12/Calprotectin ELISA compared to H3/Calprotectin ELISA (P=0.03). Khosravi found fecal CLP levels were higher in 68 MM patients compared to 25 controls using ELISA. In 10 patients, a decrease in CLP levels after treatment indicated remission, while an increase suggested relapse (P=0.001). Long found increased BM expression of S100A8, S100A9, and S100A12 in 4 MM patients compared to 4 controls using qRT-PCR ($P< 0.05$, $P< 0.05$, and $P< 0.01$, respectively). Gedük measured serum CLP in 55 MM patients and 32 controls using ELISA. CLP levels decreased due to binding with paraprotein produced by heavy chain MM (P=0.012).

Conclusion: This study indicates that CLP levels are higher in MM patients compared to healthy individuals and decrease with treatment, suggesting that CLP could serve as a promising diagnostic and therapeutic biomarker for MM.

Keywords: Multiple myeloma, Calprotectin, Biomarker, Diagnosis

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Abstract: A-10-2486-1

Alternative Egg Yolk IgY-Based Treatment for Helicobacter Pylori: A Systematic Review

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Background: Helicobacter pylori (H. pylori) is a leading cause of peptic ulcers, gastritis, and gastric cancer. While antibiotics are the standard treatment, rising antibiotic resistance due to misuse and poor patient compliance necessitates alternative therapies. Egg yolk-derived immunoglobulin Y (IgY) antibodies have emerged as a promising option. This study aims to systematically review the efficacy of IgY antibodies in animal models, exploring their potential as an alternative to traditional antibiotic treatments for H. pylori.
Methods: A systematic review was conducted following PRISMA guidelines, searching databases including PubMed, Web of Science, Scopus, and Google Scholar for grey literature. Keywords used were "Helicobacter pylori," "H. pylori," "IgY," and "egg yolk." Inclusion criteria were limited to animal studies, while exclusion criteria included reviews, human studies, and letters to editors. Two authors independently screened and extracted the data, with any discrepancies resolved by a third author. The results were presented in an extraction table.
Results: A total of 124 studies were discovered in databases, with 37 duplicates. Of the 87 studies, 72 irrelevant articles were excluded, resulting in only 15 articles due to proper information. Serology and histopathology confirmed a considerable reduction of inflammation in infected animal models. In the reviewed studies, H. pylori antigens were used to produce IgY, with UreC showing greater effectiveness and utility. Although there was some variation in the dosage of treatment, all selected studies demonstrated a significant improving effect of IgY on the treatment of H. pylori in vivo.
Conclusion: The present study demonstrates that oral administration of egg yolk IgY-based treatment is a promising alternative approach to the treatment of H. pylori infection.

Keywords: H pylori, Helicobacter pylori, Egg yolk, IgY

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Abstract: A-10-2398-1

Evaluation of the Cell Growth Inhibitory and Apoptotic Effects of the Pollen Alcoholic Extracts Against Breast Cancer Cell Lines

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Background: Breast cancer is the second leading cause of cancer-related deaths among women, with over 1.5 million diagnoses each year, accounting for 25% of all cancer cases in women globally. Treatment options include surgery, radiation therapy, chemotherapy, hormone therapy, targeted therapy, and immunotherapy. However, these treatments often come with significant side effects. As a result, the use of medicinal plant extracts has emerged as a low-risk, simple, and cost-effective alternative for treating cancers, including breast cancer. This study aims to explore the effects of alcoholic extracts from Amaranthus, Chenopodium, Artemisia, Juniperus, and Cypress on the MCF-7 breast cancer cell line and normal fibroblast cells.
Methods: These five plants were collected, and alcoholic extracts were obtained. Using the MTT method, the cytotoxicity levels of Amaranthus, Chenopodium, Artemisia, Juniperus, and Cypress on MCF-7 cells were determined. Subsequently, a Hoechst staining test was performed to assess the expression of anti-apoptotic and pro-apoptotic genes. The expression levels of Bax and BCL genes were investigated by qRT-PCR.
Results: The results of this research showed that the alcoholic extracts of these plants, especially Cypress and Artemisia, decreased the survival of cancer cells. Additionally, the cytotoxic effects of these extracts on cancer cells were equal to or even stronger than the effects of methotrexate. On the other hand, their cytotoxicity on normal cells was lower than that of the control group. The expression of Bax genes increased, while BCL2 expression decreased, indicating that apoptosis occurs in this cell type.
Conclusion: Due to the decrease in cell viability after the application of these plants and their significant efficacy in killing tumor cells, the combined effects of these plants may be used as a therapeutic potential for the treatment of breast cancer.

Keywords: Breast cancer (BC), Pollen alcoholic extracts, MCF-7, Normal fibroblast cells

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Abstract: A-10-2829-1

The Use of Polyamidoamine Alginate Nanosystem in the Treatment of Lung Cancer

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Background: Lung cancer treatment is associated with numerous challenges, prompting the development of nanocarriers as drug delivery systems. Fourth-generation polyamidoamine dendrimer, with its active amide amine nodes and empty cavities, is a suitable polymer for nanocarrier synthesis. Alginate, a polyelectrolyte with high biodegradability, can help reduce polyamidoamine toxicity.
Methods: In this study, a therapeutic agent carrier nanosystem was synthesized using polyamide amine alginate and combined with folic acid for targeted delivery to cancer cells. The quality of the synthesized nanosystem was characterized using FTIR and DLS, and the release rate of the therapeutic agent sodium butyrate from the nanosystem was investigated.
Results: The release rate of sodium butyrate from the synthesized nanosystem was reduced by 47% compared to free sodium butyrate at normal pH. Additionally, the release rate of sodium butyrate from the synthetic nanosystem was higher at acidic pH than at normal pH, which is advantageous for targeting cancer cells, as they have an acidic environment.
Conclusion: Lung cancer treatments often have disadvantages such as affecting the immune system, disrupting normal bodily functions, and indiscriminate drug distribution. Nanosystems in medicine have been effective in mitigating some of these drawbacks.

Keywords: Lung cancer, Polyamidamine, Sodium butyrate, Alginate

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Abstract: A-10-2858-1

A Quantum Mechanical Investigation on Betamethasone

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Background: Betamethasone is a corticosteroid used to treat inflammation, severe allergies, and autoimmune conditions. It's typically administered via injection under medical supervision due to potential side effects like mood changes, increased appetite, and immune suppression. Long-term use requires careful monitoring and gradual dose reduction to avoid complications.
Methods: The study utilized quantum mechanics (QM) calculations conducted through the density functional theory (DFT) method using the GAUSSIAN 09 software. The structure of the Betamethasone drug was first optimized through gradient procedures at both restricted Hartree-Fock (HF) and hybrid density functional B3LYP levels of theory using the 6-311G basis set. Examination of the results revealed that the optimized structure achieved in this research was situated at the minimum point on the potential energy surface, displaying no negative modes.
Results: This study conducted calculations for structural parameters like bond lengths, angles, and dihedrals, as well as thermodynamic parameters at the B3LYP/6-311G level of theory and provided the results. The electronic energy of the molecule was determined to be -835636.9202 kcal/mole. Additionally, the Mulliken atomic charge, spin density, and molecular orbital energies were calculated. The highest occupied molecular orbital (HOMO) was found to be -0.24266 eV and the lowest unoccupied molecular orbital (LUMO) was -0.06918 eV. The dipole moment in Debye was measured as X=-3.7977, Y=-0.7622, Z=3.4441, with a total of 5.1832.
Conclusion: Optimization of the drug was performed using the B3LYP/6-311G method. The study focused on Betamethasone's electronic characteristics, specifically the energy difference between the HOMO and the LUMO. The HOMO-LUMO gap energy was determined to be 0.17348 eV. This provides insights into Betamethasone's electronic behavior, which could have applications in various fields.

Keywords: Keywords: BETAMETHASONE, DFT, B3LYP/6-311G, HOMO-LUMO gap

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Abstract: A-10-2471-1

Comparison of the Apoptotic Effects of Lactobacillus casei on Two Different Cell Lines of Breast Cancer

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Background: Lactobacillus casei, known as probiotics, have garnered significant attention as potential supportive treatments in chemotherapy for various types of cancer, particularly breast cancer. This research examines the apoptotic effects of Lactobacillus casei on MCF-7 and MD-231 breast cancer cell lines compared to normal control cells.

Methods: The cytotoxic effect of Lactobacillus casei supernatant on MCF-7 and MD-231 breast cancer cell lines was assessed using the MTT assay. The apoptotic effect of various supernatant concentrations was evaluated by analyzing the gene expression of BAX-BCL2 ratio, Caspase-3, and Caspase 9 using quantitative Polymerase Chain Reaction (q-PCR).

Results: Major cytotoxicity was observed in MCF-7 and MD-231 breast cancer cell lines attributed to the low pH of the supernatants. The increase in the BAX-BCL2 ratio, leading to an upregulation of Caspase-3 and Caspase-7, indicated the induction of apoptosis ($P<0.05$).

Conclusion: The notable decrease in the expression of apoptotic genes involved in apoptosis highlights the importance of conducting comparative studies on various breast cancer cell lines to determine the potential anti-proliferative effects of Lactobacillus casei supernatant.

Keywords: Apoptosis, breast cancer, Lactobacillus Casei

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Abstract: A-10-2498-1

Examining the Serum Level of MDA, TAC, and TOS in Patients with Metabolic, Non-Metabolic Fatty Liver and Control Subjects

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Background: Liver inflammation can lead to fibrosis, cirrhosis, and ultimately, liver failure. Free radicals and oxidative stress are key contributors to liver damage. This study investigated the levels of three biomarkers: total oxidative status (TOS), malondialdehyde (MDA), and total antioxidant capacity (TAC) in patients with metabolic and non-metabolic fatty liver disease (FLD) compared to healthy controls. The aim was to understand the impact of these markers on liver health.
Methods: The study recruited 37 patients with metabolic FLD, 26 patients with non-metabolic FLD, and 22 healthy individuals. Serum samples were analyzed for MDA, TOS, and TAC using specific manual methods. Statistical analysis was performed using SPSS version 16 on the collected data.
Results: MDA levels were significantly higher in both FLD groups compared to the healthy control group. Furthermore, MDA levels were significantly higher in the metabolic FLD group compared to both the non-metabolic FLD and healthy control groups ($p = 0.001$ for metabolic vs. healthy and $p = 0.01$ for non-metabolic vs. healthy). TAC levels were significantly lower in the metabolic FLD group compared to the control group ($p = 0.001$). However, no significant difference was observed in TAC levels between the non-metabolic FLD group and the control group ($p = 0.16$) or between the metabolic and non-metabolic FLD groups ($p = 0.063$). TOS levels were significantly lower in both the metabolic and non-metabolic FLD groups compared to the control group ($p = 0.001$ for metabolic vs. healthy and $p = 0.021$ for non-metabolic vs. healthy). There was no significant difference in TOS levels between the metabolic and non-metabolic FLD groups ($p = 0.162$).
Conclusion: Elevated serum MDA levels and decreased TAC and TOS levels in patients with fatty liver disease suggest that these markers are associated with the development and progression of the disease.

Keywords: fatty liver, oxidant, total antioxidant capacity, non-metabolic fatty liver disease

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Abstract: A-10-2871-2

Metabolic Reprogramming in Tumor Microenvironments: A Comprehensive Meta-Analysis of Biochemical Alterations and Their Therapeutic Significance

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Background: Cancer cells develop metabolic changes that provide tumor development, survival, and treatment resistance. These changes depend on the tumor microenvironment (TME). This meta-analysis comprehensively reports on these alterations and their potential for therapy.

Methods: The review was developed through an in-depth literature search across PubMed, Google Scholar, and Web of Science for studies from 2010 to Jan-Feb 2024. In this review, we summarize all the published peer-reviewed studies that focus on TME-mediated metabolic changes and their impact on cancer therapy. The objectivity and dependability of our findings result from the search in which all relevant research was included, and our rigorous quality rating process overseen by two independent reviewers. The pooled effects of interest were calculated using a fixed- or random-effects model.

Results: In this meta-analysis, 25 studies with almost 5,000 participants analyzed. They concluded that abnormalities in glucose, lipid, and amino acid, especially in glutamine, were present in the TME (pooled OR 2.15, 95% CI 1.68-2.75). These abnormalities, such as increased glycolysis and increased lipid production, transformed cancer into more aggressive forms and were related to cancer aggressiveness and poor patient outcomes (HR 1.42, 95% CI 1.19-1.70). Therapeutic approaches targeting these metabolic pathways were observed, especially with immune checkpoint inhibitors. These strategies regulated metabolic pathways in the TME and demonstrated promise in overcoming therapeutic resistance (pooled OR 1.75, 95% CI 1.32-2.31). However, there was significant variability among the studies, indicating a need for further research and more targeted interventions (I^2 = 73%). The results emphasize the significance of metabolic reprogramming in cancer and the potential for therapeutic opportunities.

Conclusion: Metabolic changes in cancer cells facilitate tumor growth and treatment resistance. Targeting these metabolic pathways is crucial to enhancing cancer therapy. Integrating metabolic therapies into current treatments warrants further investigation, as it may play a significant role in the future.

Keywords: Tumor Microenvironment, Metabolic Networks and Pathways, Reprogramming, Drug Therapy, Immunotherapy.

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Abstract: A-10-2879-1

Altered Expression of Interleukin-6 and Heparin-1 Binding Epidermal Growth Factor, in the Endometrium of Women with Hydrosalpinx

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Background: Hydrosalpinx is a condition affecting the fallopian tubes that can decrease embryo implantation rates and in vitro fertilization (IVF) success. It can cause inflammatory conditions in the uterine endometrium, leading to alterations in the expression of transcription factors and cytokines such as interleukin-6 (IL-6) and heparin-binding epidermal growth factor (HB-EGF), which are involved in endometrial receptivity (ER) and embryo implantation. The alterations of these markers in the endometrium of patients with hydrosalpinx have not been previously investigated. Therefore, we aimed to evaluate the mRNA expression levels of IL-6 and HB-EGF in the endometrium of women with hydrosalpinx compared to a fertile control group.
Methods: In this case-control study, 30 subjects were enrolled: 15 patients with communicating hydrosalpinx (aged 20-37 years) and 15 age-matched fertile women as the control group. All subjects underwent uterine endometrial sampling using a Pipelle on days 19-24 of the menstrual cycle. Gene expression was quantitatively analyzed using real-time polymerase chain reaction (PCR). Data analysis was conducted using the Wilcoxon rank test.
Results: The mRNA expression level of IL-6 showed a significant increase in patients with hydrosalpinx compared to the control group (P=0.022). Conversely, HB-EGF gene expression was significantly reduced in the hydrosalpinx group compared to fertile women (P=0.007).
Conclusion: The presence of hydrosalpinx altered the expression of endometrial IL-6 and HB-EGF mRNA levels in the implantation window, which may explain the reduced implantation rate and success in in-vitro fertilization (IVF) outcomes.

Keywords: Hydrosalpinx, Endometrial receptivity, Interleukin-6, HB-EGF

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Abstract: A-10-2908-1

Toxicity Study of Aqueous Extracts of White and Brown Rice and Rice Bran in Zebrafish Larvae

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Background: This article examines the effects of rice contamination with heavy metals, particularly arsenic, on zebrafish larvae up to 96 hours post-fertilization. Zebrafish larvae were selected for their 70% genetic similarity to humans and the ability to make observations due to the transparent covering of the larvae during the 96 hours after fertilization, which facilitates the monitoring of organ growth, blood flow in the abdominal aorta, and heartbeat through a stereo microscope. Due to its morphological structure, rice can accumulate heavy metals, especially arsenic, which is a significant concern.

Methods: Samples of white rice, brown rice, and rice bran from the Hashemi variety in Gilan province were collected, and arsenic levels were measured using the ICP MASS device. Zebrafish larvae were treated with five different concentrations of the aqueous extract of each substance, along with a control group. Each concentration was replicated three times, with each repetition including 120 larvae. The larvae were examined, and observations were recorded for 96 hours post-fertilization.

Results: The arsenic levels in white rice were 0.07 mg/kg, in brown rice, they were 0.11 mg/kg, and in rice bran, they were 0.18 mg/kg, with rice bran showing the highest levels. At lower concentrations (0.1 and 1 mg/kg), larvae developed normally up to 96 hours. However, at higher concentrations (10 mg/kg), several abnormalities were observed.

Conclusion: Arsenic contamination in rice and related products can adversely affect the growth and survival of zebrafish larvae, indicating potential health risks for humans.

Keywords: rice ،rice bran ،arsenic ،zebrafish ،toxicity

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Abstract: A-10-2740-1

Investigating polymorphisms that play a role in colorectal cancer recurrence

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Background: Colorectal cancer (CRC) is the leading cause of mortality linked to gastrointestinal malignancies globally. Despite surgical interventions and subsequent chemotherapy, a significant percentage of patients experience recurrence. Recent research has underscored genetic variations as crucial factors influencing the progression and prognosis of colon cancer. A deeper understanding of these polymorphisms may enhance risk assessment and therapeutic outcomes for patients with locally advanced CRC.

Methods: A comprehensive systematic search of relevant studies up to 2024 was conducted by exploring databases such as PubMed, MEDLINE, SCOPUS, and Google Scholar. The keywords "Colorectal cancer," "Polymorphisms," and "Relapse" were utilized in this search. Only articles with fully accessible English texts were included in the search parameters. Articles that were reviews, duplicates, or irrelevant were excluded.

Results: In this systematic review, 95 articles were retrieved from the databases, of which only 9 met our inclusion criteria. Genetic variations, including PLS3 rs6643869 and LCP1 rs4941543, were identified as significant factors influencing the risk of tumor recurrence. Single nucleotide polymorphisms (SNPs) associated with angiogenesis, specifically VEGF C+936T and IL-8 T2251A, were linked to a reduced time to recurrence, suggesting their potential as prognostic indicators. Furthermore, the miRNA-encoding genes miR219-1 and miR-608 exhibited varying associations with survival rates in patients undergoing 5-FU-based chemotherapy. Conversely, the effect of HSPB1 rs2070804 on colorectal cancer (CRC) progression remains unclear, as it showed limited connections with clinical factors such as tumor aggressiveness and metastasis.

Conclusion: The discovery of specific SNPs within plastin genes, angiogenesis-related genes, miRNA-encoding genes, and heat shock proteins (HSPs) holds potential for developing personalized treatment approaches and risk evaluation in CRC patients. Future investigations should aim to confirm these results in larger populations and assess their clinical relevance for enhancing patient outcomes.

Keywords: Polymorphisms, Colorectal cancer, Relapse

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Abstract: A-10-2861-1

Emerging Threats and Management Strategies for CTX-M-15 Producing Escherichia coli in Horses: A Review

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Background: The emergence of CTX-M-15-producing Escherichia coli in horses presents a significant challenge in veterinary medicine, indicating a shift in antibiotic resistance trends. This review examines the prevalence, mechanisms, and management strategies associated with this multidrug-resistant strain.
Methods: A systematic review was conducted, encompassing a thorough search of 34 articles from PubMed, Google Scholar, and Iran Paper systems. Articles pertaining to CTX-M-15 E. coli and antibiotic resistance in horses were filtered from 2010 to 2023, with two authors reviewing the articles and conducting in-depth studies.
Results: The review revealed a notable presence of CTX-M-15-producing E. coli in equine fecal samples, demonstrating the strain's resistance to extended-spectrum cephalosporins. The genetic mechanisms involve horizontal gene transfer, exacerbated by environmental factors and close animal contact.
Conclusion: The increasing prevalence of CTX-M-15-producing E. coli in horses underscores the urgent need for enhanced antibiotic stewardship and interdisciplinary approaches. Education for veterinarians and horse owners, along with research into alternative therapies and vaccines, is crucial for effectively combating antibiotic resistance. Collaborative efforts are essential to develop strategies for managing this emerging threat.

Keywords: Escherichia coli, CTX-M-15, Antibiotic Resistance, Antibiotic Stewardship

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Abstract: A-10-2861-2

Systematic Review: Exploring the Impact of Dexmedetomidine and Isoflurane on Brain Development in Rodents and Potential Neuroprotective Strategies

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Background: Brain development in rodents has been extensively researched due to its close relationship with the development of the nervous system in humans and neurological disorders. Recent studies have concentrated on the effects of surgical anesthetics, particularly dexmedetomidine and isoflurane, on this process, underscoring the potential risks associated with these procedures during this critical period of brain development. Clinical research presents mixed findings on the effects of single versus repeated anesthetic exposure on the developing brain, while preclinical studies seek to uncover the underlying mechanisms of anesthetic-induced neurotoxicity in immature brains. This strategy aims to enhance our understanding of anesthesia-induced neurotoxicity and explore protective mechanisms for the immature brain, highlighting the necessity for further research in this complex and evolving field.

Methods: This review synthesized the findings of 23 articles retrieved from the PubMed and Science Direct databases, focusing on studies that investigate the effects of dexmedetomidine and isoflurane on brain development in rodents and potential neuroprotective strategies. These articles were screened and selected based on predefined inclusion criteria to ensure relevance and data quality. The search concentrated on articles published from 2001 to 2024 in both Iranian and international journals, with specific filters and keywords applied.

Results: Clinical studies mainly focus on anesthesia exposure parameters, including dose, time, and frequency of anesthesia, and suggest that occasional or short periods of anesthesia may not significantly affect cognitive outcomes such as IQ scores.

Conclusion: concerns remain about the potential for cumulative effects on aspects such as processing speed, motor skills, and social abilities after repeated anesthetic events.

Keywords: Brain Development, Rodents, Neurotoxicity, Single-Cell Sequencing

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Abstract: A-10-2368-1

The Emerging role of T Cell Chemokine Trafficking for the Treatment of Colon Cancer

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Background: Colon cancer is the most prevalent cancer globally and a significant cause of mortality. Chemokines are chemotactic cytokines that facilitate the migration of immune cells throughout the body. The emerging role of chemokines may be crucial in recruiting T cells and various immune cells into the gastrointestinal tumor microenvironment. T cells, which serve as the primary agents of the adaptive immune system, exhibit specific modes of chemotaxis and versatile immune activities. Furthermore, the accumulation of T cells, which possess a strong capacity to recognize and eliminate malignant and viral inflammatory cells, can trigger immune responses with the assistance of chemokines. The infiltration of cancer cells is characterized by T cell subsets with a chemokine gene signature. Given that chemokines and their receptors play a vital role in cancer, previous studies on colon cancer have indicated that the expression of CXCR3 and CXCL10 is linked to metastasis in various cancers, including colon cancer.

Methods: This abstract was conducted using articles published on PubMed and Google Scholar until June 2024. The keywords used were T cells, chemokines, immune system, and colon cancer treatment. By searching these two databases, over 30 articles were reviewed, and 21 articles were excluded. Consequently, 9 articles were selected based on the inclusion criteria.

Results: Our statistics show an effective relationship between CD8, CXCL9, and CXCL10, and the expression of CD8, CXCL9, and CXCL10 is undoubtedly related to the survival of colon cancer patients. In support of these observations, CD8+ T cells and Th1-type chemokines play an important role in predicting the outcome of most patients.

Conclusion: Therefore, the intelligent manipulation of targeted T cells using receptors and chemokine signals and directing and infiltrating them to the foci of cancer lesions may be a new strategy for colon cancer.

Keywords: Colon Cancer, T cells, Chemokine, Immune system

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Abstract: A-10-2826-1

Development of Covid-19 neutralizing antibody detection test using a truncated recombinant ACE2 protein

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Background: COVID-19 is the third most prevalent viral disease of the coronavirus family in the 21st century. The interaction between the ACE2 receptor and the receptor binding domain (RBD) of the S protein is crucial for the entry of the SARS-CoV-2 virus into host cells. The Coronavirus S protein can activate the immune system and generate neutralizing antibodies against it. The efficacy of a vaccine is evaluated by assessing the cellular and humoral immune responses (neutralizing antibodies) for each of the COVID-19 vaccines. Our long-term objective is to design and produce a truncated recombinant human ACE2 protein and utilize it to develop a coronavirus-neutralizing antibody detection kit by simulating viral infection (ACE2-S-protein interaction).

Methods: The target sequence was selected from ACE2 using bioinformatics analysis. The sequence was designed for expression in a eukaryotic host within the pcDNA3.1 vector. The synthesized genes were transfected into HEK293 cells for protein expression. The efficiency of protein expression was confirmed by SDS-PAGE gel and Western blotting. The binding of the recombinant ACE2 protein with the spike protein was assessed through an ELISA test using an anti-His tag antibody. The neutralizing antibody was detected by analyzing the blocking of the ACE2-RBD interaction.

Results: In summary, we present an efficient expression system and refolding procedure for preparing a functional recombinant ACE2 using the pcDNA3.1 expression system and HEK293 cells. The recombinant ACE2 produced in this study demonstrated effective binding ability in the ELISA assay. More importantly, the expressed recombinant ACE2 can detect and bind to SARS-CoV-2.

Conclusion: The recombinant ACE2 produced in the present study can be used as starting material in the development of diagnostic kits and screening of potential vaccines

Keywords: ACE2, neutralizing antibody, SARS-CoV-2, spike protein, vaccine

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Abstract: A-10-2859-1

The effect of monobenzone cream on oxidative stress and its relationship with serum levels of IL-1β and IL-18 in vitiligo patients

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Background: Monobenzyl ether hydroquinone (MEBHQ) is a cream that enhances the spread and uniformity of skin patches in vitiligo. Our objective was to investigate the oxidative and inflammatory effects of this cream on vitiligo patients using MEBHQ.

Methods: A case-control study was conducted with three groups of 30 individuals each: a control group, vitiligo patients before treatment, and vitiligo patients after treatment. A specialist doctor determined the percentage of vitiligo spots. The levels of biochemical factors, oxidative stress profiles, and inflammatory factors were measured using enzymatic, colorimetric, and ELISA methods, respectively.

Results: Vitiligo patients exhibited elevated levels of inflammation and oxidative stress compared to healthy individuals. After three months of using MEBHQ cream, the percentage of skin spots in vitiligo patients increased from an average of 63% to 91%, and the skin color became nearly uniform; however, this also led to an increase in oxidative stress and inflammation levels in these patients. Despite the significant rise in oxidative stress, there was no notable increase in malondialdehyde levels. The absence of significant differences in biochemical factor levels between healthy individuals and vitiligo patients before and after treatment indicates a lack of side effects.

Conclusion: The use of MBEHQ increased the size of skin spots and uneven skin color in vitiligo patients. Although MBEHQ did not show side effects such as diabetes, liver and kidney diseases, it increased the levels of oxidative stress and inflammatory cytokines, which needs further study.

Keywords: Vitiligo, Monobenzyl ether of hydroquinone, malondialdehyde, Total oxidant status, Inflammation, Oxidative stress

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Abstract: A-10-2471-2

Targeted Development of carbon Dot and Paclitaxel Co-Delivery by Chitosan Nano-carrier Decorated with Folate to the MCF-7 Cancer Cell Line Theranostic Application

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Background: Chitosan nanoparticles for therapy and tracking applications are eminent co-delivery nanoparticles widely used as polymeric nano-carriers in the nanomedicine domain. Development in targeted delivery and imaging is contingent on attaching efficient ligands to chitosan polymer as target delivery.
Methods: Here, we have described our recent experiences, carbon dot synthesis, decoration of chitosan by folate, the formulation of carbon dot and paclitaxel as a hydrophobic drug, characterization of nano-carrier, human mammary carcinoma (MCF-7) cancer cell imaging, and evaluation of the therapeutic effects of paclitaxel by real-time PCR. The carbon dots were synthesized by hydrothermal method with a 3-7 nm mean size. The conjugation of folate and chitosan polymer accomplished by EDC/NHS chemistry and formulation of carbon dot and paclitaxel was occurred by ionic gelation method. The conjugates showed a uniform size distribution of 220 ± 30 nm. DLS, FTIR, FESEM, TEM, and UV-visible techniques performed the characterization of constructs. The chitosan@ carbon dot@ paclitaxel@ folate conjugates were tracked under fluorescence microscopy to evaluate the cell uptake. Also, Chinese hamster ovary cells (CHO) were used as a non-express folate receptor.
Results: The results exhibited a good size distribution of ~ 80 nm with an acceptable loading capacity for paclitaxel of approximately 43%. After 4 h incubation of MCF7 and CHO cells with conjugates, fluorescence imaging shows the transferring of nanoparticles to cancer cells. Real-time PCR of apoptotic genes confirmed the theranostic efficiency of nanoparticles. The BAX/BCL2 ratio shows increased cancer cell apoptosis.
Conclusion: This investigation demonstrates that chitosan@ carbon dot@ paclitaxel@ folate nanoparticles provide a unique construction for cancer-specific fluorescent imaging capable of loading therapeutic agents.

Keywords: Cancer, Chitosan, Co-Delivery, Nano-carrier, Theranostic

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Abstract: A-10-3062-1

Effects of Buffers on chondroitinase ABC form Proteus vulgaris Activity and stability of the Enzyme

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Background: Chondroitinase ABC I (cABC I) is an enzyme isolated from the bacterium Proteus vulgaris. Its enzymatic activity and potential applications in biomedical research and biotechnology make it a significant subject of interest in biochemistry and molecular biology, as it degrades glycosaminoglycan chains that hinder axon regeneration following spinal cord injury. However, the thermal instability of cABC I primarily limits its medical applications. This study assessed the effects of phosphate and tris buffers on cABC I activity and thermal stability.

Methods: The genes encoding the wild type from P. vulgaris were transformed into competent cells in a previous study. The harvested cells were lysed, and soluble protein was extracted using a Ni-NTA agarose column. Protein elution was performed with 50 mM phosphate or tris buffer. The activity assay for the expressed cABC I enzymes was conducted by measuring the increase in absorbance at 232 nm. Long-term stability of the enzyme was measured at -20, 4, and 25°C, while thermal stability was assessed at 40 °C.

Results: Our results indicate that there is no significant difference in enzyme catalytic activity between the phosphate and tris buffers (data not shown). The findings revealed that the long-term stability of cABC I at 25°C improved in phosphate buffer compared to tris buffer. However, experiments demonstrated that the effect of phosphate buffer on the thermal stability of cABC I was not substantial.

Conclusion: This study was conducted to investigate the effect of phosphate and tris buffers on activity and thermal stability of rcABC I. Our data showed an improvement in catalytic activity of rcABC I using phosphate buffers. Therefore, the use of phosphate buffer show signs of enhancement in shelf-life, so it can be improvement medical applications of this drug enzyme.

Keywords: Chondroitinase ABC I, Enzyme activity, Thermal stability

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Abstract: A-10-2261-2

Ferulic acid exerts a protective effect against cyclosporine-induced liver injury in rats via activation of the Nrf2/HO-1 signaling, suppression of oxidative stress, inflammatory response, and halting the apoptotic cell

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Background: Drug-induced liver injury is a significant challenge that leads to the withdrawal of various drugs in clinical settings. Cyclosporine is one such drug whose long-term administration has devastating effects on hepatocytes. In this study, we aimed to evaluate the impact of ferulic acid, a natural compound found in plants, on cyclosporine-mediated hepatotoxicity.
Methods: Forty-eight male Wistar rats were treated with cyclosporine and/or ferulic acid to assess the function and morphology of liver cells.
Results: We found that ferulic acid dose-dependently improved both functional and histopathological parameters of liver cells, as evidenced by the reduction of hepatocellular vacuolation, portal fibroplasia, and necrosis. Furthermore, this phenolic compound was able to restore the balance of the redox system in cyclosporine-treated rats by activating the nuclear factor erythroid 2-related factor 2 (Nrf2)/heme oxygenase-1 (HO-1) signaling axis. Notably, the protective effects of ferulic acid against cyclosporine-mediated liver toxicity were not limited to the induction of potential antioxidant properties; in the presence of this agent, the expression of pro-inflammatory cytokines such as nuclear factor (NF)-κB, tumor necrosis factor (TNF)-α, and interleukin-1β was also reduced. Additionally, ferulic acid shifted the balance between the expression levels of pro-apoptotic and anti-apoptotic proteins, thereby preventing the development of cyclosporine-induced liver injury.
Conclusion: Overall, these findings highlighted that ferulic acid can reduce cyclosporine-induced liver injury due to its antioxidant properties.

Keywords: Cyclosporine, Ferulic acid, Oxidative stress, Nrf2/HO-1 axis, Apoptotic cell death

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Abstract: A-10-2974-1

From molecular mechanisms to novel therapies: using TGF B as a therapeutic target in cancer

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Background: The molecular biology of cancer cells is a rapidly advancing field of medical science. Understanding the molecular mechanisms underlying cancer cells is crucial for cancer prevention. Recent research indicates that the TGF β protein plays a vital role in regulating the tumor microenvironment and cancer progression.
Methods: This study is a review based on data from the SId, PubMed, and Google Scholar databases, utilizing keywords such as TGF-B, cancer, tumor, and SAMD4. After reviewing the titles and abstracts of the articles, irrelevant studies were excluded. This study results from a comprehensive review of available related articles.
Results: Based on the analysis of 37 articles (20 international and 17 domestic) over five days from September 5 to 9, TGF-β is identified as a significant factor in regulating cell growth and differentiation, influencing various stages of cancer. The findings reveal that TGF-β can function both as a suppressive and a stimulating factor in tumor progression. The application of TGF-β antagonists, particularly in combination with other treatments like immunotherapy and chemotherapy, holds promise for enhancing clinical outcomes. These strategies may help amplify immune responses and inhibit tumor growth. Additionally, this protein may serve a protective role in the early stages of cancer. TGF β is notably involved as an inducer of epithelial-mesenchymal transition during wound healing and in pathological conditions such as fibrosis and cancer.
Conclusion: The use of TGF-β as a therapeutic target in cancer is a promising field that could lead to the development of new treatments and improved patient outcomes. However, a deeper understanding of the various roles of TGF-β in cancer biology and the design of more detailed clinical studies are necessary to realize this goal.

Keywords: TGF-B, cancer, SAMD4

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Abstract: A-10-3048-2

Whole Exome Sequencing in Biochemical Disorders: A Comprehensive Review

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Background: Whole exome sequencing (WES) has emerged as a powerful diagnostic tool for identifying genetic mutations underlying biochemical disorders. This systematic review aims to evaluate the effectiveness of WES in diagnosing these disorders, analyze its clinical utility, and highlight the challenges posed by incomplete penetrance and variable expressivity in patients.

Methods: A systematic literature search was conducted using PubMed, Scopus, and Web of Science databases. Keywords included “whole exome sequencing,” “biochemical disorders,” “metabolic disorders,” “inborn errors of metabolism,” and “genetic diagnosis.” The search was limited to articles published between 2013 and 2023. Inclusion criteria required studies reporting WES as a diagnostic tool for biochemical disorders with patient outcome data. A total of 185 articles were identified initially. After excluding duplicate records and studies without relevant clinical data, 52 articles fulfilled the inclusion criteria.

Results: The review demonstrates that WES has significantly improved the diagnostic yield for biochemical disorders, particularly in patients with complex, undiagnosed conditions. Across studies, WES identified pathogenic variants in 35-50% of cases. It was valuable in detecting rare mutations associated with inborn errors of metabolism, enabling early intervention and targeted treatments. However, the review also identified challenges such as incidental findings, difficulties interpreting variants of unknown significance (VUS), and cases of incomplete penetrance, where individuals carrying pathogenic mutations remained asymptomatic. Furthermore, the findings highlighted the variability in clinical outcomes, even among patients with identical mutations.

Conclusion: WES has proven to be a crucial diagnostic tool for biochemical disorders, improving diagnostic accuracy and guiding clinical management. However, the complexity of interpreting results, especially in cases of incomplete penetrance and asymptomatic individuals, underscores the need for improved bioinformatics tools and genetic counseling. Continued research is needed to optimize the interpretation of WES data and understand the full clinical spectrum of biochemical genetic disorders.

Keywords: Whole Exome Sequencing, Biochemical Disorders, Asymptomatic Individuals

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2680-1

Investigation of hematology and biochemical characteristics of coliform mastitis in the occurrence of acute laminitis in dairy cows

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Background: Mastitis and laminitis are common diseases affecting dairy cows, significantly influencing their economic value and overall welfare. Mastitis, an infection of the mammary gland, often results in lameness, a condition known as laminitis, which can further intensify the severity of mastitis. This study aims to investigate the hematological and biochemical characteristics of coliform mastitis in relation to acute laminitis in dairy cows, with the ultimate goal of identifying potential preventive measures and enhancing the management of these diseases.
Methods: A comprehensive search was conducted across three leading scientific databases: PubMed, Science Direct, and Iran Paper, yielding a total of 83 articles. These articles underwent rigorous screening based on predetermined filters and criteria designed to ensure relevance and quality. This search focused on articles published from 2009 to 2024 in Iranian and foreign journals, and the articles were selected according to the filters, with specific keywords examined. Following this thorough selection process, 33 articles were identified and included in this review, providing a solid foundation for evaluating the hematological and biochemical characteristics of coliform mastitis in the context of acute laminitis in dairy cows.
Results: Coliform mastitis has been recognized as a significant risk factor for the development of acute laminitis in dairy cows. The hematological and biochemical abnormalities observed, including neutropenia, reduced iron and zinc levels, and positive ethanol gelatinization tests, highlight the complex interplay between mastitis and laminitis.
Conclusion: These findings highlight the importance of early detection and intervention in managing these diseases to minimize economic losses and improve animal welfare. Further research is warranted to explore the underlying mechanisms and develop targeted therapeutic strategies.

Keywords: Coliform Mastitis, Acute Laminitis, Dairy Cows, Neutropenia, Iron Deficiency, Zinc Deficiency

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3018-1

Reviving Vision: Cutting-Edge Stem Cell Therapies for Optic Nerve Regeneration

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Background: Optic nerve damage can lead to irreversible blindness, significantly impacting quality of life. Recent advances in stem cell therapy offer promising avenues for regenerating damaged optic nerves. This review synthesizes findings from systematic reviews and meta-analyses to evaluate the efficacy and safety of stem cell-based therapies for optic nerve regeneration.

Methods: A systematic review was conducted by searching databases including PubMed, Cochrane Library, and Web of Science. The search was performed using keywords such as "optic nerve regeneration," "stem cell therapy," "mesenchymal stem cells," and "induced pluripotent stem cells." The search covered studies published from 2000 to 2023. Inclusion criteria were studies on stem cell therapy for optic nerve regeneration, published in peer-reviewed journals, and written in English. Exclusion criteria included non-peer-reviewed articles and studies not directly related to optic nerve regeneration. Data about stem cells, efficacy, and associated safety concerns were extracted. The number of articles initially identified, excluded, and included were documented. Meta-analyses were performed where applicable.

Results: A total of 150 articles were identified, of which 120 were excluded based on the inclusion and exclusion criteria. Thirty articles were included in the final analysis. Various stem cells, including mesenchymal stem cells (MSCs), induced pluripotent stem cells (iPSCs), and neural stem cells (NSCs), have been investigated. Meta-analyses indicate that stem cell therapy significantly improves optic nerve function and visual acuity in animal models. However, clinical trials in humans are still in the early stages. Systematic reviews highlight potential risks such as tumorigenicity and immune rejection. Strategies to mitigate these risks include genetic modification and immunosuppressive therapy.

Conclusion: Stem cell therapy represents a promising approach for optic nerve regeneration. While preclinical studies are encouraging, further research is needed to establish its efficacy and safety in humans. Continued advancements in molecular biology and regenerative medicine are essential to bring this therapy closer to clinical application.

Keywords: Optic nerve regeneration, stem cell therapy, mesenchymal stem cells, induced pluripotent stem cells

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3066-1

The Role of Monoclonal Antibodies in Cancer Treatment: Mechanisms and Clinical Applications

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Background: Monoclonal antibodies have significantly transformed the landscape of cancer treatment over the past few decades. Unlike chemotherapy, which can damage healthy cells, mAbs specifically target cancer cells by recognizing unique proteins on their surfaces. This targeted strategy helps to reduce side effects and enhance treatment outcomes. Consequently, mAbs have become a cornerstone of modern oncology, providing patients with more precise and less toxic options for combating cancer.

Methods: We conducted a thorough review of the literature by searching for five primary keywords in databases such as PubMed, Scopus, and Web of Science from 2014 to 2024 to collect studies on the application of monoclonal antibodies in cancer therapy. A total of 95 articles were included based on their relevance to the mechanisms of action, clinical effectiveness, and recent advancements in the field. Studies that lacked detailed information or did not directly pertain to cancer immunotherapy were excluded.

Results: Monoclonal antibodies have demonstrated remarkable success in improving survival rates and reducing tumors across a wide array of cancers. For instance, trastuzumab has significantly enhanced survival for patients with HER2-positive breast cancer, while pembrolizumab has resulted in lasting remissions in advanced melanoma. These antibodies function by activating the immune system to more effectively attack cancer cells and by blocking signals that promote tumor growth. Newer types of mAbs, such as bispecific antibodies and antibody-drug conjugates, have been developed to further amplify these effects, providing even more powerful tools against challenging-to-treat cancers.

Conclusion: Monoclonal antibodies have revolutionized cancer treatment by providing more targeted, effective, and safer therapies. As research continues, we can expect even more breakthroughs in this field, leading to better outcomes for patients and new strategies to overcome the challenges of drug resistance.

Keywords: Monoclonal antibodies, Cancer therapy, Immune activation, Bispecific antibodies, Antibody-drug conjugates

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Abstract: A-10-2494-2

The relationship between physical activity and intestinal microbiota composition: A systematic review

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Background: The intestinal microbiota, a complex ecosystem of microorganisms residing within the gastrointestinal tract, is increasingly recognized as a crucial determinant of human health. Emerging evidence suggests a potential bidirectional relationship between physical activity and the composition of this microbial community. While the mechanisms underlying this association remain to be fully elucidated, alterations in microbial diversity, composition, and metabolic function have been observed in response to exercise interventions.

Methods: By searching the keywords of physical activity and gut microbiota in PubMed, Web of Science, and Scopus, we included all studies that met our criteria. We did not restrict the language, and our search continued until June 2024.

Results: Out of 2081 studies, 19 were included. Reviews, observational, animal, and laboratory studies were excluded. The main results vary significantly depending on the level of physical activity in the studies, but most indicated positive effects. One study utilized the Mediterranean Diet and physical activity to associate with microbiota. This study shows that long-term lifestyle improvements aimed at weight loss through this protocol lead to increases in certain diversity, such as Ruminococcaceae, which may respond to energy restriction. Conversely, the reduction of other diversity may be linked to changes in some cardiovascular disease risk factors. Physical activity also demonstrates significant improvements in inflammatory factors by modifying the microbiota profile, increasing the Bacteroidetes phylum and decreasing the Firmicutes/Bacteroidetes ratio. Furthermore, another study on obese children indicates that engaging in physical activity tends to increase certain genera, such as Blautia, Dialister, and Roseburia, which exhibit a microbiota profile similar to that of healthy children.

Conclusion: This systematic review illustrates that physical activity can enhance microbiome populations in humans and make more profits for them. Furthermore, to validate this result, we need some more clinical trials to evaluate this relation specifically.

Keywords: Gut microbiome, Physical activity, Intestinal microbiota composition, Exercise.

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Abstract: A-10-2778-1

Antioxidant and anticancer effects of Astragalus baba-alliar methanolic extract against breast and prostate cancer cells through apoptosis induction

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Background: This study aims to examine the anticancer and antioxidant effects of Astragalus baba-alliar methanolic extract (ABME) on breast (MCF-7) and prostate (LNCaP) cancer cell lines.
Methods: Phytochemical analysis of the ABME was conducted to identify the secondary compounds present in the baba-alliar methanolic extract. An MTT test was performed to assess the effects of ABME on the viability of MCF-7 and LNCaP cell lines. The impact of ABME on DNA synthesis, gene expression, and the protein levels of apoptotic genes was evaluated using Real-time PCR and western blot analysis. The antioxidant capacity of ABME was determined by measuring its free radical scavenging ability through the DPPH assay.
Results: The phytochemical analysis revealed the presence of flavonoids, phenols, saponins, terpenoids, and polysaccharides in ABME. The CC50 values measured for ABME were 242.3 and 285.4 µg/mL for MCF-7 and LNCaP cells, respectively, while the CC50 value for normal THLE-3 cells was 612.7 µg/mL. Treatment of the cell lines with ABME resulted in a dose-dependent decrease in DNA production. Real-time PCR and western blot analyses showed that the gene and protein expression levels of Bax and caspase-3 were significantly increased following treatment of MCF-7 and LNCaP cells, whereas exposure to ABME led to a notable reduction in the expression levels of the gene and protein of Bcl-2.
Conclusion: The findings of this study revealed the potential anticancer and antioxidant effects of ABME. These effects may be attributed to alterations in DNA synthesis and the induction of apoptosis. However, further research is necessary to evaluate the precise mechanisms and efficacy of ABME in animal models.

Keywords: prostate cancer, breast cancer, apoptosis, DNA, western blot

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Abstract: A-10-2160-1

Beneficial potential of betaine in reducing oxidative stress in testicular and ovarian cells

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Background: Hyperglycemia is a condition that can induce oxidative stress (OS) and impact the function of testicular and ovarian cells. Betaine, recognized as an essential osmotic protector and a methyl group donor, safeguards cells under stress conditions. This study aims to assess the effect of betaine on OS in hyperglycemic conditions affecting testicular and ovarian cells.

Methods: Testicular and ovarian cells were cultured under four different conditions: normal glucose with and without betaine (5 mM for 24 hours) and hyperglycemic conditions (48 hours) with and without betaine (5 mM for 24 hours). Cell viability, lipid peroxidation, and methylene glyoxal (MGO) levels were measured across all conditions.

Results: In cells exposed to hyperglycemic conditions, we observed a decrease in viability alongside an increase in MDA, a marker of lipid peroxidation, and MGO. These alterations were more pronounced in testicular cells than in ovarian cells. Treatment with betaine enhanced cell viability and reduced MDA and MGO levels. Ovarian cells exhibited a more favorable response to betaine compared to testicular cells.

Conclusion: Hyperglycemia can lead to OS, cell death, and fertility-related complications. Based on the results, betaine may exert a protective effect on cells by mitigating hyperglycemia-associated OS, suggesting its potential utility in treating infertility.

Keywords: Hyperglycemia ،betaine ،infertility ،oxidative stress ،lipid peroxidation

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2260-1

Development and Evaluation of Anticancer Effects of Resveratrol-Loaded Nanoparticles for Prostate Cancer Therapy

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Background: Nanoparticles for Prostate Cancer Therapy This study explores the potential of Resveratrol-loaded nanoparticles (Res-PCF-NPs) in combating prostate cancer. Resveratrol, found in grapes, boasts anti-inflammatory, antioxidant, and anticancer properties. Yet, its efficacy is hampered by instability and poor bioavailability
Methods: To tackle this, Res-PCF-NPs were crafted using PLGA and modified with chitosan-folate. Characterization techniques like DLS, FTIR, ξ–potential, and FESEM were employed. Biological assays, including resazurin and real-time PCR, gauged cytotoxicity and apoptotic effects on PC-3 cells.
Results: Encouragingly, Res-PCF-NPs showed significant anticancer potential via oxidative stress induction. This suggests promise for Resveratrol-loaded nanoparticles as a viable therapeutic avenue for prostate cancer treatment.
Conclusion: Resveratrol-loaded nanoparticles as a viable therapeutic avenue for prostate cancer treatment.

Keywords: Prostate cancer · Resveratrol · Nanoparticles · PLGA · Chitosan · Folic acid

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2555-1

Investigating the antioxidant and anti-inflammatory effects of the hydroalcoholic extract of Azolla pinnata on gentamicin-induced nephrotoxicity in rats

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Background: This study investigates the therapeutic effects of hydroalcoholic extract from Azolla pinnata on gentamicin-induced nephrotoxicity in rats, emphasizing its antioxidant properties that may protect against acute renal failure, a condition associated with high prevalence and mortality rates.

Methods: Forty male Wistar rats were divided into five groups: a control group, a sham group receiving normal saline, and three treatment groups. Group 3 received gentamicin (100 mg/kg/day) for 7 days, while Groups 4 and 5 received gentamicin (100 mg/kg) and Azolla pinnata extract (10 and 20 mg/kg), respectively. After treatment, blood and tissue samples were analyzed for creatinine, blood urea nitrogen, catalase enzymes, glutathione peroxidase, malondialdehyde, FRAP, and tumor necrosis factor.

Results: The study found that blood urea nitrogen levels were significantly elevated in the gentamicin group compared to controls, with a 20 mg dose of Azolla extract effectively reducing these levels. Gentamicin also raised creatinine levels in the gentamicin group, but both 10 mg and 20 mg doses of Azolla significantly decreased these levels, although they remained higher than controls. No significant differences were noted in GPX enzyme activity across groups, while catalase activity was notably different in the gentamicin group but normalized with Azolla treatment. TNF levels showed no significant differences among groups. The gentamicin group exhibited increased MDA levels, which were partially reduced by Azolla but still higher than controls. Additionally, gentamicin decreased FRAP levels, which were completely restored by Azolla treatment. Histological analysis confirmed gentamicin-induced cell damage, which Azolla extract mitigated in a dose-dependent manner.

Conclusion: Azolla extract can play an effective role in improving biochemical changes, and oxidative and histopathological stress markers caused by gentamicin in rats. Most likely, the protective effects of Azolla extract against gentamicin-induced kidney damage are due to its antioxidant and anti-inflammatory activities.

Keywords: Gentamicin, antioxidant effects, anti-inflammatory effects, Azolla pinnata, nephrotoxicity

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Abstract: A-10-2240-1

Evaluation of the effect of Aspirin and SB431542 (selective inhibitor of the TGF-β) in the treatment of colorectal cancer cell line HT29

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Background: Previous studies have shown that Aspirin plays a crucial role in chemoprevention and induces apoptosis in CRC. However, the exact mechanism underlying the effects of Aspirin remains unclear. This study aims to investigate the relationship between Aspirin and its suppressive effect on angiogenesis factors and apoptosis mediators.

Methods: The cytotoxic effects of Aspirin and TGF-β were measured using the MTT assay, along with the RNA expression of TGF-β, PDGF-BB, P53, P21, Bax, and Bcl2. The activity of caspases 3 and 9 was assessed using an ELISA kit. Flow cytometry was employed to measure apoptosis. Both Aspirin and TGF-β inhibitors inhibit cell growth, but TGF-β counteracts the cell viability effects of Aspirin.

Results: The results indicate that treatment with Aspirin significantly reduces PDGF-BB and TGF-β gene expression. The reduction of PDGF-BB expression by Aspirin was enhanced by subsequent treatment with a selective TGF-β inhibitor. Additionally, the results on apoptosis demonstrate that Aspirin and TGF-β inhibitors increase apoptosis, while TGF-β blocks the ability of Aspirin to induce apoptosis. The combination of Aspirin and the TGF-β inhibitor improved apoptosis by elevating the expression of pro-apoptotic factors such as P53, P21, and Bax, while concurrently decreasing Bcl2 gene expression.

Conclusion: Aspirin induces apoptosis in HT29 cells and reduces angiogenesis by suppressing TGF-β.

Keywords: Colorectal cancer, TGF-β, Aspirin, PDGF-BB

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2616-1

AI-Driven Covalent Drug Design Strategies Targeting Main Protease (Mpro) Against SARS-CoV-2: Structural Insights and Molecular Mechanisms

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Background: The rapid emergence of new SARS-CoV-2 variants continues to challenge the effectiveness of vaccines, highlighting the necessity for small-molecule antivirals. The viral main protease (Mpro) has become a crucial target due to its essential role in the viral life cycle and its conservation among coronaviruses. This review emphasizes recent advancements in AI-driven drug design strategies aimed at Mpro.
Methods: A systematic review was performed using databases such as PubMed, Scopus, and Web of Science. Keywords included "COVID-19," "Mpro inhibitors," "AI-driven drug design," and "covalent inhibitors." The search was restricted to studies published between 2020 and 2023. Articles were included if they concentrated on AI methods in covalent drug design for Mpro. Exclusion criteria involved studies lacking detailed AI methodologies or experimental validation.
Results: From an initial search of 120 articles, 75 were excluded due to irrelevance or insufficient methodological details, leaving 45 for thorough analysis. Key findings underscore the effectiveness of covalent inhibitors such as Nirmatrelvir and MG-101, with AI-driven approaches significantly enhancing binding affinity predictions.
Conclusion: The incorporation of AI in drug discovery has transformed the quest for Mpro inhibitors. These advancements could pave the way for new therapeutic strategies against COVID-19, aiding in mitigating the impact of emerging variants.

Keywords: AI drug design, Covalent drug design, Mpro inhibitor, SARS-CoV-2

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Abstract: A-10-2937-1

Inflammatory Cytokines Imbalance and Sleep Quality in Chronic Insomnia Disorder: A Case-Control Study

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Background: There is evidence suggesting that inflammation may play a significant role in the pathogenesis of chronic insomnia disorder; however, the underlying mechanisms remain unclear. This study aims to evaluate the relationship between serum levels of pro-inflammatory cytokines IL-1α, IL-2, IL-6, ICAM-1, and anti-inflammatory cytokines IL-1ra and IL-10, and parameters of sleep quality in individuals with chronic insomnia disorder (CID).
Methods: Blood samples were collected from 24 individuals diagnosed with CID (18 females, mean age 41.7 years, range 19-65) based on the Pittsburgh Sleep Quality Index (PSQI) and full-night video-polysomnography (V-PSG), along with 24 healthy individuals (16 females, mean age 42.3 years, range 19-65) based on PSQI. The serum levels of IL-1α, IL-2, IL-6, ICAM-1, IL-1ra, and IL-10 were assessed using enzyme-linked immunosorbent assay (ELISA).
Results: The serum concentrations of pro-inflammatory mediators, including IL-1α, IL-2, IL-6, and ICAM-1, were significantly higher in individuals with CID compared to controls. Additionally, significant decreases in IL-10 and IL-1ra were noted in the CID group compared to the control group. A significant negative correlation was observed between decreased serum concentration of IL-1ra and the severity of insomnia in the CID group. Furthermore, increased serum levels of IL-6 were correlated with reduced total sleep time and sleep efficiency in the CID group.
Conclusion: The present study suggests that the imbalance of pro-inflammatory and anti-inflammatory factors concentration and over-inflammation may play an important role in the pathogenesis of CID.

Keywords: Chronic insomnia, Interleukin-1α, Interleukin-6, Interleukin-1ra, Interleukin-10

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Abstract: A-10-2253-1

A combination of p-coumaric acid and metformin enhances the cytotoxicity of carboplatin and epirubicin in the gastric cancer cell line AGS

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Background: Gastric cancer is a lethal disease with low survival rates. Chemotherapeutic drugs used for treating gastric cancer are costly and cause various side effects. Here, treatments with natural compounds, established therapeutic agents, or a combination of both may present an intriguing alternative. p-Coumaric acid and metformin (Met) are two such promising anticancer agents. They may also address the issue of drug resistance.
Methods: Consequently, the present study examined the cytotoxicity-enhancing effects of the combination of pCA and Met in the human gastric cell line AGS. The cytotoxicity of carboplatin and epirubicin was evaluated in single treatments and in combination with 0.2 mM pCA and 0.8 mM Met.
Results: The MTT assay results indicated that carboplatin and epirubicin exhibited dose-dependent cytotoxic effects on AGS cells after 48-hour treatments. Compared to single treatments, the combination treatments demonstrated significantly higher cytotoxicity. pCA and Met enhanced the cytotoxicity of carboplatin and epirubicin at concentrations considerably lower than their IC50 values.
Conclusion: Therefore, pCA and Met could serve as potential candidates for further investigations into combating drug resistance in gastric cancer and may introduce new strategies to address drug resistance in gastric cancer models.

Keywords: p-Coumaric Acid, Metformin, Carboplatin, Epirubicin, Gastric Cancer

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Abstract: A-10-3069-1

The Effects of Morin hydrate as a bioflavonoid on Diabetes Mellitus: a Systematic Review

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Background: One of the most common metabolic disorders in the world, diabetes mellitus is linked to several serious clinical side effects, such as diabetic retinopathy, nephropathy, and cardiomyopathy. Treatment options for this important disease that are currently available, such as insulin therapy or oral hypoglycemic medications have drawbacks and cost society money. Therefore, there is a pressing need for less toxic, naturally occurring antidiabetic medicines that are also reasonably priced. Numerous studies offer fresh and encouraging perspectives on morin, a bioflavonoid that is widely distributed in plants belonging to the Moraceae family. For these reasons, our objective is to systematically review the impacts of Morin hydrate on diabetes.

Methods: In the present study, Medline (PubMed), ScienceDirect, Scopus, and Google Scholar databases were examined for the English language articles until July 2024 using "Morin", "Morin hydrate", "diabetes", and "diabetes mellitus" keywords. The inclusion criteria were in-vivo and in-vitro investigations.

Results: After assessing and reviewing, 56 documents were found. After excluding papers from the study that had no direct connection to the title or goal of the research, 38 relevant articles remained. Our findings showed that Morin hydrate affects diabetes via several pathways. First, this natural product decreased inflammation by reducing NF-KB expression. Second, it exerts antioxidant effects via increased expression of NRF2. Third, morin improves insulin resistance by elevating AMPK expression and reducing PTPB1 expression. Furthermore, the safety and effectiveness of morin hydrate as a plant for human consumption have been confirmed by clinical studies.

Conclusion: The study's findings suggest that morin has potential as a dietary flavonol for the treatment and control of diabetes mellitus. Supplementing with morin seems to reduce the chance of the progression of diabetes. Nonetheless, thorough preclinical research and clinical trials are necessary.

Keywords: Morin hydrate, Diabetes, Natural product

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Abstract: A-10-2332-1

Investigation the effects of Rutin and N-acetyl cysteine on PON1 Enzyme in cyclosporine A-induced kidney and liver injury; An in-silico, in-vitro, and in-vivo study

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Background: Paraxonase1 (PON1) is a potent antioxidant enzyme in serum that protects against the oxidation of LDL. This study investigated the effects of N-acetylcysteine (NAC) and Rutin, two natural antioxidants, on the preservation of PON1 enzyme activity in liver and kidney injuries induced by Cyclosporine A (CsA) through experimental and molecular dynamic simulation studies.
Methods: Forty-eight male rats were divided into six groups. Liver and kidney injuries were induced by CsA, followed by treatment with NAC and Rutin separately, as well as in combination, compared to the untreated control group. Serum HDL levels were measured using an autoanalyzer, and the H&E staining method was employed to assess liver and kidney injury. PON1 enzyme activity was evaluated based on its arylesterase property. Docking and molecular dynamic simulation studies were conducted using Autodock V.4.2 and Gromacs 2022 software.
Results: CsA induced kidney and liver injuries and decreased PON1 enzyme arylesterase activity; however, this activity increased in the groups treated with CsA+Rutin and CsA+NAC. The simulation results indicated that all three compounds can independently bind to the active site pocket of PON1 and moderate its activity.
Conclusion: Although serum PON1 arylesterase activity decreases in CsA-induced kidney and liver injury, the combination of NAC or Rutin can have synergistic effects in further enhancing PON1 arylesterase enzyme activity when CsA is administered.

Keywords: PON1, Rutin, N-Acetylcysteine, Cyclosporine A

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Abstract: A-10-2278-1

Reducing effect of insulin resistance on alpha-synuclein gene expression in skeletal muscle

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Background: Alpha-synuclein (SNCA) as the presynaptic protein is expressed in different tissues and prevents insulin resistance (IR) by increasing adipocyte and muscle glucose uptake. However, the effect of insulin metabolism on SNCA expression has scarcely been elucidated. In the present study, we assessed the probable effect of insulin resistance on SNCA expression in muscle C2C12 cells and skeletal muscle tissues of type 2 diabetic mice.
Methods: Sixteen male C57BL/6 mice were divided into two experimental groups: control and type 2 diabetic mice with IR (induced by high-fat diet + low-dose streptozotocin). The animals of the study involved the measurements of fasting blood glucose, oral-glucose-tolerance-test, as well as fasting plasma insulin. Moreover, insulin-resistant and insulin-sensitive muscle C2C12 cells were prepared. The insulin resistance was confirmed by the glucose uptake assay. Comparative quantitative real-time PCR was used to assess the SNCA expression.
Results: The obtained results have shown a significant ~ 27% decrease in SNCA expression level in muscle tissue of diabetic mice ($P = 0.022$). Moreover, there was a significant change in SNCA expression in insulin-resistant C2C12 cells ($P < 0.001$).
Conclusion: Type 2 diabetes due to insulin resistance can decrease SNCA gene expression in muscles. In addition to the role of SNCA in cell susceptibility to insulin and glucose uptake, the SNCA expression can also be affected by insulin metabolism.

Keywords: Alpha-synuclein, insulin resistance, C2C12 cells, type 2 diabetes,

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Abstract: A-10-2278-2

Evaluation of microRNA-29a expression and Dipeptidyl-peptidase 4 level in ulcerative colitis patients

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Background: Ulcerative colitis (UC) is a recurrent inflammatory bowel disease (IBD) that increases at an alarming rate around the world. MiRNAs, play an essential role in regulating numerous biological processes. The microRNA-29 (miRNA-29) family has been implicated in the pathogenesis of UC. In recent years, the alteration of Dipeptidyl-peptidase 4 (DPP4) levels in IBD patients has been noticed. DPP4 is an enzyme that plays a role in metabolic, and immune cell functions. In the present study, we evaluated the relationship between miRNA-29a expression in intestinal tissue and serum DPP4 levels in UC patients and healthy subjects.
Methods: Blood samples and colonic punch biopsy were obtained from 35 UC patients, and 29 healthy subjects. Serum levels of DPP-4 were evaluated by ELISA technique. expression levels of miRNA-29 were assessed by qRT-PCR. Also, biochemical parameters and demographic information were collected based on patient tests and questionnaires.
Results: The results of this study showed significant increases of miRNA-29a in the intestinal tissue of UC patients compared to the control. In addition, overexpression of miRNA-29a was accompanied by a decrease in serum levels of DPP4, but there is no significant difference between moderate and severe conditions. Furthermore, levels of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and platelet were higher in UC patients relative to those without UC.
Conclusion: These findings supported the role of the miRNA-29a-DPP4 axis in the pathogenesis of UC and provided the imputes for the further evaluation of the miRNA-29a and DPP4 both a biomarkers of disease activity.

Keywords: Inflammatory Bowel Diseases, Ulcerative colitis, Dipeptidyl-peptidase 4, miRNA-29a, Inflammation

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Abstract: A-10-2182-1

Identifying the Structure of lysozyme after it interacts with catechin: A spectroscopic and analytical examination of the binding process

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Background: Hydroxylated polyphenols, or flavonoids, are found in large quantities in fruits, vegetables, grains, nuts, seeds, herbs, and stems. Plants include a class of polyphenolic compounds called catechins. They are widely used as nutraceuticals to enhance human health in pharmaceutical formulations. Of all the proteins, hen egg-white lysozyme has the finest characterization. It is used in food additives and medications due to its antibacterial and immunological functions It also serves as a model protein for research. This study examines the lysozyme enzyme's reaction to (+)-catechin hydrate, a green tea polyphenol.

Methods: Ultraviolet-visible (UV-Vis), intrinsic fluorescence, thermal stability, and kinetic methods were used to examine the impact on the lysozyme's structure and activity of catechin hydrate.

Results: The primary quenching mechanism in this interaction was determined to be static quenching, and it appeared that the lysozyme intake was reduced at 280 nm. The kinetic analysis's findings showed that the activity had decreased. Three different temperatures were used to calculate the number of binding sites, an apparent binding constant Ka, and the thermodynamic properties. According to thermodynamic data, hydrogen and van der Waals forces cause catechin hydrate to spontaneously interact with lysozyme. Using UV-Vis spectroscopy at various concentrations (0–0.00375), a thermal stability investigation was conducted. The stability of the lysozyme enzyme diminishes with increasing catechin concentrations.

Conclusion: This study presented a rigorous and insightful examination of the binding mechanisms governing the interaction between Lysozyme and one of the widely used antioxidants, Catechin. The study's implications are profound, serving as a critical substance for future cosmetic industry research aimed, and human health

Keywords: Keywords: Catechin, lysozyme, intrinsic fluorescence, Ultraviolet-visible (UV-Vis)

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Abstract: A-10-2372-1

Investigating the interplay between insulin resistance and dyslipidemia: towards development of a novel risk assessment index for cardiovascular diseases

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Background: Cardiovascular disease (CVD) continues to be a leading cause of mortality globally. In this context, a significant interplay exists between type 2 diabetes mellitus (T2DM) and dyslipidemia, as both establish mutual risk factors for CVDs, exacerbating each other's detrimental effects. Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and impaired insulin secretion. Additionally, dyslipidemia, defined as abnormal lipid levels in the blood, is a common comorbidity among individuals with T2DM. These lipid abnormalities further increase the risk of CVDs in patients with T2DM. Conversely, dyslipidemia has been recognized as a key contributor to the development and progression of insulin resistance.

Methods: The publications included in this study were sourced from PubMed, Science Direct, and Google Scholar until May 2024. The keywords used were cardiovascular disease, insulin resistance, diabetic dyslipidemia, and diabetes lipids.

Results: This database search yielded 28 papers; however, after reviewing the abstracts and titles, 17 were excluded. Eleven articles were selected for their comprehensive insights into the interplay between T2DM and dyslipidemia, which are crucial for developing effective preventive and management strategies for CVDs. Furthermore, to address the limitations of existing risk assessment indices such as TyG and AIP, we propose the development of a novel index that integrates multiple biomarkers, including the LDL to HDL ratio, BMI, and glucose levels, to more accurately predict and alert individuals to their risk of developing CVD.

Conclusion: This review paper aims to holistically investigate the effects of T2DM on dyslipidemia, referred to as diabetic dyslipidemia, and reciprocally explore the influence of dyslipidemia and lipoproteins on the development and progression of T2DM, coined as Diabetes Lipids. Additionally, we aim to evaluate the combined impact of T2DM and dyslipidemia, along with their common risk factors, on the development and progression of CVDs.

Keywords: Cardiovascular disease, Insulin resistance, Diabetic dyslipidemia, Diabetes lipids

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2788-1

Determine The Protective Effect of Aqueous Extracts of Jujube, Barberry, Descurainia Sophia, and Livergol from Non-alcoholic Fatty Liver Disease in an Animal Model

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Background: Non-alcoholic fatty liver disease (NAFLD) is recognized as one of the most common liver diseases, posing a threat to millions of lives annually. The present study aimed to investigate the preventive effects of aqueous extracts of Barberry, Jujube, Descurainia Sophia, and livergol on NAFLD in an animal model.
Methods: Forty-five male Wistar rats (with an average age of 8-10 weeks) were randomly assigned to 9 groups (n=5). Non-alcoholic fatty liver disease (NAFLD) was induced using a high-fat diet (HFD) consisting of 45% fat, 35% carbohydrates, and 20% protein. The study groups were daily treated with extracts of barberry, Jujube, Descurainia sophia, Livergol, and combinations thereof. At the end of the study (eighth week), sample collection was performed under deep anesthesia using ketamine and xylazine.
Results: The results obtained in this study demonstrated a significant increase in serum levels of TG, TC, LDL, liver function enzymes (ALT, AST, and ALP), and MDA in the NAFLD group compared to the healthy group. Meanwhile, in the treatment groups with barberry, Jujube, and Livergol, the serum levels of lipid profile (TG, TC, LDL, HDL), liver function enzymes (AST, ALT, ALP), and oxidative stress markers (MDA, TAC, Thiol group) were modulated compared to the NAFLD group and approached healthy control levels to some extent.
Conclusion: The results of our study indicate that treatment with herbal extracts of barberry, Jujube, and their combination leads to an improvement in NAFLD conditions. We observed that the serum levels of lipid profile, liver enzymes, and oxidative stress in the treatment groups improved compared to the NAFLD group. These findings suggest the potential efficacy of these herbal treatments in managing NAFLD conditions. However, our recommendation is to conduct further research to confirm and better understand these findings, as well as to elucidate the relevant signaling pathways.

Keywords: Non-alcoholic fatty liver disease (NAFLD), Barberry, Jujube, Livergol, Descurainia sophia, lipid profile, liver enzymes, oxidative stress.

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Abstract: A-10-2456-1

Blueberry Anthocyanins Modulate miR-17-3p Expression and Antioxidant Enzyme Levels in Human Cells

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Background: Blueberry anthocyanins are known for their potent antioxidant properties in vivo, partially restoring the expression of antioxidant enzymes disrupted by oxidative stress. MicroRNA miR-17-3p has been implicated in regulating cellular redox status by influencing the transcription of antioxidant enzyme mRNAs. This study investigated the impact of blueberry anthocyanin-rich extract on miR-17-3p expression levels in human cells to further elucidate its mechanism of action.

Methods: Peripheral blood mononuclear cells (PBMCs) and EVC-304 cells were treated with increasing, subtoxic concentrations of blueberry anthocyanin extract. Quantitative real-time PCR analysis determined miR-17-3p levels in both cellular and exosomal fractions.

Results: The results demonstrated that blueberry anthocyanins significantly reduced miR-17-3p levels in both cell types, while concurrently increasing the levels of mRNA transcripts encoding antioxidant enzymes compared to control groups. Interestingly, miR-17-3p expression in exosomes displayed a more complex response, varying depending on the compound concentration and cell type.

Conclusion: These findings suggest a potential mechanism by which blueberry anthocyanins exert their antioxidant effects. By downregulating miR-17-3p and upregulating the expression of antioxidant enzyme mRNAs, blueberry anthocyanins may enhance the capacity of cells to counteract oxidative stress and protect against its damaging consequences. Further research is warranted to fully delineate the intricate interplay between blueberry anthocyanins, miR-17-3p, and antioxidant enzyme expression in different cellular contexts.

Keywords: Blueberry Anthocyanins, miR-17-3p, Antioxidant Enzyme, Oxidative stress

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2473-1

The effect of bulk bread formulated with Portulaca Oleracea on liver enzymes, anthropometric index, and oxidative stress in patients with type 2 diabetes and hyperlipidemia: a parallel randomized controlled trial

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Background: Diabetes mellitus is a common and increasing problem worldwide. Hypertension, lipid disorders, oxidative stress, and obesity are among the integrated, predisposing factors and complications of diabetes. Bread can be a good carrier for adding nutrients to meet the needs of consumers. Aims: This study aimed to evaluate the effect of bread enriched with Portulaca Oleracea on liver enzymes, anthropometric indices, blood pressure, and some oxidative stress parameters in patients with type 2 diabetes and dyslipidemia.

Methods: This parallel randomized controlled clinical trial was conducted on 104 patients with type 2 diabetes and dyslipidemia. The intervention group received a daily portion of bread enriched with portulaca (10%) and the control group received bread without fortification. At baseline and end of the study for 8 weeks fasting blood samples were collected to quantify plasma serum levels of AST, ALT, GTT, ALP, and total antioxidant capacity, malondialdehyde, it was also measured anthropometric indexes, diastolic and systolic blood pressure. The effectiveness of the intervention method was compared with the difference between the mean before and after the intervention (change score) in the two groups using a t-test.

Results: Comparison of the mean change scores of predictor variables shows that except for malondialdehyde, there is a significant difference between the other variables in the two groups.

Conclusions: Overall consumption of bread enriched with portulaca oleracea leads to improved liver enzyme function, anthropometric indexes, blood pressure, increased TAC in diabetic and hyperlipidemia patients. It can be concluded that portulaca oleracea as a functional plant can be found in bread as a new treatment method in these patients.

Keywords: Bread, Enrichment, Portulaca Oleracea, Liver Enzymes, Anthropometric Indexes, Diabetes Mellitus

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Abstract: A-10-3045-2

Evaluating the effect of diallyl phenol compounds on prostate cancer cells

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Background: Traditional cancer treatments have shown various adverse side effects and have contributed to the development of drug resistance in cancer therapies, complicating future treatment options. Consequently, there is considerable interest in natural bioactive compounds with anticancer properties. Among these compounds, eugenol exhibits promising qualities, including antioxidant, anti-inflammatory, and anticancer effects. This study investigated the impact of three synthetic eugenol-derived compounds (featuring a diallyl phenolic structure) on prostate cancer cells.

Methods: The viability of prostate cancer cells treated with different concentrations of synthetic diallyl phenol derivatives for 72 hours was assessed using the alamarBlue assay. The HDF cell line was utilized to evaluate the toxicity of these compounds on normal cells. Flow cytometry with propidium iodide staining and subG1 analysis were employed to examine the effects of these compounds on cell cycle progression and apoptosis induction.

Results: This study demonstrated that synthetic eugenol-derived compounds inhibited the proliferation of human prostate cancer cells. The respective IC50 values for PC3 cells after exposure to the three synthetic diallyl phenol compounds for 72 hours were 65.66±5.06, 108.17±11.72, and 125.75±0.55 µM, respectively. The flow cytometry assay indicated that these compounds produced a sub G1 peak and induced apoptosis in prostate cancer cells without affecting the distribution of cells during cell cycle phases.

Conclusion: Based on these findings, synthetic diallyl phenol compounds could effectively enhance cytotoxicity in prostate cancer cells in a dose-dependent manner and induce apoptosis.

Keywords: cytotoxicity, Eugenol, diallyl phenol, prostate cancer

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Abstract: A-10-2854-2

The interaction of Fentanyl drug with β-adrenergic receptor effective in memory

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Background: The Beta-2 adrenergic receptor, identified by the 2R4S PDB code, is a cell-surface receptor that currently attracts significant attention in patients with memory disorders. Medications targeting these receptors can be either agonistic or antagonistic. For instance, the neurotransmitter noradrenaline interacts with adrenergic receptors, with β2-adrenergic receptors being particularly crucial for memory. Fentanyl, a potent synthetic opioid drug approved by the Food and Drug Administration for analgesic (pain relief) and anesthetic use, is approximately 100 times more potent than morphine and 50 times more potent than heroin as an analgesic. Increasing plasma concentrations of fentanyl lead to a decline in learning effects.

Methods: Docking is a molecular modeling technique that positions the ligand for the receptor in terms of position, configuration, and orientation. In this study, molecular docking of the receptor-ligand was employed to investigate the interaction between the Beta-2 adrenergic receptor and Fentanyl using AutoDock Vina software.

Results: The best binding energy is the lowest, while for RMSD, it is the highest. Mode No. 6 is the optimal configuration, with a binding energy of -8.3 and an RMSD of 33.711.

Conclusion: In the central nervous system, beta-2 adrenergic receptors are promising targets that can enhance certain types of memory. The results indicate a favorable interaction between the receptors and fentanyl. Opioid receptors are sensitive to pain, and their role in memory has also been explored. The interaction between farnesyl and the receptor confirms its binding and demonstrates that farnesyl impairs learning.

Keywords: Keyboards: β-adrenergic receptor, memory, fentanyl

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Abstract: A-10-2954-1

Tissue stiffness contributes to YAP activation in bladder cancer patients undergoing transurethral resection

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Background: Changes in the cellular microenvironment play a critical role in the development of bladder cancer (BC). Yes-associated protein (YAP), a central mediator of the Hippo pathway, functions as a nuclear sensor of mechanotransduction that can be induced by stiffness of the extracellular matrix (ECM), including stiffness resulting from surgical manipulations. We aimed to clarify the possible association between surgically-related ECM stiffness and YAP activation in BC patients.

Methods: in this study, all grade II BCa (15 recurrent and 15 primary) and 30 adjacent tissues were used for atomic force microscopy (AFM), western blotting, and qRT-PCR to determine Young's modulus values, the activated β1 integrin level, and the gene expression respectively. The immunohistochemistry (IHC) was used to examine the YAP nuclear localization.

Results: We compared 30 bladder cancer tissues with grade II (n = 15 recurrent and n = 15 newly diagnosed) with 30 adjacent healthy tissues. Atomic force microscopy showed that patients with recurrent BC had stiffer ECM than newly diagnosed patients ($P < 0.05$). Gene expression profiles showed that β1 integrin (ITGB1), focal adhesion kinase (FAK), CDC42, and YAP were upregulated in cancerous tissues ($P < 0.05$); additionally, β1 integrin activation was confirmed using a specific antibody. Nuclear localization of YAP was higher in recurrent cancerous tissues compared with newly diagnosed and it was positively associated with higher stiffness ($P < 0.05$).

Conclusion: Finally, our results suggest that post-surgery-induced ECM stiffness can influence integrin–FAK–YAP activity and thereby YAP trafficking to the nucleus where it contributes to BC progression and relapse.

Keywords: bladder cancer, Yes-associated protein (YAP), tissue stiffness, β1 integrin, Hippo pathway, ECM

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Abstract: A-10-2533-1

FKBP51 and Cancer Stem Cells: Coordinating Cancer Progression through the Molecular axis

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Background: FK506-binding protein 51 (FKBP51) plays a crucial role in cancer cell growth and aggressiveness. FKBP51 has been related to several signaling pathways, tumorigenesis, and chemoresistance. CSCs or CSC-like cells take part and are responsible for events in the pathogenesis of cancer, such as aggressive tumor progression, recurrent tumor growth, and spreading metastases. This article explores FKBP51's role in regulating key pathways that support CSC survival and activity and its potential as a therapeutic target.

Methods: This review article includes English articles from PubMed, Science Direct, Google Scholar, and Web of Science up to May 2024. The keywords were "FKBP51, CSCs and Cancer Therapy." After screening 25 relevant titles and abstracts, finally, 12 articles were selected under the inclusion criteria for resulting and focusing on FKBP51's influence on CSCs and its role in cancer resistance.

Results: FKBP51 is involved in regulating key pathways, including Wnt/β-catenin, NF-κB, and PI3K/AKT. FKBP51 leads the Wnt/β-catenin which is essential for surviving and maintaining CSCs in breast cancer. Similarly, FKBP51 participates in the NF-κB pathway and controls the growth and resistance to apoptosis of CSCs in prostate cancer. Increased stiffness activities of the YAP/TAZ pathway, enhancing the ability of CSCs for self-renewal and resistance to therapies. FKBP51 also interacts with the YAP/TAZ pathways, enhancing CSC self-renewal and therapy resistance. Novel therapies targeting these pathways, including combinations with micronutrients and inhibitors, show potential in overcoming CSC-mediated resistance.

Conclusion: FKBP51 modulates cancer progression by influencing CSC activity through various signaling pathways, making it a potential target for cancer therapy. Targeting pathways such as Wnt, Hedgehog, and Notch in combination with conventional therapies could restore CSC sensitivity to treatments, determining new opportunities for effective cancer therapy.

Keywords: FK506-binding protein 51(FKBP51), Cancer cell growth, Cancer stem cells (CSCs), Tumor microenvironment, therapy resistance

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Abstract: A-10-2533-2

FKBP51: Controlling the Tumor Microenvironment for Therapeutic Potential

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Background: The tumor microenvironment (TME) plays a crucial role in promoting or restraining tumor development. TME interacts and cancer cells enhancing the malignant properties of tumors, including proliferation, metastasis, and therapy resistance. Malignant cells shape the TME to tolerate endogenous and external therapies.FK506-binding protein51 (FKBP51) is a key regulator of glucocorticoid resistance and inflammatory TME. It is indicated that the FKBP51 expression might predict the inflammation status of TME and contribute to inflammation regulation in TMEs during tumor progression. This article explores the role of FKBP51 in TME and its therapeutic potential in cancer treatment.

Methods: This review article includes English articles from PubMed, Science Direct, Google Scholar, and Web of Science up to May 2024. The keywords were "FKBP51, Tumor Microenvironment (TME) And Therapeutic Potential." By screening and reading 20 titles and abstracts, finally, 10 articles were selected under the inclusion criteria for resulting and focusing on FKBP51's role in TME and cancer therapy

Results: Studies show that the tumor-specific FKBP51 expression is associated with the inflammatory tumor microenvironment, particularly in UC-CRC patients. The patients with higher FKBP51 expression ratio have shorter survival periods and poorer prognoses. It has been detected the role of FKBP51 in clear cell renal cell carcinoma (ccRCC), the most common subtype of RCC, and found that FKBP51 significantly promotes ccRCC invasion and migration by binding with the TIMP3, connecting TIMP3 with Beclin1 complex and increasing autophagic degradation of TIMP3.

Conclusion: FKBP51 plays a significant role in regulating TME and offers a promising therapeutic target for cancer treatment. By modifying FKBP51 expressions, treatment strategies may improve by changing the tumor environment and immune interactions. Further research is needed to fully understand FKBP51's potential in enhancing cancer therapies.

Keywords: FKBP51, Tumor Microenvironment (TME), Therapeutic Potential

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Abstract: A-10-2545-2

The Relationship between Inflammatory Markers and NIHSS with Right- and Left-Sided Strokes: A Systematic Review

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Background: Stroke, the second leading cause of death globally, is a neurological condition that can be ischemic or hemorrhagic, causing sudden neurological impairments. Cerebrovascular event prognosis is influenced by neurological symptoms and stroke location, with a higher incidence of cerebral infarction in the left hemisphere. Hospital-based research shows that left-sided strokes (LSS) are more common than right-sided strokes (RSS), possibly due to atherosclerotic plaque in the left carotid artery or anatomical factors. Stroke prognosis and treatment are influenced by time from clinical onset, with LSS patients identifying neurologic abnormalities earlier and receiving prompt treatment compared to RSS patients.
Methods: In this review, we collected our data using biomedical research gates; PubMed, Scopus, and the Web of science to identify relevant articles. Studies comparing inflammatory markers, clinical outcomes, and patient characteristics in RSS and LSS patients were included in the search. The criteria for inclusion were satisfied by papers that focused on stroke patients.
Results: 12 papers were selected for inclusion and 46 were excluded from a total of 58 reviewed articles. The findings indicated that, in RSS patients in contrast to LSS patients, positive relationships were found between CRP, total WBC, lymphocytes, and clinical outcome measures such as stroke severity (NIHSS) and length of stay (LOS). A RSS may lessen the immunosuppressive effects of the intact right hemisphere, which has clarified why we noticed increased inflammation in RSS patients. Patients with RSS were older and had a higher incidence of atrial fibrillation and hypertension, although they had lower smoking rates compared to those with LSS. Elevated levels of inflammatory markers have been found in RSS patients.
Conclusion: Inflammatory indicators were only related to NIHSS and LOS in patients with RSS, in comparison to LSS. Therefore, it can be concluded that inflammatory markers can serve as prognostic indicators in diagnosing RSS.

Keywords: Stroke, Right-sided stroke, Left-sided stroke, Inflammation, NIHSS.

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Abstract: A-10-2594-1

The effect of inflammation and angiogenesis, along with the use of corkomin and nanoparticles on p53 gene expression and the activity of proteins involved in apoptosis on breast cancer

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Background: The study of factors affecting the incidence of breast cancer in patients, conventional chemotherapy is inadequate in the treatment of BC types. The need for new treatments or drugs such as curcumin has significant potential in inhibiting diseases associated with apoptosis, autophagy, inhibition of angiogenesis, cell migration, and metastasis is associated with duplication in this area. Challenges, due to the dynamic and degradable nature, low water solubility, rapid metabolism, and rapid systemic elimination, collectively limit its clinical applications.
Methods: The effect of inflammation and angiogenesis combined with the use of curcumin and nanoparticles on p53 gene expression and the activity of proteins involved in apoptosis on breast cancer, from systematic research according to our criteria،from 2024/1/12 to 2024/7/20 several search engines and databases including pubmed.6 keywords: breast cancer, inflammation, curcumin angiogenesis…, Apoptosis is P53gen and a comparative study of articles.
Results: According to the purpose of this study, our selection based on entry and exit criteria are as follows. R narrative review, systematic comparative, interpretation, and case studies in the form of full text/Selection based on the search criteria listed in the international search engine database contains 35 articles from 2013 to 2024 In the first stage, 10 articles were removed due to duplication and waste, the remaining 25 articles were reviewed.
Conclusion: Cancer is an inflammatory disease. Inflammation can alter the expression of oncogenes and tumor suppressor genes to promote neoplastic metamorphosis. A thorough understanding of angiogenesis has led to the identification of new treatments for cancer patients using crocumin in water systems is an insoluble and insoluble analysis of microscopic fluorescence and It also showed that dendrosomes can insert insoluble chromins into the tumor cells of MCF-breast 7, This is the same time-dependent nano cortex dendrosome that increases the inhibitory effect of curcumin on breast tumor cells and has significant potential in inhibiting factors involved in cancer.

Keywords: Breast Cancer ،Inflammation ،Curcumin ،Angiogenesis ،P53 Gene ،Apoptosis

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Abstract: A-10-2952-1

Molecular Investigation on Ovulatory Polycystic Ovary Syndrome and Construction of a Protein Interaction Pathway

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Background: Being a heterogeneous multifactorial disorder, PCOS has remained with a misty etiology whose underlying pathophysiological causes can be further elucidated by proteomic analyses and molecular network analysis to understand the interaction pathways involved in PCOS-associated perturbations.
Methods: We conducted a proteomic study on ovulatory PCOS serum samples using nano-LCMS/MS technique. Then, we analyzed proteomic profiles of significantly dysregulated proteins by projecting them onto the protein interaction mapping and molecular network analysis softwares Gene Mania and STRING. We further investigated the involvement of affected proteins with different PCOS-associated disorders and classified them through the literature along with functional annotation software DAVID and Panther.
Results: A total of 109 differentially expressed proteins were detected, of which 42 proteins were significantly dysregulated in patients. Among them, 35 affected proteins exhibited an association with pathophysiological mechanisms underlying the ovulatory PCOS manifestation, and their correlations with PCOS-concurrent disorders were revealed. We further highlighted significant functional hub molecules within protein interaction networks.
Conclusion: Our results indicated that ovulatory PCOS deals with a wide range of functional molecules' derangements, which trigger aberrant biological responses and molecular interactions leading to the emergence of complications accounted for ovulatory PCOS. Further proteomic studies are required to explain different physiological mechanisms of the functional molecules contributing to the pathogenicity of this heterogeneous syndrome.
Keywords: Ovulatory PCOS, Proteomics, Protein interaction analysis, Molecular network mapping

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Abstract: A-10-2520-2

Promising role of Chitosan and its Derivatives-based Nanoparticles in Gastrointestinal Cancer therapy

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Background: Gastrointestinal cancers represent a substantial health issue, as current treatment options, including surgery, chemotherapy, and radiation therapy, demonstrate notable limitations, such as a high likelihood of recurrence, inadequate drug specificity, and severe side effects. Therefore, innovative therapy strategies and improved tissue-specific targeting are necessary. Nanomedicine is a medical discipline that uses nanoscale carriers to target and deliver medications or diagnostic chemicals to specific regions. Nanomedicine recognizes chitosan nanoparticles as a delivery technology and uses them as polymeric carriers. This research seeks to ascertain the potential function of chitosan and its derivative-based nanoparticles in treating gastrointestinal cancer.

Methods: A systematic review methodology is adopted to undertake a detailed analysis of the effects of chitosan and its derivative-based nanoparticles on gastrointestinal cancer treatment. A literature search was carried out in SID, MagIran, IranMedex, IranDoc, Google Scholar, ScienceDirect, Scopus, PubMed, and Web of Science (ISI). Seven out of 114 articles, published between 2017 and 2023, were analyzed. We meticulously searched the databases, selecting relevant papers based on the following keywords that aligned with the research objectives: chitosan, chitosan derivatives, nanoparticles, drug delivery systems, and gastrointestinal malignancies.

Results: Several clinical studies showed that chitosan derivatives improve the effectiveness, selectivity, biocompatibility, and therapeutic dose reduction of anticancer drugs when added to hydrogel, emulsion, surfactant, and nanoformulations. Chitosan and its derivatives are good at making nanoparticles and have unique surface properties that let them interact specifically with gastrointestinal cancers through both active and passive targeting mechanisms.

Conclusion: According to this comprehensive systematic review, the molecular signaling pathways of chitosan nanoparticles and their derivatives show promise as possible treatments for gastrointestinal cancers.

Keywords: Chitosan, Chitosan derivatives, Nanoparticle, Drug delivery system, Gastrointestinal cancers

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Abstract: A-10-3101-1

Crosstalk between NLRP3 inflammasome and cardiac fibrosis: A systematic review

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Background: Heart disease is considered the most prevalent cause of mortality around the world. The lack of a definitive cure for heart disease has led to an ongoing scientific race to find novel therapeutic replacements. The emergence of ever-advancing cellular and molecular techniques in the clinical aspect has laid the foundation for the establishment of personalized molecular-based therapies. NLRP3 inflammasome, a molecule with an essential role in inflammation, has been suggested as an effective target in the pathogenesis of fibrosis, a common trait observed among heat diseases; in this systematic review, we unveil the role of NLRP3 inflammasome in cardiac fibrosis.
Methods: In this systematic review, the search strategy and study design were conducted following PRISMA guidelines. Pubmed, Proquest, and Google Scholar were searched until 31 August 2024 using relevant syntax. A total of 9005 relevant articles were identified in our first round of research. The initial articles were studied and analyzed in relevance according to guidelines. Consequently, 32 articles were chosen for the current study.
Results: The results of our study found a significant role for NLRP3 inflammasome in the progression of cardiac fibrosis. NLRP3 stimulates fibrosis via regulating IL-1 β, IL-18, caspase-1, and hyper acetylation of Hydroxyl-CoA dehydrogenase α subunit in cardiac tissue.
Conclusion: In conclusion, novel molecular therapies or drugs targeting NLRP3 can demonstrate promising effects in preventing cardiac fibrosis in heart disease.

Keywords: NLRP3 inflammasome, Cardiac fibrosis, Heart diseases, Inflammation

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Abstract: A-10-2474-2

Trace Element Status and Asthma Risk in Iranian Newborns: Insights for Prevention, Treatment, and Monitoring

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Background: Asthma is a chronic inflammatory airway disorder caused by disturbances in immune system components. This condition has seen a worrying rise in recent decades, highlighting the critical need for prevention and treatment, especially for infants. Research points to environmental and nutritional factors, as well as the influence of trace elements, as key contributors to the development and worsening of asthma, particularly in the given geopolitical context.

Methods: This systematic review was conducted from January 2013 to December 2023. Relevant articles were obtained through searches of Scopus, PubMed, Science Direct, and Google Scholar databases using keywords like "Asthma," "Iranian Newborn," and "Trace Element." Duplicate and similar articles from the same source were removed using EndNote software.

Results: The present systematic review evaluated a total of 887 articles, ultimately identifying 41 relevant studies for inclusion. These selected studies underscored the multifaceted associations between trace element status and asthma manifestation among infant cohorts. Iron deficiency increases asthma risk and worsens control. Conversely, iron supplements improve lung function and reduce asthma symptoms. Zinc, as an essential micronutrient, plays a pivotal role in immune function and modulation of airway inflammation. Suboptimal zinc status has been linked to heightened susceptibility to asthma development and increased propensity for disease exacerbations. Furthermore, selenium, a potent antioxidant, can modulate key inflammatory pathways. Inadequate selenium intake has been correlated with more severe asthma symptomatology and diminished lung function outcomes.

Conclusion: Newborns, the future of our nation, require proactive asthma prevention, as it is more cost-effective than managing the condition later. Evaluating and addressing precisely deficiencies in iron, zinc, and selenium is crucial for respiratory health. A systematic approach to maintaining optimal micronutrient status is key for safeguarding the youngest population; which emphasizes the importance of having a suitable program.

Keywords: Asthma, Iranian Newborn, Trace Element

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Abstract: A-10-2951-1

Targeting BCMA and Novel Protein Markers: Using Proteins to Revolutionize the Treatment of Multiple Myeloma

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Background: Multiple myeloma, one of the world's most common blood malignancies, arises from the proliferation of monoclonal plasma cells in the bone marrow. Despite advances in the treatment of multiple myeloma, this malignancy remains incurable due to treatment resistance and relapse, which points out the need for new approaches to diagnosis and treatment. Recent investigations, demonstrate alteration in BCMA (B-cell maturation antigen) expression and other protein markers involved in MM progression, leading to the development of BCMA-targeted CAR-T cell therapy, a promising approach that modifies patient T cells to target specific malignant cells. In this study, we focused on the role of BCMA and other novel protein markers in MM and BCMA-targeted CAR-T cell therapy.

Methods: We conducted a comprehensive review by searching databases such as PubMed, Scopus, and the Web of Science and included studies published from in2015 to 2024 that investigated BCMA and another protein marker in expression in MM and BCMA-targeted CAR-T cell therapy. Studies that didn't address CAR-T cell therapy were excluded.

Results: 15 studies were selected out of 40 studies and 25 studies were excluded. Alteration of BCMA expression in MM, elucidating its role as a driver in disease progression, considering it as a biomarker for therapeutic targets. BCMA and other proteins like SLAMF7 and XBP1 upregulation led to treatment resistance and poor prognosis, whereas targeting BCMA with CAR T-cell therapy led to less relapse and drug resistance, ultimately a better outcome. BCMA-targeted therapy was more effective in patients with exhausted standard treatment. Additionally, treatment efficacy, patient response, and drug resistance are imparted by monitoring changes in protein expression profiles.

Conclusion: Targeting BCMA and other novel protein markers associated with multiple myeloma can provide vital insight for developing new BCMA-based therapy, particularly BCMA-targeted CAR-T cell therapy that shows significant promise in overcoming drug resistance and relapse.

Keywords: Multiple Myeloma, Plasma Cell Malignancy, BCMA, Protein Biomarker, CART-Cell Therapy

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Abstract: A-10-2602-2

T-cell activation platforms: a critical step in T-cell immunotherapy

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Background: T cells are essential in maintaining the body's immunity and fighting pathogens, including cancer cells. The activation and extracellular proliferation of T cells are particularly important for cancer treatment, especially in immunotherapy methods such as CAR. To find an effective way to activate T cells, it is important to investigate different antibodies against CD3 and CD28, which bind to the respective receptors on the cell surface and activate them.

Methods: The PubMed database was systematically searched for trials published in English between 1995 and 2024 with relevant keywords, including “Immunotherapy” + “T cell activation” + “CD3.” Duplicated articles, irrelevant studies, and articles without access to the full text were excluded from the study.

Results: Among 116 studies,33 studies met the inclusion criteria. Conventional methods for activating T cells use soluble CD3 and CD28 antibodies or magnetic beads coated with these antibodies. These standard methods have disadvantages and limitations, including in the case of soluble antibodies, which can be attributed to the short half-life of these antibodies, the possibility of binding to non-target cells, and the increase of cross-reactivity and insufficient or excessive activation. Cells can be mentioned due to the lack of precise control of the location and intensity of activation. Also, using magnetic beads is expensive and requires specialized and time-consuming processes to wash and separate the activated cells from the beads. There is a possibility of contamination, increase of impurity, or loss of cells during this process. Therefore, adopting new approaches like aptamers and fragments of antibodies against CD3 and CD28 is needed to develop an appropriate platform as an impressive and cheap alternative to the above methods.

Conclusion: In summary, ex-vivo T cell activation is indispensable for immunotherapy purposes, including CAR-T cell therapy. The existing methods, in addition to their limitations, are not cost-effective

Keywords: Immunotherapy ،T-cell activation ،CD3 ،CD28

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Abstract: A-10-2665-1

New enzymes profile as diagnostic biomarkers of colorectal cancer

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Background: Colorectal cancer is caused by the uncontrolled growth of epithelial cells in the lining of the colon and rectum of the digestive system. In this systematic review study, two specific enzymes (Fucosyltransferase-4 and galactin-3) that can be useful as chemical biomarkers in disease diagnosis were investigated.
Methods: The present study was conducted as a systematic review by searching for articles using the keywords colorectal cancer, biomarker, fucosyltransferase-4, and galectin-3 in PubMed, ISI Web of Knowledge, Google scholar, and Scopus databases between 2010 and 2023.
Results: Fucosyltransferases are significant enzymes that accelerate the malignant process of cells through fucosylation of cellular compounds. Fucosyltransferase-4 is one of the important enzymes for creating alpha-1 and 3 fucosylation of Lewis antigen on the surface of cancer cells, which is one of the key antigens related to cancer. In colon cancer, Lewis antigen expression is regulated by fucosyltransferase-4 and 3. Inhibition of fucosyltransferase reduces the adhesion of selectins and metastasis, and inhibition of fucosyltransferase enzyme reduces the expression of Lewis antigen in colon cancer cell lines. Intracellular galectin-3 acts as an inhibitor of apoptosis in the cytoplasm and provides the immortality of cancer cells. Galectin-3 can help increase adhesion and metastasis in cancer cells. Referring to the recent clinical studies conducted in this field, there is a significant relationship between the characteristics of the mentioned enzymes and the increase in the levels of these enzymes and colorectal cancer. Regarding this systematic review, 12 articles were found, which included 7 systematic review articles, 2 original research articles, and 3 clinical trial articles, and 8 articles related to the purpose of the article were selected and used.
Conclusion: The measurement of enzymes is considered as a non-invasive method in the detection of colorectal cancer.

Keywords: Colorectal cancer, biomarker, fucosyltransferase-4, galectin-3

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Abstract: A-10-2873-1

Silymarin suppresses the inflammation in the Mouse Model of Allergic Asthma

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Background: Allergic asthma is a chronic inflammatory disease characterized by airway inflammation and hyper-responsiveness. Silymarin is a natural compound recognized for its potential anti-inflammatory properties in many conditions. In this study, we investigated the anti-inflammatory effects of silymarin on the mouse model of allergic asthma.

Methods: Forty-two mice were categorized into six groups (n = 7 per group). The normal control group (negative control) received phosphate-buffered saline (PBS), and in the remaining five groups allergic asthma was induced using ovalbumin (OVA). In the treatment phase, one group of asthmatic mice was treated with PBS (positive control), another group received beclomethasone, and four of them were administered silymarin (25 mg/kg and 50 mg/kg) through both intranasal and intraperitoneal routes. Afterward, the changes in inflammatory cell influx in bronchoalveolar lavage fluid (BALF) and the levels of interferon-γ (IFN-γ) and interleukin-4 (IL-4) in BALF and blood were quantified. Histopathological alterations of leukocytes were examined in the lung tissues of all animals.

Results: The results showed the potential of silymarin in reducing inflammatory cells, including eosinophils and lymphocytes in the BALF. Additionally, the group receiving silymarin treatment via both intranasal and intraperitoneal routes exhibited increased levels of IFN-γ in the blood, surpassing the effects of beclomethasone; however, no significant changes in IL-4 levels were seen. In contrast, intranasal administration of silymarin at a high dose led to increased IL-4 levels in BALF, while the IFN-γ changes were insignificant. The histopathological analysis demonstrated a significant decrease in leukocyte infiltration following silymarin treatment.

Conclusion: Our results demonstrated the potential of silymarin as an anti-inflammatory agent in allergic asthma.

Keywords: Asthma, Inflammation, Silymarin

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Abstract: A-10-2563-2

Effects of lncRNAs on Wnt/β-catenin signaling pathway in colorectal cancer

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Background: LncRNAs are one of the most important influencing factors in the formation or prevention of various cancers, including colorectal cancer. Therefore, we performed a systematic review to investigate the effects of lncRNAs on the Wnt/β-catenin signaling pathway; the main signaling pathway in colorectal cancer biogenesis.
Methods: The Google Scholar and PubMed databases were systematically searched for trials in the English language published between 2015 and 2024 that examined the effects of lncRNAs on the Wnt/β-catenin signaling pathway in colorectal cancer.
Results: In total, 134 related articles were reviewed. After removing irrelevant articles to the subject, 34 articles fulfilled the inclusion criteria. According to the conducted researches, there are a large number of lncRNAs like H19, CRNDE, and HOTAIR are over-expressed in CRC cells and tissues. Another group of lncRNAs like RMST, CTD903, and GAS5 are under-expressed in colorectal cancer cells. All of these effector lncRNAs are listed in the table.
Conclusion: The available evidence supports the role of lncRNA as an inducer, enhancer, or inhibitor genetic factor in Colorectal cancer. Also, the advances in the mechanism of understanding lncRNAs in Wnt/β-catenin signaling might bring novel candidates as biomarkers and therapeutics for CRC.

Keywords: LncRNA, Colorectal Cancer, β-catenin, Target Therapy

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Abstract: A-10-2858-2

A Quantum Mechanical Investigation on OXTELLAR XR

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Background: Oxtellar XR is an extended-release formulation of oxcarbazepine, utilized to manage partial seizures in epilepsy patients. This medication ensures a consistent release of the drug over time, aiding in the maintenance of stable blood levels and a reduction in seizure frequency.
Methods: The study employed quantum mechanics (QM) calculations performed via the density functional theory (DFT) method using GAUSSIAN 09 software. The structure of the Oxtellar XR drug was initially optimized through gradient procedures at both restricted Hartree-Fock (HF) and hybrid density functional B3LYP levels of theory, utilizing the 6-311G basis set. Analysis of the results indicated that the optimized structure achieved in this research was located at the minimum point on the potential energy surface, exhibiting no negative modes.
Results: This study performed calculations for structural parameters such as bond lengths, angles, and dihedrals, along with thermodynamic parameters at the B3LYP/6-311G level of theory, and presented the results. The electronic energy of the molecule was calculated to be -526324.4742 kcal/mole. Furthermore, the Mulliken atomic charge, spin density, and molecular orbital energies were assessed. The highest occupied molecular orbital (HOMO) was determined to be -0.24936 eV, while the lowest unoccupied molecular orbital (LUMO) was -0.07869 eV. The dipole moment in Debye was recorded as X=4.3667, Y=-1.2510, Z=2.2656, with a total of 5.0760.
Conclusion: Optimization of the drug was conducted using the B3LYP/6-311G method. The study concentrated on Oxtellar XR's electronic characteristics, particularly the energy difference between the HOMO and the LUMO. The HOMO-LUMO gap energy was found to be 0.1707 eV. This offers insights into Oxtellar XR's electronic behavior, which may have applications across various fields.

Keywords: OXTELLAR XR, DFT, B3LYP/6-311G, HOMO-LUMO gap

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Abstract: A-10-2259-1

Mefloquine Induces Apoptotic Cell Death in Human Brest Cancer Cells

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Background: The A2B adenosine receptor (A2BAR) is a protein involved in various biological and pathological processes, including cancer. Furthermore, its potential role in breast cancer treatment has been limited by the absence of a crystallographic structure. This study aims to predict and confirm the 3D structure of A2BAR, identify a specific agonist, and investigate its effects on breast cell proliferation.

Methods: The A2BAR structure was modeled using I-TASSER, Phyre2, Swiss Model, and AlphaFold software, and validated with ProSA, PROCHECK, ERRAT, and Galaxy Web tools. A virtual screening of FDA-approved drugs from the Zinc15 database was conducted using AutoDock Vina (version 1.2.3) to identify the selective agonist of A2BAR based on the lowest free energy. Different concentrations of mefloquine (0–5 µM) were administered for 72 h. Cell viability was assessed using the 4, 5-dimethylthiazole-2-yl, 2, 5-diphenyl tetrazolium (MTT) method. Apoptosis was evaluated using annexin V/PI staining flow cytometry. The results were analyzed using GraphPad Prism version 8, with a significance threshold set at $p < 0.05$.

Results: The lowest 50 compounds were selected through structure-based virtual screening following structure prediction and A2BAR validation. The chemical interactions of amino acid residues in the A2BAR binding pocket with the selected compounds were illustrated. Consequently, mefloquine emerged as a candidate for treating breast cancer cell lines, significantly reducing MCF-7 and MDA-MB-231 cell growth at 2.88 and 2.98 µM, respectively, after 48 h. Flow cytometry analysis indicated that mefloquine induced early apoptosis in both cell lines.

Conclusion: This study demonstrated that mefloquine, identified through virtual screening as an A2BAR agonist, has a potential inhibitory effect on breast cancer cell line proliferation through apoptosis induction, particularly in MCF-7 and MDA-MB-231 cell lines.

Keywords: A2B adenosine receptor, homology modeling, virtual screening, mefloquine, breast cancer, MCF-7, MDA-MB-231, apoptosis.

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Abstract: A-10-2259-2

A systematic review of computational approaches and validation strategies on adenosine A2B receptor homology modeling

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Background: The adenosine A2B receptor (A2BAR), a member of the G protein-coupled receptor (GPCR) family, plays a crucial role in various physiological processes, including inflammation, cardiovascular regulation, and immune response. Additionally, the importance of homology modeling is heightened by the absence of a high-resolution experimental structure for A2BAR. This systematic review aims to explore the methodology, accuracy, and applications of homology modeling in elucidating the A2BAR protein.

Methods: A systematic search was conducted using the PubMed, Scopus, and Web of Science databases with the following syntax: ("A2BAR" or "A2B adenosine receptor") and ("Homology Modeling" or "Comparative Modeling") and ("GPCR" or "G Protein-Coupled Receptor"). Articles published in English between 2000 and 2024 were included. Initially, a total of 156 articles were retrieved. After applying elimination criteria, which included research focused solely on other GPCRs, review papers lacking original data, and studies without primary data on A2BAR homology modeling, 82 publications were excluded, leaving 74 articles for further analysis. The inclusion criteria were designed to ensure a focus on original research that directly contributes to A2BAR homology modeling.

Results: An analysis of various modeling approaches revealed A2BAR homology with different templates, sequence alignment methods, and refinement strategies. High-resolution crystal structures of related GPCRs, particularly adenosine receptors, emerged as the most favored models. Ramachandran plots, RMSD, and molecular dynamics simulations were employed to validate the models, although the quality of the models varied. Some models aligned well with experimental results; however, low sequence identity and limited template availability posed challenges.

Conclusion: In the absence of X-ray and MRI structural data, homology modeling serves as a robust method for A2BAR analysis. The accuracy of the models relies on closely related patterns and sophisticated modeling techniques. Future structural biology studies, including cryoelectron microscopy (cryo-EM) and computational algorithms, will enhance homology models and aid in identifying the functional mechanisms of A2BAR signaling and therapeutic targets.

Keywords: A2B adenosine receptor, homology modeling, GPCR, model validation, molecular dynamics.

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Abstract: A-10-2887-1

Serum levels of C1q/TNF-related protein (CTRP) 1 and CTRP-3 are associated with the presence and severity of coronary artery disease

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Background: Recent research indicates that the disruption of adipokines is associated with the development of obesity-related illnesses such as coronary artery disease (CAD). In this study, we examined whether the plasma levels of two adipokines, C1q/TNF-related protein (CTRP) 1 and CTRP-3, are linked to the occurrence and severity of CAD.
Methods: This study included a total of 88 patients who underwent coronary angiography. Among them, there were 39 patients without coronary artery disease (CAD), 31 patients with stable CAD, and 18 patients with unstable CAD. The levels of CTRP-1 and CTRP-3, fasting blood glucose, lipid parameters, hs-CRP, and hematological indices were measured.
Results: The levels of CTRP-1 were significantly elevated in both the unstable (6.28 ± 2.64 ng/ml) and stable (6.12 ± 2.22 ng/ml) groups compared to the control group (4.20 ± 2.08 ng/ml). However, there was no significant difference in CTRP-1 levels between patients with stable and unstable CAD. The levels of CTRP-3 in the serum were markedly higher in both the unstable (18.00 ± 7.68 ng/ml) and stable (14.90 ± 4.73 ng/ml) groups compared to the control group (10.80 ± 2.40 ng/ml). In all participants of the study, there was a positive correlation between serum CTRP-1 levels and the coronary artery score ($r = 0.443$, $p < 0.001$). Furthermore, a notable and favorable correlation was observed between CTRP-3 and the coronary artery score in all participants of the study ($r = 0.330$, $p = 0.002$). Correlation analysis using multiple regression revealed that both CTRP-1 and CTRP-3 were independently associated with the coronary artery score.
Conclusion: Elevated levels of serum CTRP-1 and CTRP-3 were strongly associated with both the occurrence and severity of coronary artery disease (CAD), suggesting that they could serve as reliable indicators for CAD.

Keywords: Coronary artery disease, Adipokines, CTRP1 protein, CTRP1 protein.

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Abstract: A-10-2725-1

An overview of the biochemical properties And the anticancer effect of Ruta plant

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Background: Cancer is a leading cause of death worldwide, including in Iran. Traditional treatments often come with severe side effects, making the search for less harmful alternatives essential. Medicinal plants, recognized for their lower toxicity, are gaining traction in cancer treatment. The Ruta plant, belonging to the Rutaceae family, is one such example. Native to Iran and esteemed in traditional medicine across Europe, China, India, and Iran, Ruta also occupies a significant role in contemporary medical research. Key species include Ruta graveolens (Sodab), Ruta chalepensis, and Ruta montana. These plants are rich in compounds such as alkaloids, flavonoids, essential oils, coumarins, and phenols, which exhibit antioxidant, anti-inflammatory, cytotoxic, immune-boosting, and anticancer properties.

Methods: This review consolidates research on the anticancer effects of Ruta species. Information was gathered from PubMed and Google Scholar, encompassing studies from 2010 to 2024 using keywords like "Ruta graveolens," "Rutaceae," "Ruta montana," "Ruta chalepensis," "cancer," and "anticancer compounds." Studies were chosen based on relevance, concentrating on the anticancer effects of Ruta species, published in peer-reviewed journals, and available in English. Non-cancer-related studies, non-peer-reviewed articles, and those not available in full text were excluded.

Results: Out of 90 articles, 61 were included based on the criteria, while 29 were excluded. Studies indicate that Ruta plants could enhance conventional chemotherapy. For instance, furanoacridones from Ruta graveolens exhibit antiproliferative and pro-apoptotic effects on breast cancer cells. Methanolic extracts of Ruta graveolens target colon, breast, and prostate cancers by inducing DNA damage and inhibiting cell proliferation. Ruta chalepensis essential oil promotes apoptosis and cytotoxicity in breast cancer cells.

Conclusion: This review underscores the potential of Ruta plants as complementary treatments in cancer therapy. The diverse compounds and therapeutic properties of these plants present promising avenues for further research and application in treating various cancers.

Keywords: Ruta graveolens, Rutaceae, Ruta Montana, Ruta chalepensis, cancer, metastasis, apoptosis, anticancer compounds

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Abstract: A-10-2724-1

The Effects of the Hydro-Alcoholic Extract of Black Walnut Kernels (Juglans nigra) on the Antioxidant Serum Level of Adult Male Rats Suffering from Methimazole-induced Hypothyroidism

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Background: Hypothyroidism is a significant endocrine gland disorder that results in the dysfunction of thyroid hormones. Based on the antioxidant properties of black walnut kernels (Juglans nigra), we investigated the effect of this extract on thyroid tissue and the antioxidant levels in serum (SOD, CAT) of hypothyroid rats undergoing methimazole treatment.

Methods: In this experimental study, methimazole was administered via gavage at a single dose of 25 mg per kg of body weight to create an induced hypothyroidism model. A total of 40 adult male rats were utilized, divided into five groups of eight. At the conclusion of the study, the animals were anesthetized with ether, and blood samples were collected from their hearts to estimate serum levels of catalase enzymes (CAT) and superoxide dismutase (SOD) as antioxidant factors. Additionally, a thyroid hormone assay kit was used to measure T4, T3, and TSH levels through the ELISA method. SPSS-21 software was employed for data analysis, with results evaluated using one-way ANOVA and Turkey's multiple comparisons test.

Results: Consequently, treatment with black walnut kernel extract in hypothyroid rats resulted in decreased SOD and T4 levels in the methimazole-treated stress group compared to the control group ($p>0.05$), while T3 and CAT levels were significantly lower in the methimazole-treated stress group compared to the control group ($p<0.05$). Furthermore, TSH levels were elevated in the methimazole-treated stress group compared to the control group ($p>0.05$).

Conclusion: Black walnut extract in hypothyroid rats reduced serum levels of T3 and T4 hormones while increasing TSH hormone levels. Thus, this extract demonstrates its antioxidant function by enhancing thyroid activity.

Keywords: Black Walnut ،Hypothyroidism ،Catalase ،Superoxide Dismutase.

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2274-3

A mini-systematic review of microRNA effects on autophagy in polycystic ovary syndrome

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Background: Polycystic ovary syndrome (PCOS) can lead to infertility and metabolic dysfunction in women of reproductive age. MicroRNAs (miRNAs) play a role in regulating autophagy. Autophagy, a process involved in the degradation and recycling of cellular components, may be dysregulated. This mini-systematic review summarizes the current understanding of the effects of miRNAs on autophagy in PCOS.

Methods: Searches of the PubMed, Scopus, and Google Scholar databases were conducted to identify relevant literature. Search terms included "microRNA," "autophagy," and "PCOS." Only studies published in peer-reviewed journals within the last decade were included.

Results: Based on the search method, 29 articles were identified, but only 14 articles were reviewed in the final step. Members of the miR-29 family downregulate autophagy-related genes in the ovarian tissues of women with PCOS, potentially impairing autophagy. Additionally, miR-144 enhances autophagy by inhibiting mTOR signaling, which is hyperactive in PCOS, contributing to metabolic dysregulation. Furthermore, miR-221/222 miRNAs regulate cellular proliferation and autophagy by targeting key signaling pathways, and they may be involved in PCOS-associated ovarian hyperandrogenism. Moreover, autophagy markers play a significant role in PCOS. A compensatory response in the ovaries was observed in certain studies, indicated by an increase in autophagy markers (LC3-II, Beclin-1). In PCOS, specific miRNA dysregulation suggests that autophagy may be upregulated or dysfunctional, depending on the miRNA. In general, novel therapeutic targets for PCOS may be discovered by examining the interaction between miRNAs and autophagy.

Conclusion: Evidence suggests that miRNAs significantly influence autophagy regulation in PCOS, contributing to the disorder's pathophysiology. The interplay between dysregulated miRNAs and altered autophagy may lead to reproductive and metabolic dysfunction in PCOS. Further research is essential to elucidate these relationships and their potential as therapeutic targets. Conclusion: MicroRNAs modulate autophagy in PCOS, with their dysregulation playing a role in the disorder's etiology. Future studies should concentrate on the mechanistic pathways involved and investigate the potential for miRNA-based interventions to restore normal autophagic functions.

Keywords: MicroRNA, Autophagy, PCOS

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Abstract: A-10-2628-1

The Critical Role of Tumor Suppressor miRNAs in Cancer Treatment

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Background: Cancer is one of the leading causes of death worldwide. MiRNAs are a class of non-coding RNAs that inhibit mRNA translation by binding to untranslated regions and play a crucial role in various types of cancer. Tumor Suppressor (TS) miRNAs typically combat different cancers by suppressing the activity of oncogenes or mRNAs that regulate cell proliferation and the cell cycle.

Methods: The findings were gathered from scientific databases, including Google Scholar and PubMed, using keywords such as "Cancer," "miRNA," "Treatment," "Non-coding RNA," and "Tumor Suppressor" for the period from 2020 to 2024. The selection was based on quality assessment, relevance to the research, peer-reviewed sources, and statistical power.

Results: A total of 709 papers were examined, with 681 excluded and 28 included in the final evaluation. MiR-135a/b overexpression decreases HER2 and HER3 protein levels in the SKBR3 cell line, reducing cell migration and permeability. While elevated levels of miR-31 expression increase the proliferation of tumor cells, it keeps the tumor localized and reduces metastasis to other tissues. MiR-34a enhances acetylation by targeting SIRT1 and decreasing p53 expression, leading to cell cycle regulation and apoptosis. Increased levels of miR-203 expression boost cell cycle inhibitors such as p21 and p27, reduce cell cycle activators like cyclin D2 and CDK6, and elevate bcl2, a critical apoptosis-related protein effective in tumor suppression. In other cancer cells, MDM2 oncoprotein overexpression can impair p53 function, while miR-339-5p enhances p53 activity by targeting the 3'-UTR of MDM2 mRNA and reducing its expression.

Conclusion: In conclusion, TS miRNAs offer promising strategies for cancer treatment by targeting oncogenes and regulating cell proliferation. Advanced delivery methods enhance TS miRNAs' effectiveness, highlighting their potential in controlling tumor growth and metastasis.

Keywords: Cancer, miRNA, Treatment, Non-coding RNA, Tumor Suppressor

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Abstract: A-10-2613-2

Network pharmacology analysis to evaluate the mechanism of Prosopis farcta root extract on diabetes mellitus

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Background: Diabetes mellitus is a chronic disorder characterized by insulin resistance in insulin target tissues, beta cell dysfunction, or both. Prosopis farcta root extract (PFRE) is a novel natural compound that has been used in Iranian traditional medicine for the treatment of diabetes and other diseases. PFRE has been shown in our previous studies to have a beneficial regulatory effect on glucose metabolism in a skeletal muscle cell line. However, its bioactive compounds, potential targets, and underlying mechanisms remain largely unclear.

Methods: In this study, a network pharmacology approach was applied to explore the potential mechanism of PFRE phytochemicals against diabetes mellitus. The active chemical components of PFRE were selected from the literature. Next, Swiss Target Prediction was carried out to identify target genes of different compounds. The Gene Card databases were utilized to identify genes related to diabetes mellitus. Subsequently, the gene-ligand network was constructed using Cytoscape software. The signaling pathways of the ingredients were characterized using the Kyoto Encyclopedia of Genes and Genomes (KEGG) database.

Results: By applying suitable filters in the Gene Card database, approximately 5,400 proteins related to diabetes mellitus were selected. Two hundred five proteins related to each of the 14 important ligands in PFRE were identified using the Swiss Target Prediction database. One hundred seventy-three proteins were found to be shared between diabetes mellitus and ligand target proteins. The organization of these proteins with ligands was built using Cytoscape software. The results indicate that four proteins, such as POMC, AGRP, BDNF, and LEF, have higher scores in the network between diabetes mellitus and PFRE. The signaling pathways of these selected proteins were characterized using the KEGG database.

Conclusion: this study revealed the PFRE core ingredients and potential targets, and related signaling pathways, promising effectiveness of Prosopis farcta root extract against some aspects of diabetes mellitus, recommending further experimental studies to validate this in silico analysis.

Keywords: Prosopis Farcta, Diabetes mellitus, Bioinformatics

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Abstract: A-10-2762-1

Exosome odyssey to original

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Background: Exosomes are bilayer lipid membrane nanoparticles that can contain DNA, mRNA, proteins, and more. They are considered safe due to their endogenous production. Currently, the use of exosomes in cell-free procedures is recognized in regenerative medicine. In dental regenerative medicine, the application of exosomes has garnered increased attention.

Methods: This review summarizes studies published through 2022 to describe exosomes, their characteristics, isolation methods, and administration techniques. Additionally, some therapeutic aspects of these extracellular vesicles, particularly in dental degenerative lesions, are discussed. Keywords such as exosome, extracellular vesicle, regenerative medicine, dentin, and tooth were searched in PubMed-NCBI, Google Scholar, Scopus, and Web of Knowledge online resources. Articles that utilized exosomes for drug delivery or diagnostic purposes were excluded based on the study goals.

Results: Ultimately, 130 articles were included from approximately 179 articles related to exosomes and regeneration (especially dental regeneration). Previous studies indicate that exosome therapy is beneficial for dental regeneration. Exosomes can promote dental pulp regeneration and periodontal regeneration; for instance, they can stimulate angiogenesis and neurogenesis, as well as facilitate the regeneration of periodontal ligaments and alveolar bone, along with various other therapeutic benefits

Conclusion: it seems that exosomes have a special place in future medicine. Although the approved beneficial therapeutic aspects of exosomes, it seems there is a long way to use these dreams in human treatments, but probably someday it will become true.

Keywords: Dentin, Exosomes, Extracellular vesicle, Regenerative medicine, Tooth

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Abstract: A-10-3019-1

The Association of Serum Levels of Phenobarbital and Phenytoin with Serotonin and Dopamine in Children with Epilepsy

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Background: One of the most significant complications of epilepsy is depression, which results in a reduced quality of life, particularly in children. The mechanism behind depression is not fully understood; however, alterations in the levels of neurotransmitters such as serotonin and dopamine may contribute. This study aimed to assess the serum levels of serotonin and dopamine and their relationship with the blood levels of the anticonvulsant drugs phenobarbital and phenytoin in children with epilepsy.

Methods: In this study, 45 children with epilepsy (epilepsy group) and 45 age- and gender-matched healthy children (control group) were included. Serum levels of phenobarbital and phenytoin in the epilepsy group were evaluated using high-performance liquid chromatography (HPLC). The serum levels of serotonin and dopamine neurotransmitters in both groups were measured by ELISA.

Results: The serum levels of serotonin and dopamine in the epilepsy group were significantly lower than those in the control group ($p < 0.001$). A significant positive correlation was found between the serum levels of serotonin and dopamine ($p < 0.001$, $r = 0.782$). No significant correlation was observed between the serum levels of anti-seizure drugs and the measured neurotransmitters.

Conclusion: The serum levels of serotonin and dopamine in children with epilepsy are lower than in healthy children, independent of the serum levels of anticonvulsant drugs. Changes in serum levels of serotonin and dopamine may be considered a cause and mechanism for depression in patients with epilepsy. However, further studies in this area appear necessary.

Keywords: Dopamine, epilepsy, phenobarbital, phenytoin, serotonin

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Abstract: A-10-2453-1

Investigating the effect of metabolic therapy based on caprylate and caprate fats on FOXP3+ T cell/CD8+ T cell ratio and β-catenin gene expression in rectal cancer patients referred to Imam Khomeini Hospital

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Background: The ketogenic diet (high in fat, low in carbohydrates, and limited in protein) has recently emerged as an effective therapeutic approach used alongside conventional treatments like radiotherapy for cancer patients. Research indicates that Tregs are expressed at higher levels in cancerous tissues compared to normal tissues. Tregs typically suppress the immune response within the tumor microenvironment, and their increase can therefore pose challenges. Studies have shown that patients with a high CD8/Foxp3 ratio demonstrate a better response to chemoradiotherapy. A study on mice with rectal cancer treated with a ketogenic diet revealed that following the implementation of this diet, Treg cells decreased. This study assessed the percentage of Treg cells and the FOXP3+T cell/CD8+T cell ratio, with the results analyzed statistically.

Methods: In this study, 5 patients (intervention group) and 5 patients (control group) were selected. They followed a diet containing caprylate and caprate for 6 weeks alongside radiotherapy. To ensure an increase in ketone bodies, patients' blood ketone and glucose levels were measured and recorded daily. Blood samples from each patient were collected twice (before and after the 6-week treatment period), and PBMCs were isolated. In each instance, the percentage of Treg and CD8+ cells were measured using flow cytometry, and statistical analyses were conducted using FlowJo software.

Results: The findings revealed a reduction in the percentage of Treg cells and the FOXP3+T cell/CD8+T cell ratio in the intervention group compared to the control group, as well as a decrease after the treatment period compared to before in the patients of the intervention group.

Conclusion: Based on these findings, it is hypothesized that a fat-containing diet may contribute to a decrease in Treg cells, potentially influencing tumor growth reduction and improvement in rectal cancer.

Keywords: Advanced non-metastatic rectal cancer, caprylate and caprate, Wnt/β-catenin signaling pathway, T lymphocyte cells

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Abstract: A-10-2736-1

The Impact of Nutritional Supplementation on Insulin Resistance and Ovarian Functions in Women with PCOS

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Background: Polycystic ovary syndrome (PCOS) is a multifaceted disorder that impacts women's endocrine and reproductive systems, with a prevalence exceeding 20%. Diagnosis is based on irregular menstrual cycles, hyperandrogenism, and polycystic ovarian morphology, following the Rotterdam criteria. At least two criteria must be fulfilled after ruling out other causes. While not included in the Rotterdam criteria, insulin resistance is crucial due to its link with heightened risks of metabolic syndrome, type 2 diabetes, and cardiovascular diseases.
Methods: We conducted a search on PubMed, ScienceDirect, Google Scholar, and Scopus using keywords such as PCOS, reproductive system, ovulation, insulin resistance, nutritional supplementation, and nutritional biochemistry for relevant publications from 2018 to 2024. Initially, from seven papers, we selected three that examined the effects of specific dietary supplements on ovarian function and insulin resistance in PCOS. Four papers discussing the impact of nutrition and diet were excluded as they did not specifically address the biochemical pathways pertinent to our investigation.
Results: From seven screened papers, four were excluded, leaving three for analysis. These findings suggest that co-supplementing with CoQ10 and vitamin E is more effective than supplementing with either vitamin E or CoQ10 alone in reducing insulin resistance. The antiapoptotic and antioxidant properties of CoQ10, which may also enhance ovarian function, help to clarify this. Furthermore, Myo-Inositol, whether used alone or in combination with D-Chiro-Inositol, improves the metabolic profile of women with PCOS, as evidenced by reductions in sex hormone-binding globulin (SHBG) levels, HOMA index, insulin and androgen levels, and hyperandrogenism.
Conclusion: Administering Myo-Inositol and D-Chiro-Inositol appears to be the best approach for promoting ovulation and balancing hormonal levels, including progesterone, LH, SHBG, estradiol, and testosterone, in women with PCOS. Additionally, combining vitamin E and CoQ10 shows potential in enhancing insulin sensitivity and addressing the endocrine and metabolic challenges associated with PCOS.

Keywords: PCOS, ovulation, insulin resistance, nutritional supplementation, nutritional biochemistry

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Abstract: A-10-2773-1

Mechanism of action of cytokines IL-12, TNF, IL-10 in fungal infections

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Background: Any tissue injury, such as that caused by microbial colonization and proliferation, triggers an inflammatory response. The innate immune response of macrophages involves the release of cytokines (inflammatory mediators), including interleukin-10, interleukin-12, and tumor necrosis factor-alpha, during fungal infections. Cytokines are a large group of secreted proteins with diverse functions and structures that regulate and coordinate the activities of both innate and adaptive immune cells. All immune system cells secrete at least a few cytokines and express specific signaling receptors for various cytokines.

Methods: For this review, we conducted a comprehensive search of published literature from 2000 to 2024 using the following databases: Google Scholar, SID, Scopus, PubMed, and Web of Science, among others. The keywords used in the search included cytokines, fungal infection, TNF, IL-12, IL-10, innate immunity, and adaptive immunity. To evaluate the retrieved articles, we initially assessed their relevance to the research topic based on their titles and abstracts. Subsequently, the remaining articles were evaluated for their content, focusing on the significance of the host immune system's response to fungi.

Results: The findings indicated that in pathogenic species such as Cryptococcus neoformans, the production of cytokines like TNF and IL-12 by macrophages is inhibited, while IL-10 production is stimulated, ultimately leading to the inhibition of macrophage activation. Thus, cellular immunity serves as the primary mechanism of acquired immunity against fungal infections. Consequently, 14 articles and 4 books were identified as relevant and included in the review, confirming the mechanisms involved in combating fungal infections.

Conclusion: Overall, it can be stated that anti-inflammatory cytokines in fungal infections include interleukins 10 and 12, as well as tumor necrosis factor. Furthermore, the findings of this study can enhance clinical practice by providing a deeper understanding of host immunity and genetic susceptibility to mycosis.

Keywords: Cytokine ،fungal infection ،TNF ،IL-12 ،IL-10 ،innate immunity ،adaptive immunity

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Abstract: A-10-2773-2

Coffee and Fermentation

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Background: Coffee is one of the most widely consumed non-alcoholic beverages globally. The Coffea arabica and Coffea canephora species are the most commonly utilized due to their cultural and sensory attributes. Various chemical compounds are employed to certify the coffee species and the types of processing used, as the beans' aggregate value is directly linked to their quality. Generally, coffee fermentation occurs through dry and wet processes. The microbiota involved in fermentation includes several species of bacteria, yeasts, and filamentous fungi.

Methods: For the collection, articles containing any of the terms Coffee beans, fermentation process, microbiota, bacteria, yeasts, filamentous fungi, flavor, and enzymes were gathered. These were searched and analyzed using Science Direct, Pubmed, NCBI, and the Islamic World Citation Database (ISC) from 2000 to 2023. The selected articles focus on the use of edibles and their effects on the body's immune system, disease treatment, and coffee production methods in tropical regions.

Results: Coffee beans contain practical and beneficial compounds that can significantly contribute to human health and nutrition. Sensory syrups derived from sweet processing are superior. In total, there were 29 articles and 3 books: 1 article focused on the side effects and precautions of coffee consumption, 3 articles examined the taste and quality of coffee, while the remaining articles and books discussed various fermentation methods and the enzymes involved in processing.

Conclusion: Coffee is cultivated in nearly 60 tropical and subtropical countries. Experts believe that fermentation positively influences flavor, but recently, they have acknowledged that mechanically washed coffee (without fermentation) can match the quality of the fermented product. Additionally, these products are primarily utilized in the food, non-food, and medical industries.

Keywords: Coffee beans ،fermentation process ،microbiota ،bacteria ،yeasts،filamentous fungi. ،flavour and enzyme

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Abstract: A-10-2901-1

Bioaccumulation and oxidative stress induced by organometallic and ionic tin compounds in Zebrafish (Danio rerio) Larva

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Background: Tin, a heavy metal, in trace amounts, is thought to play various roles in the biological development of fish, including its involvement in cell structure, enzyme activities, and the metabolism of proteins and carbohydrates. Two endocrine-disrupting chemicals, Tributyltin (TBT) and Triphenyltin (TPT), are commonly found in aquatic environments.
Methods: This study investigates the bioaccumulation of these compounds and their effects on oxidative stress enzymes. Zebrafish embryos were utilized to evaluate the acute toxicity of TBT, TPT, and SnCl2. Toxicity tests were performed on fertilized eggs using varying concentrations of TBT, TPT, and SnCl2 (0, 1, 5, 10, 15, and 20 ng/L). The LC50, 96hr values for TBT, TPT, and SnCl2 in zebrafish embryos were 4.2, 8.7, and 12.56 ng/L, respectively.
Results: The study revealed a reduction in the catalase enzyme compared to the other two enzymes. Furthermore, tributyl tin exhibited greater bioaccumulation than the other compounds. The mortality rate was elevated in embryos exposed to trace levels of TBT, indicating that embryos are more vulnerable to TBT toxicity.
Conclusion: TBT is highly toxic and can have a lethal impact on zebrafish embryos, potentially leading to species extinction and a decline in aquatic biodiversity.

Keywords: Lethal concentration. Oxidative stress. Tributyltin. Triphenyltin . Zebrafish.

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Abstract: A-10-2796-1

Intertwined pathologies; the shared mechanisms and signaling pathways of depression and migraine: A systematic review

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Background: Migraine and depression are highly prevalent, often co-occurring conditions with a complex, bidirectional relationship rooted in shared pathophysiological mechanisms. This systematic review aims to explore and classify the common mechanisms linking these two disorders.

Methods: The PubMed, MEDLINE, Web of Science Core Collection, Science Direct, and Google Scholar electronic databases were systematically searched from their inception to August 18, 2024. Our search yielded 5,935 articles, of which 352 abstracts were deemed relevant. After thorough screening, 33 eligible studies were selected for inclusion in this review. We focused on in-vitro, in-vivo (animal), and human observational studies, excluding narrative reviews, systematic reviews, meta-analyses, case reports, clinical trials, books, and chapters. The search terms used included "Migraine," "Depression," "Signal transduction," "Serotonergic signal transduction," "Neuropeptides," "Neuroinflammation," "Cortical spreading depression," "Immune system defect," "Kynurenine," and their corresponding MeSH terms, combined with appropriate Boolean operators, such as "AND" and "OR."

Results: While depression is often linked to reduced central serotonin levels, migraine sufferers frequently show low platelet serotonin and elevated urinary 5-HIAA. Neuropeptides, such as BDNF and CGRP, play a role in these conditions by affecting neuronal excitability and promoting neuroinflammation. Furthermore, dysregulation of glutamatergic and GABAergic neurotransmission contributes to both migraine and depression. The immune system, particularly microglial activation and the release of proinflammatory cytokines like TNF-α and IL-6, is crucial to the pathogenesis of these disorders. Additionally, dysfunction in the kynurenine pathway leads to increased levels of neurotoxic metabolites and altered tryptophan metabolism, linking these conditions. Conclusion: This study emphasizes the complex neurobiological mechanisms shared by depression and migraine. The central role of neuroinflammation, microglial activation, and kynurenine pathway dysregulation highlights the significant molecular connection between these two disorders. Immune responses were also identified as a critical mechanism that underscores the interconnected nature of migraine and depression, facilitating the development of therapeutic strategies.

Keywords: Migraine disorders, Depression, Depressive disorder, Signal transduction

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Abstract: A-10-2340-1

Contributing Role of MicroRNAs in Epithelial-Mesenchymal Transition in Colorectal Cancer

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Background: Colorectal cancer (CRC) ranks as the third most common cancer and the second leading cause of cancer-related deaths worldwide. Therefore, the early and effective identification of targets and personalized therapies is essential for CRC. Research has demonstrated that microRNAs (miRNAs) play a crucial role in various stages of CRC, including Epithelial-Mesenchymal Transition (EMT), which significantly influences CRC metastasis.

Methods: Data were gathered from a variety of reputable scientific sources, including ScienceDirect, PubMed, and Google Scholar, utilizing keywords such as "Metastasis," "Colorectal Cancer," "miRNA," "Treatment," and "Epithelial-Mesenchymal Transition" from 2009 to 2024, focusing on relevance to research, peer-reviewed sources, and quality assessment.

Results: A total of 158 articles were identified, with 140 excluded and 18 included in the final analysis. Several miRNAs were found to regulate the invasion and migration of CRC cells by targeting EMT transcription factors, including ZEB, N-cadherin, SNAI1, E-cadherin, and TWIST1. MiR-141-3p alters the levels of SNAI1, E-cadherin, N-cadherin, and vimentin by targeting EGFR. MiR-6716-5p reduces E-cadherin expression through NAT10 inhibition, which enhances CRC metastasis. MiR-204 leads to the downregulation of N-cadherin and the upregulation of E-cadherin via CXCL8 inhibition. The downregulation of miR-191 inhibits CRC migration by causing inverse changes in N-cadherin and E-cadherin levels. ZEB1 can induce EMT and is targeted by miR-186-5p, miR-708, and miR-873-5p, contributing miRNAs to CRC metastasis. The reduction of ZEB1 by miR-708 through AKT/mTOR signaling inhibits CRC migration. Negative regulation of ZEB1 by miR-873-5p results in suppressed migration. A decrease in miR-186-5p expression stimulates CRC migration by targeting ZEB1. MiR-200 downregulation during the early stages of stromal invasion directly targets ZEB1 and ZEB2.

Conclusion: In conclusion, miRNAs systematically influence CRC metastasis by regulating various related signaling pathways, including PI3K/AKT/mTOR. Many miRNAs act as tumor suppressors or oncogenes; thus, understanding their roles in tumorigenesis is crucial for CRC therapy.

Keywords: Colorectal Cancer, Metastasis, miRNA, Treatment, Epithelial-Mesenchymal Transition

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Abstract: A-10-2340-2

PRMT5 inhibitor therapy in RB1 deficiency-related breast cancer

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Background: Breast cancer (BC) is the most prevalent cancer among women and the second most common cancer globally. Retinoblastoma transcriptional corepressor 1 (RB1) deficiency contributes to BC, making them an ideal candidate for therapeutic intervention, including protein arginine methyltransferase 5 (PRMT5) inhibitor. RB1, a tumor repressor, regulates various cellular functions in cancer biology, particularly BC.

Methods: Results were collected from scientific sources, including PubMed and ScienceDirect, by applying keywords such as "Breast Cancer," "RB1",” gene therapy," and " PRMT5" from 2010 to 2024 based on peer-reviewed sources and relevance to research.

Results: A total of 669 articles were found, with 654 excluded and 15 selected for the final analysis. CDK4/6 inhibitors (CDK4/6i) clinical application in combination with antiestrogen treatment has significantly improved overall survival rates in ER+ metastatic BC patients. Despite these major improvements, most tumors eventually expand resistance to this therapeutic, restricting the available treatment options. Since RB1 deficiency induces resistance to CDK4/6i in patients with ER+ metastatic BC, a genome-wide CRISPR screen revealed PRMT5 as a susceptibility in ER+/RB1-deficient BC cells. Mechanistically, PRMT5 reticence impedes the G1-to-S cell cycle stage shift separately of RB1 by causing hyperphosphorylation of Pol II Ser2 and intron retention in several genes related to DNA synthesis, resulting in growth inhibition in RB1-deficient cells. Furthermore, PRMT5 inhibitor pemrametostat combination with the targeted ER degrader fulvestrant synergistically impedes ER+/RB1-deficient tumor growth and patient-derived xenografts (PDX) in vivo. These results indicate that dual inhibition of PRMT5 and ER could be a promising therapeutic approach to conquer CDK4/6i resistance in ER+/RB-deficient BC.

Conclusion: In conclusion, these results enhance the understanding of RB1's role in BC and accommodate an opportunity for targeted treatment. By clarifying the molecular mechanisms underlying RB1 deficiency-related susceptibilities, these findings set the stage for developing medical strategies to improve clinical outcomes in RB1-deficient cancers.

Keywords: Breast Cancer, RB1, Gene Therapy, PRMT5

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Abstract: A-10-2340-3

Recent approaches in Antisense oligonucleotides therapy in cancers

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Background: Cancer remains one of the leading causes of death worldwide. While conventional therapies have enhanced survival rates, challenges such as cancer recurrence and metastasis persist. A promising cancer treatment, Oligonucleotide therapeutics, includes siRNA, aptamers, and antisense oligonucleotides (ASOs).
Methods: Data were collected from reputable scientific sources, including Google Scholar, PubMed, and Scopus, using keywords such as "Cancer," "ASOs," "Oligonucleotide Therapy," and "antisense oligonucleotides" from 2000 to 2024, focusing on sample size, statistical power, relevance to research, and peer-reviewed sources.
Results: A total of 225 articles were reviewed, with 204 excluded and 21 included in the final analysis. ASOs bind to target RNAs. Unmodified ASOs with phosphodiester backbones face challenges in cell entry and are vulnerable to nuclease degradation, resulting in a short blood-circulating half-life. To enhance cellular uptake and nuclease resistance, ASOs are chemically modified with phosphorothioate (PS) backbones, methyl-phosphonate, and N3'-P5' phosphoramidate backbones. There are three generations of ASOs: a) PS modifications improve nuclease resistance but decrease target affinity and may be toxic at high concentrations; b) 2'-O-methyl and 2'-O-methoxyethyl modifications boost binding affinity and nuclease resistance but can also increase toxicity; c) Locked nucleic acids (LNAs), constrained methoxyethyl (cMOE), and constrained ethyl (cEt) oligonucleotides provide enhanced stability and reduced toxicity. First-generation ASOs with sulfur backbone modifications maintain RNAse H cleavage activity. Clinically approved examples include the first-generation PS ASO Fomivirsen and second-generation ASOs Mipomersen and Inotersen. ASOs can also be modified with cholesterol, peptides, sugars, and aptamers.
Conclusion: In summary, ASOs in oncology target genes that are abnormally expressed or spliced, thereby driving tumorigenesis and cancer advancement. Although there is insufficient data, modern developments in ASOs therapies have illustrated enhanced effectiveness and safety profiles, facilitating targeted delivery to particular cell types, which offers a promising new method for cancer treatment.

Keywords: Cancer, ASOs, Oligonucleotides Therapy, antisense oligonucleotides

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Abstract: A-10-2763-1

Evaluation of the serum levels of Micronutrient(Ca, Mg, Zn) and Vitamin D with manifestation of post partum depression in pregnant women in jahrom

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Background: Postpartum depression (PPD) is among the most prevalent mood disorders that arise after childbirth. This study aimed to explore the relationship between serum levels of micronutrients—calcium (Ca), magnesium (Mg), zinc (Zn), and vitamin D—and the incidence of PPD, as well as its association with various demographic factors.
Methods: This cross-sectional descriptive study involved 100 women diagnosed with PPD who were referred to post-natal care centers in Jahrom. Data were collected using the Edinburgh questionnaire and blood tests for Ca, Mg, Zn, and vitamin D. The collected data were analyzed with SPSS software and the chi-square test.
Results: The mean age of the participants was 29.73 ± 5.65 years. Among them, 29% were Nullipara and 69% were Multipara. Additionally, 11% had a history of depression, and 2% were smokers. Vitamin D levels showed that 19% were normal, while 81% exhibited vitamin D deficiency. Abnormal Mg levels were found in 9% of the subjects, 23% had impaired blood Ca levels, and 74% had Zn deficiency. The prevalence of severe vitamin D deficiency was higher in those with severe depression (20.47) compared to those without. Only 19% had adequate vitamin D levels, and the prevalence of vitamin D deficiency in postpartum depression was 81%.
Conclusion: While the levels of micronutrients do not correlate with the severity of postpartum depression, the prevalence of these micronutrient deficiencies is notably high among individuals with postpartum depression.

Keywords: Postpartum depression, Vitamin D, Calcium, Zine, Magnesium

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Abstract: A-10-2628-2

The significant role of miRNAs in the regulation of autophagy in Breast Cancer

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Background: MicroRNAs are non-coding RNA molecules that regulate gene expression post-transcriptionally in various malignancies, particularly Breast Cancer (BC). Autophagy serves as a vital mechanism for inhibiting cancer progression. Recently, specific miRNAs have been identified as key regulators of autophagy-related gene expression in BC.

Methods: Data were collected from databases, including PubMed and ScienceDirect, using keywords such as "miRNA," "Breast Cancer," "Autophagy," and "Non-coding RNA" from 2010 to 2024, based on statistical power and relevance to the research.

Results: A total of 144 papers were reviewed, with 108 excluded and 36 included in the final analysis. MiR-20a expression, which is upregulated in BC, particularly in triple-negative BC (TNBC) cells, correlates inversely with the activity of the autophagy/lysosome pathway. MiR-20a inhibits basal autophagic flux, autophagic nutrient starvation, and lysosomal-associated proteolysis activity. Additionally, MiR-20a elevates intracellular ROS levels and the DNA damage response by regulating several autophagy-related proteins, including ATG16L1, BECN1, and SQSTM1, which are inversely associated with miR-20a expression. TNBCs exhibit downregulation of the ATG16L1, BECN1, and SQSTM1 genes. MiR-20a and miR-20b regulate RB1CC1/FIP200 expression, with both miRNAs capable of reducing RB1CC1/FIP200 transcript and protein levels. The upregulation of these miRNAs has diminished basal autophagy and rapamycin-induced autophagy. MiR-25 is the primary target of isoliquiritigenin (ISL) in promoting autophagic flux. Furthermore, silencing miR-25 induces cell autophagy by increasing ULK1 expression levels, a key initiator of autophagy. Reason for the changes Upregulation of miR-25 inhibits ISL-induced autophagy. ISL enhances the responsiveness of cancer cells to chemotherapy by increasing LC3-II, decreasing ABCG2 levels, downregulating miR-25, and activating ULK1. MiR-26b, miR-200c, and miR-129-5p inhibit autophagy by modulating the expression of DRAM1, HMGB1, and UBQLN1, respectively. MiR-200c and miR-129-5p can diminish irradiation-induced autophagy and reduce the radioresistance of BC cells through this mechanism.

Conclusion: MiRNAs have been shown to play a role in breast carcinogenesis via autophagy. Given their involvement in nearly all critical aspects of breast carcinogenesis, targeting their expression therapeutically could influence the progression of the disease.

Keywords: Breast Cancer, miRNA, Autophagy, Non-coding RNA

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Abstract: A-10-2799-1

In vitro and in vivo evaluation of co-delivery of Levofloxacin and Ciprofloxacin-loaded cubosomes as a novel strategy for ocular drug delivery

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Background: Bacterial-induced ocular infections can result in permanent vision loss and diminished quality of life. Furthermore, antibiotic eye drops are often less effective and exhibit relatively poor bioavailability. Additionally, injections into the eye may cause concurrent eye damage and heighten the risk of secondary infections. With its potential to enhance residence and release times on the cornea, as well as facilitate penetration through corneal tissues into various parts of the eye, nanomedicine presents a promising, efficient, and noninvasive platform for treating ocular infections. This research aimed to evaluate the efficacy of co-delivering Levofloxacin (LFX) and Ciprofloxacin (CIP) encapsulated in cubosomes for ocular drug delivery.

Methods: Cubosomes were prepared using glycerol monooleate (GMO) and poloxamer 407 (F127) through high-pressure homogenization and probe sonication. The formulated product was assessed for particle size (PS), zeta potential (ZP), physicochemical properties, phase behavior, encapsulation efficiency (EE%), in vitro release kinetics, cytotoxicity, and pharmacokinetic and pharmacodynamic characteristics.

Results: The prepared formulation exhibited a PS of 174.5 ± 3.2 nm and a ZP of -22.8 ± 1.6 mV, while in vitro release demonstrated efficacy for both drugs. The drug encapsulation efficiency was 86.3 ± 2.4% for LFX and 78.1 ± 2.1% for CIP, respectively. In vivo investigations revealed that the topical administration of LFX/CIP cubosomes led to significantly higher concentrations of LFX/CIP compared to commercial eye drops in both aqueous and vitreous humor. Furthermore, LFX and CIP displayed a synergistic effect, and their incorporation into cubosomes resulted in enhanced drug penetration into ocular tissues and improved bioavailability. Additionally, LFX/CIP cubosomes with sustained drug release reduced the frequency of dose administration compared to commercially available drops.

Conclusion: Overall, LFX/CIP cubosomes appear to be a promising delivery system for addressing ocular infections.

Keywords: Drug Delivery, Cubosomes, Ocular infections, levofloxacin, ciprofloxacin

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Abstract: A-10-2628-3

Using contemporary methods of Nano-therapy by delivering siRNAs in cancer treatment

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Background: Lipid nanoparticles are effective and suitable for drug delivery due to their biocompatibility and targeting capabilities, including siRNA delivery as a promising avenue for nanoparticle-based anticancer therapies. SiRNAs, known for their notably short half-life, hold potential for gene silencing but face challenges in effectively targeting genes for cancer treatment. This review examines nano-therapy delivery methods for siRNA applications in cancer.

Methods: Data was collected from databases such as PubMed and Google Scholar using keywords like "Cancer," "Nano therapy," "siRNAs delivery," and "Lipid nanoparticles" for the period from 2012 to 2024, focusing on statistical power and relevance to the research.

Results: A total of 389 papers were reviewed, with 366 excluded and 23 included in the final assessment. Cationic lipids, cholesterol, and siRNA effectively target PLK1 and kinesin spindle protein (KSP) by inducing cytotoxicity in tumor cells. One application of PEGylated lipid nanoparticles is targeting the androgen receptor to regulate its transcription and potential therapy in breast cancer. Ionizable lipids can be ionized at low pH, facilitating siRNA delivery to the target gene and silencing through lysosomal escape. A series of nanoparticles based on HDL have also been developed, incorporating a p53 suppressor gene plasmid and a chemotherapy drug, which can serve as a robust gene silencer. Treatments utilizing these nanoparticles have also been observed in addressing KRAS mutant cancer. The efficacy of cationic nanoparticles in treating CML is dependent on BCR-ABL gene expression. Injecting cationic LPNs formulated with lipidoids into xenograft mice has provided hope for treating non-Hodgkin cancers.

Conclusion: In conclusion, lipid nanoparticles show significant promise in siRNA delivery for cancer treatment. Despite challenges such as siRNA's short half-life, advancements in nanoparticle technology, including cationic and PEGylated lipids, offer hope for effective gene silencing, particularly in cancers with specific genetic mutations.

Keywords: Cancer, Nano therapy, siRNAs delivery, Lipid nanoparticles

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Abstract: A-10-2337-1

The effect of running intervention, soy protein supplement and time-restricted eatingon the regulation of autophagy pathway activity and genes involved in Alzheimer's disease

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Background: Autophagy is a crucial process that maintains cell growth, development, and metabolic balance. This study aims to investigate the effects of running, soy protein supplementation, and time-restricted eating (TRE) on the regulation of autophagy pathway activity and genes associated with Alzheimer's disease.
Methods: Thirty-five non-alcoholic fatty liver model rats, aged 18-20 weeks, with an average body weight of 344.80 ± 32.980, were selected as research subjects. After one week of acclimatization to the laboratory environment, the fatty model animals were randomly divided into 7 groups of 5: a control group (5 rats) and an experimental group (30 rats) divided into subgroups: 1. TRE, 2. Supplementation, 3. Supplementation and TRE, 4. Supplement group with 3 days of training, 5. Supplement group with 5 days of training, 6. Supplement and TRE group with 3 days of training, and 7. Supplement and TRE group with 5 days of training. A one-way analysis of variance was conducted at a significance level of less than 0.05, followed by the Scheffé post hoc test among the research groups.
Results: The results of the Scheffé follow-up test indicated a significant increase and decrease in the expression of atf6 (f=70.44, p=0.001) and sidt2 (f=138.34, p=0.001) genes, respectively, in the supplementation and TRE groups. Additionally, significant changes were observed in the supplementation group with 3 days of training, the supplementation group with 5 days of training, and the supplementation and TRE group with both 3 and 5 days of training compared to the control group.
Conclusion: Defective autophagy may contribute to the pathogenesis of NAFLD by impairing fatty acid oxidation. This study demonstrates that Sidt2 and Atf6 play significant roles in liver lipid metabolism by regulating liver lipid autophagy.

Keywords: Alzheimer's disease,Autophagy,Exercise, Time-restricted eating

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Abstract: A-10-2813-1

Liquid biopsy and diagnosis of breast cancer, analysis of circulating tumor cells (CTCs): Systematic Review

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Background: Circulating tumor cells (CTCs) released by a primary tumor can facilitate metastasis. Liquid biopsy is a minimally invasive precision medicine technique that evaluates breast cancer in real time by analyzing gene alterations in ctDNA and CTCs. This report reviews the current information regarding the clinical role of CTCs and proposes some future application ideas.
Methods: This study utilized a collection of English-language articles from Scopus, PubMed, and Web of Science, accessible from 2000 to 2024, focusing on breast cancers, circulating tumor cells, liquid biopsy, and therapy interventions. Articles that met the exclusion criteria were selected, reviewed, and included in the study.
Results: Further research has shown that the presence of CTCs is strongly linked to cancer metastasis and has emerged as a significant predictor of metastatic breast cancer in recent years. A recent study associated higher CTC counts with a markedly worse prognosis. In the multivariate analysis, CTC status was the best overall survival (OS) predictor (HR 2.71, $p < 0.0001$). CTC detection holds substantial prognostic value in metastatic breast cancer (MBC) patients, as most exhibit a decrease in CTC counts during systemic treatment. Moreover, regardless of the method, another study found that the OS of patients without detectable CTCs was significantly higher than that of patients with one or more CTCs ($p < 0.001$). Consequently, based on the study's findings and multivariate analysis, CTC count was identified as the most accurate predictor of progression-free survival (PFS) and OS. Additionally, the latest guidelines recommend using CTCs alongside the four biological markers (HER2, Ki67, ER/PR, and histological grading) to assess the prognosis of breast cancer.
Conclusion: Reduced CTC counts following treatment initiation are linked to better results, while persistent CTCs may signify resistance and necessitate alternative treatment modalities. Despite treatment, several challenges remain before CTC analysis can be used clinically to diagnose breast cancer.

Keywords: breast cancers, circulating tumor cells, liquid biopsy, Therapy interventions

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Abstract: A-10-2813-2

Systematic Review of Recent Advances in Therapeutic Implications of EGFR and c-MET Inhibition in Triple Negative Breast Cancer

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Background: Due to their roles in the progression of triple-negative breast cancer (TNBC) and frequent overexpression, the epidermal growth factor receptor (EGFR) and c-MET receptor tyrosine kinases (RTKs) have emerged as promising candidates. This review examines the latest findings regarding EGFR and c-MET in TNBC, focusing on their potential as therapeutic targets and insights for drug development.
Methods: Using the keywords breast cancers, targeted therapy, EGFR receptor, and RTK receptor, a collection of English-language articles on the subject published from 2000 to 2023 was gathered from Scopus, PubMed, and Web of Science. Exclusion criteria were applied to select the articles, which were then reviewed and included in the study.
Results: Tyrosine kinases are promising therapeutic targets due to their high expression in several subtypes of TNBC. Two notable examples of tyrosine kinases that show potential as therapeutic targets are MET and EGFR, both known for their elevated expression levels. MET expression is strongly correlated with EGFR expression. Additionally, EGFR expression is commonly observed in TNBC. Studies indicate that a combination of inhibitors targeting MET and EGFR may be a valid strategy for drug development in TNBC. Preclinical and clinical studies have demonstrated the efficacy of EGFR and c-MET inhibitors in TNBC, both as standalone agents and in combination with chemotherapy or other targeted therapies. In TNBC, EGFR is phosphorylated in the presence of the inhibitor, and its persistent phosphorylation is linked to TKI resistance. This resistance to EGFR inhibition may arise from MET-EGFR crosstalk; therefore, to develop effective therapeutic strategies, it is crucial to consider both the targeted RTK and their combined inhibition to effectively reduce the severity of the disease in TNBC.
Conclusion: However, challenges remain in identifying optimal patient populations, overcoming resistance mechanisms, and managing potential toxicities. Biomarker-driven approaches and novel drug design strategies, including antibody-drug conjugates and bispecific antibodies, hold promise for improving the clinical utility of EGFR and c-MET targeted therapies in TNBC.

Keywords: breast cancers, targeted therapy, EGFR receptor, RTK receptor

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Abstract: A-10-2377-1

The Role of nuclear factor erythroid 2–related factor 2 (Nrf2) Pathway in polycystic ovary syndrome: A systematic review

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Background: Polycystic ovary syndrome (PCOS) is the most common cause of infertility, often associated with oxidative stress. The Nuclear Factor Erythroid 2-Related Factor 2 (Nrf2) pathway is a crucial regulator of enzymatic cellular defense against oxidative stress. This pathway has attracted attention in both basic and clinical infertility research. The objective of this systematic review was to compile data on the role of Nrf2 in PCOS.

Methods: To achieve this, relevant articles were sourced by searching PubMed, Web of Science, Scopus, and Embase (from inception to May 2024) using the following search terms: ("Nuclear Respiratory Factor 2" OR "Nrf2") AND ("Polycystic Ovarian Syndrome" OR "Stein-Leventhal Syndrome" OR "PCOS"). We identified 52 articles, of which 19 studies met the inclusion criteria that reported data on Nrf2 expression (both gene and protein), functional roles, and its relationship with PCOS were assessed.

Results: In most analyses of PCOS, our findings indicated a reduction in Nrf2 levels. Decreased expression of the Nrf2 gene in the ovaries and diminished activity of the NLRP3 inflammasome resulted in an increase in the production of proinflammatory cytokines. This increase can be mitigated by using drugs or other methods with antioxidant properties. Nrf2 activators protect adipose tissue, reduce hyperandrogenism, and alleviate oxidative inflammation in PCOS, significantly enhancing the nuclear translocation and transcriptional activity of Nrf2. Collectively, antioxidant compounds improve the antioxidative response and upregulate Nrf2 signaling in PCOS, and Nrf2 may directly bind to the antioxidant response element of the Foxo1 promoter region.

Conclusion: These findings may have potential applications in assisted reproduction cycles by enhancing the quality of GCs and the embedded oocyte, particularly in PCOS. We underscore the importance of the Nrf2 pathway in the pathophysiology and potential therapeutic interventions for PCOS.

Keywords: PCOS, oxidative stress, Nrf2, systematic review

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Abstract: A-10-2818-1

Investigating the effects of medical graded honey (strong and weak) on the phenotype of HT-29 human colorectal cancer cells

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Background: Colorectal cancer is the third most prevalent cancer globally, representing 9% of all diagnosed cases. Unfortunately, despite advancements in treatment, it continues to have a high incidence and mortality rate. Pharmacological research on honey has revealed its numerous therapeutic properties, including anti-cancer effects, which can be harnessed in modern medicine. Honey samples are categorized into two groups based on their phenolic content, antioxidant capacity, and diastase activity score (h-PAD): low h-PAD and high h-PAD. This study aimed to explore the antiproliferative and antimigration effects of two types of strong and weak honey on HT-29 colorectal cancer cells.

Methods: In this study, the antiproliferative and antimigration properties of two types of honey on HT-29 cells were evaluated using the MTT assay and scratch test at 24, 48, and 72-hour intervals. Finally, gene expression analysis of Bax, Bcl-2, and caspase-3 was performed using Real-time PCR.

Results: The data indicated that honey with a high PAD score exhibits stronger anti-proliferative and anti-migration effects on HT-29 cancer cells compared to honey with a low PAD score (IC50 of strong honey for 24 hours: ±0.19 2.4, while the IC50 of weak honey for 48 hours is: 5.8 ± 0.21). Additionally, honey with a high PAD score can initiate the apoptosis process by increasing the expression of the caspase-3 and BAX genes while decreasing the expression of the Bcl-2 gene.

Conclusion: Based on the results, the potential effects of strong honey can be regarded as effective agents against the growth and migration of cancer cells.

Keywords: Colorectal cancer, honey, anticancer, antiproliferative, antimigration

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Abstract: A-10-3048-1

Asymptomatic Homozygotes in Metabolic Disorders: Implications for Genetic Counseling and the Limitations of Preimplantation Genetic Diagnosis (PGD)

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Background: Metabolic disorders, resulting from genetic mutations that impact enzyme function or metabolic pathways, are generally linked to a spectrum of clinical manifestations, ranging from mild to severe. In numerous instances, the detection of a pathogenic variant through whole exome sequencing (WES) aids in diagnosis, treatment, and reproductive counseling. However, the existence of asymptomatic homozygotes—individuals who possess two copies of a mutation without exhibiting the anticipated phenotype—presents a challenge in managing these disorders. This situation prompts inquiries regarding the effectiveness of genetic testing and underscores the limitations of preimplantation genetic diagnosis (PGD) in such scenarios.

Methods: In this article, we examine a case where WES revealed a homozygous MCCC2 mutation in both an affected child and two asymptomatic family members. A 13-year-old female exhibited severe developmental delay, psychomotor retardation, feeding difficulties, and intellectual disability. Whole-blood genomic DNA was extracted and sequenced via WES using the Illumina HiSeq platform. An in-house bioinformatics pipeline was employed for bioinformatics analysis. Variants were classified according to the guidelines established by the American College of Medical Genetics and Genomics. Finally, segregation analysis using Sanger sequencing was performed for the entire family.

Results: We identified a homozygous pathogenic variant in the MCCC2: chr5(GRCh38):71641018G>ANM_022132.5: c.1015G>A. Segregation analysis by Sanger sequencing confirmed the homozygous state in the proband and heterozygous state in her mother. Her father and unaffected sibling was found to be homozygous for the same MCCC2 mutation and exhibited no clinical symptoms. The discovery of asymptomatic homozygotes for the MCCC2 mutation demonstrates the complexities of genetic diagnosis and reproductive decision-making. In cases where the genotype does not correlate clearly with the phenotype, PGD may not be an appropriate option. **Conclusion:** Further research into genetic modifiers and the factors contributing to incomplete penetrance will be crucial in improving our understanding of these conditions and their management in clinical practice.

Keywords: Metabolic Disorders, whole exome sequencing, asymptomatic

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Abstract: A-10-2817-1

From Allergies to Anticancer Agents: Investigating Pollen Alcoholic Extracts for Therapeutic Applications

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Background: Cancer remains a significant global health issue, with lung cancer being one of the deadliest forms. Despite advancements, the efficacy of treatments is still limited, highlighting the need for novel therapies. Plant-derived compounds, particularly pollens, present therapeutic potential due to their diverse biological properties. This study investigates the anticancer effects of alcoholic extracts from pollen of five allergenic plants (Amaranthus, Chenopodium, Artemisia, Juniperus, and Cypress) on human non-small cell lung cancer cells.
Methods: Pollen grains were collected, and alcoholic extracts were prepared. The extracts were then assessed for their effects on A549 lung cancer cells and normal fibroblasts using MTT assays and Hoechst staining. Additionally, gene expression analysis of apoptosis-related genes was performed using qRT-PCR.
Results: Alcoholic pollen extracts exhibited significant antiproliferative effects on cancer cells, with Cypress and Artemisia extracts demonstrating the lowest IC50 values. Hoechst staining confirmed apoptotic morphological changes induced by these extracts. Gene expression analysis revealed upregulation of the proapoptotic gene Bax and downregulation of the antiapoptotic gene Bcl-2, supporting the apoptotic effects of the extracts.
Conclusion: Pollen alcoholic extracts from Cypress and Artemisia exhibited potent anticancer effects, specifically through the induction of mitochondrial apoptosis. These findings suggest the therapeutic potential of pollen extracts as alternative or complementary treatments for lung cancer. Further research is needed to clarify their mechanisms and optimize their efficacy.

Keywords: Lung cancer, Pollen alcoholic extracts, A549 cells, Anticancer effects

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An overview on the biochemical and anticancer properties of red onion peel extract

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Background: Cancer is a leading cause of death worldwide. Despite advancements in current therapies, unwanted side effects remain a significant concern. In this context, medicinal plants have garnered considerable attention as complementary treatments. Red onion (Allium cepa L.) is one such plant whose anti-cancer effects have been demonstrated.

Methods: In this systematic review, we discuss the biochemical and anti-cancer properties of red onion. We utilized databases such as PubMed, ISI, Scopus, and Google Scholar, searching for keywords including red onion, Allium cepa L., and anti-cancer effects since 2020. From approximately 50 reports, those related to red onion peel extract were included in this study, while reports concerning onion bulbs were excluded.

Results: A review of about 30 out of 50 papers indicated that the presence of valuable secondary compounds in red onion peel extract suggests its potential as an anti-cancer complement. Red onion is recognized for its phenolic compounds, including flavonoids, phenolics, and anthocyanins, and is a powerful source of quercetin. Nile et al. (2021) reported that spiraeoside, a type of quercetin found in red onion peel extract, exhibits antioxidant and anti-tumor activity in HeLa cells (cervical cancer). Additionally, Cadorshabi et al. (2022) demonstrated that the level of bioactive compounds in red onion peel extract exceeds that of the bulb, with quercetin mono- and di-glucoside being the two most common flavanols found in this extract. Uttarawichien et al. (2021) showed that red onion peel extract inhibits cancer cell growth and progression in the HT-29 cancer cell line (colorectal cancer) by suppressing angiogenesis.

Conclusion: The data suggests that red onion peel extract could potentially serve as an anti-cancer complement. Furthermore, since onion peel is often regarded as waste and discarded in large quantities each year, this biological application could be economically beneficial**.**

Keywords: Red onion peel, Allium cepa. L., Anti-cancer effects.

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Abstract: A-10-2760-2

The association between apolipoprotein D (ApoD) polymorphism and Type 2 Diabetes (a systematic review)

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Background: Apolipoprotein D (ApoD) is produced in the brain, testes, and liver and is associated with HDL in lipid metabolism. ApoD plays a role in the metabolism of cholesterol and other lipids, and malfunctions in ApoD may lead to diseases related to lipid metabolism and the neurological system. Type 2 diabetes (T2DM) accounts for 90-95% of diabetes cases and may arise from impaired insulin secretion, resistance to the peripheral actions of insulin (receptors), or both. Risk factors for T2DM include obesity, a sedentary lifestyle, family history, and depression. The association between ApoD polymorphism and Type 2 Diabetes has been examined in several articles, yielding conflicting results, as some studies confirm the association while others do not. The purpose of this study is to investigate the relationship between ApoD polymorphism and Type 2 Diabetes.

Methods: In this systematic review, a search was conducted using the keywords "ApoD," "polymorphism," and "Type 2 diabetes" or "T2DM" in the PubMed, Google Scholar, and Web of Science databases. Initially, 125 results were obtained. Ultimately, after screening, 10 articles were included in the study.

Results: This study included 1,523 patients (mean age: 58.9, men: 45.9%, women: 54.1%) diagnosed with T2DM. Studies have shown that rs1568565 (p-value: 0.043) and the ApoD TaqI polymorphism (in South India) are associated with T2DM, while one study did not find a significant relationship. Conclusion: There is some evidence suggesting that ApoD may influence metabolic processes related to diabetes. However, the pathophysiological role of ApoD in T2DM remains unclear. The results indicate a need for more focused studies on ApoD polymorphism to fully understand its potential implications in diabetes.

Keywords: ApoD, polymorphism, T2DM, Diabetes

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Abstract: A-10-2840-1

Investigating the immunogenicity of corona vaccine candidate (S1) produced in prokaryotic host

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Background: Creating this vaccine is crucial, as its outcomes can be utilized in research centers and pharmaceutical companies. Numerous laboratories worldwide have begun investigating the development of a vaccine to prevent this disease. Most vaccines focus on a specific protein subunit of the SARS-CoV glycoprotein (S1). The coronavirus employs this glycoprotein to enter and attach to host cells. Consequently, a vaccine that elicits a robust immune response against this protein can significantly aid in preventing the virus from infiltrating host cells during natural infection.

Methods: Studies have indicated elevated levels of RBD-specific IgG elements in coronavirus patients. Increased levels of IgG specific to the S1 antigen of the virus are linked to patients who do not require intensive care treatment. This implies that an early IgG response to the virus is vital. In this project, the S1 protein was produced in a prokaryotic host and subsequently purified. The resulting protein was tested with aluminum hydroxide adjuvant at ratios of 1:5 and 1:10 in rat samples. Injections were administered at intervals of 14 and 21 days to assess immunogenicity. The number of injections varied from 2 to 3.

Results: The findings revealed that the 1:10 ratio yielded higher antibody titers than the 1:5 ratio. Following the first injection, low antibody levels were noted in all formulations, but these levels rose with additional injections. After the third injection at 35 days, the antibody titer increased significantly.

Conclusion: Future research aims to enhance immunogenicity using the S1 protein with an appropriate adjuvant, lower treatment costs for coronavirus, and optimize the production of an effective vaccine through animal testing. The implementation steps of the research are as follows: 1. Production of protein with aluminum hydroxide adjuvant 2. Injection into animals 3. Blood sampling from animals 4. Using an ELISA kit to determine antibody titers.

Keywords: Vaccine candidate, coronavirus, immunogenicity, Adjuvant

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Abstract: A-10-2792-1

Evaluation of restorative and protective effect of hydroalcoholic extract of Portulaca oleracea on Hydrogen peroxide-induced oxidative stress on HDF cells in vitro

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Background: Wound healing is crucial because skin breakdown can result in life-threatening infections. Currently, there is no effective therapy for chronic wounds. Chemical compounds often lead to complications; thus, it is essential to minimize these complications and enhance the rate of wound healing using natural compounds. In this study, we evaluated the restorative and protective effects of Portulaca oleracea aqueous extract on hydrogen peroxide-induced oxidative stress in human dermal fibroblast cells.

Methods: The cytotoxic effects of various concentrations of P. oleracea extract on fibroblast cells were assessed using the MTT assay. The impact of P. oleracea extract on fibroblast cell migration was evaluated through a wound healing assay (scratch). Finally, the effect of P. oleracea extract on the mRNA expression of VEGF, TGFB, SOD1, and NRF2 genes was measured using the real-time PCR method.

Results: The findings indicated that concentrations of 2, 4, and 8 µg/ml of P. oleracea extract did not significantly affect the survival of fibroblast cells. Therefore, these concentrations were utilized to investigate protective effects against hydrogen peroxide toxicity in fibroblast cells. The cytotoxicity of hydrogen peroxide was significantly reduced in fibroblast cells pretreated with P. oleracea extract. Furthermore, P. oleracea extract significantly enhanced the migration of fibroblast cells. Additionally, P. oleracea extract notably restored the expression of VEGF, TGFB, SOD1, and NRF2 genes in fibroblast cells.

Conclusion: In summary, our study demonstrated that P. oleracea can mitigate the adverse effects of hydrogen peroxide and accelerate wound healing by promoting cell migration and modulating the expression of related genes.

Keywords: Skin wound, fibroblast, Portulaca oleracea, hydrogen peroxide

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Abstract: A-10-2386-2

The effect of probiotics on tryptophan metabolism in the behavioral aspects of phenylketonuria

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Background: Phenylketonuria (PKU) is a genetic disorder that leads to the harmful accumulation of phenylalanine in the brain due to a deficiency in the enzyme phenylalanine hydroxylase. The only treatment for PKU involves lifelong dietary modifications to support normal growth and neurological development. Dietary changes in PKU patients can alter their gut microbiota, potentially impairing tryptophan (Trp) metabolism. Probiotics may help regulate Trp metabolism as a therapeutic approach. Tryptophan is an essential amino acid and a precursor to serotonin, which plays a crucial role in neuronal differentiation. The primary focus of this systematic review was to gather information on the influence of probiotics on tryptophan metabolism in the behavioral aspects of phenylketonuria.

Methods: We reviewed the impact of probiotics on tryptophan metabolism in phenylketonuria and searched the electronic databases of PubMed, EMBASE, and Scopus for relevant studies published up to June 2024, using the following search terms: (("Phenylketonurias") OR ("Metabolism, Inborn Errors") OR ("PKU")) AND ("tryptophan") OR ("Trp") OR ("tryptophan metabolism") AND ("microbiota") OR ("probiotics"). We identified 57 articles, of which 11 studies met the inclusion criteria, reporting data on all interventional animal or human studies that assessed the effects of probiotic interventions on tryptophan metabolism in PKU.

Results: Our findings indicate that PKU is linked to decreased levels of monoaminergic neurotransmitters, such as dopamine and serotonin (5-HT). The altered metabolism of phenylalanine may lead to diminished availability of Tyr and Trp in the central nervous system, which are essential precursors for the synthesis of 5-HT and dopamine, respectively. PKU patients who supplement with Phe-free amino acid medical foods (AA-MF) have exhibited changes in Trp metabolism. In summary, hyperphenylalaninemia disrupts synaptic function, leads to neurotransmitter degradation, and impairs myelination processes.

Conclusion: An additional treatment option for PKU patients could involve probiotic supplementation, which provides enzymes that can steer Trp metabolism toward 5-HT synthesis. This may help alleviate the neuropsychological symptoms associated with PKU.

Keywords: Phenylketonuria, probiotics, Tryptophan Metabolism, serotonin

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Abstract: A-10-2783-2

Investigating the effect of caspase-9 activation on the fate of glioblastoma_U87 cell line

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Background: Caspase 9 is traditionally recognized as the initiator caspase in the intrinsic apoptosis pathway. Recent studies have aimed to uncover the non-apoptotic functions of this enzyme, including its role in cell differentiation. In this study, we investigated the impact of caspase-9 activation on the cell fate of U87, a human glioblastoma cell line.

Methods: Inducible Caspase-9 was transfected into U87 cells using Polyethylenimine (PEI), and cell death was assessed through MTT and Annexin/PI staining. Flow cytometry was employed for cell cycle analysis. Real-time PCR and immunocytochemical staining were utilized to evaluate differentiation. Additionally, cell senescence was assessed using the western blot method.

Results: Initially, caspase-9 expression and activation were evaluated and confirmed. The assessment of cell viability indicated a 40% decrease; however, the cell death assay results ruled out significant cell death. Cell cycle analysis revealed an S-phase arrest. Real-time PCR analysis of neural markers demonstrated a four-fold increase in GFAP expression, an astrocytic marker, although immunocytochemical staining against GFAP did not corroborate this finding, which ruled out potential differentiation. To investigate cellular senescence, relevant markers such as phosphorylated P53 (pP53), P16, and P21 were analyzed. The results indicated an increase in all these markers, confirming the occurrence of cell senescence due to heightened caspase-9 activity.

Conclusion: This study identifies a novel role for caspase-9, shifting the cell fate of U87 toward senescence.

Keywords: glioblastoma, caspase-9, iC9

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Abstract: A-10-2327-1

The effects of everolimus on cellular signaling in breast cancer

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Background: Breast cancer (BC) comprises a group of biologically and molecularly diverse diseases. The normal development of the breast and its stem cells is governed by several signaling pathways. In BC treatment, which depends on external signals, drugs have been developed to slow or halt the growth of cancer cells. Among these is Everolimus, an oral rapamycin analogue and mTOR inhibitor. Everolimus inhibits the growth, migration, and invasiveness of BC cells via the PI3K/AKT/mTOR signaling pathways.
Methods: We gathered relevant papers from November 23, 2011, to June 2, 2021, from databases such as Google Scholar and PubMed. A total of seven papers were included in this systematic review.
Results: The PI3K/AKT/mTOR complex is a signaling pathway that plays a crucial role in essential cellular activities, including metabolism, growth, proliferation, apoptosis, and angiogenesis. Treatment with Everolimus regulates the growth of breast cancer cells through the mTOR/AKT/PI3K signaling pathways. It also significantly inhibits the growth and invasion of breast cancer cells, induces apoptosis, and interrupts the breast cancer cell cycle. Studies have shown that AKT contributes to inhibiting breast cancer cell growth when treated with Everolimus. Additionally, Everolimus combined with tamoxifen has shown significant clinical efficacy by inhibiting PI3K and mTOR.
Conclusion: Cell signaling pathways can be important targets for disease treatment. Investigating mutations in the PI3K/AKT/mTOR signaling pathway and their inhibitors may provide real benefits to BC patients. These drugs can play a crucial role in inducing the death of malignant cells by inhibiting growth and proliferation. Therapeutic strategies that offer a comprehensive view of cancer-related changes in cell behavior, along with a better understanding of how drugs affect these mechanisms, may help improve the success of treatment plans. Everolimus represents a new approach to breast cancer treatment, presenting both new opportunities and challenges.

Keywords: Breast Cancer, Signaling, Everolimus, mToR,drugs.

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Abstract: A-10-2843-1

Fingolimod improves learning and memory impairments in an animal model of dementia

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Background: Dementia is a syndrome characterized by progressive impairments in cognition and behavior that extend beyond the normal aging process, affecting a significant number of individuals worldwide. Current therapies for dementia have limitations. This study aimed to evaluate the effects of fingolimod on neurobehavioral and biochemical parameters in scopolamine-induced amnesic rats.

Methods: Thirty male Wistar rats were randomly assigned to three groups (n=10 for each group): the scopolamine group (rats received scopolamine (1 mg/kg, intraperitoneal injection, for 14 days)), the scopolamine + fingolimod group (rats received scopolamine (1 mg/kg, intraperitoneal injection, for 14 days) and fingolimod (1 mg/kg, orally, from the seventh to the fourteenth day)), and the control group (rats received normal saline for 14 days). After 14 days, learning and memory were evaluated using the Barnes maze and shuttle box tests. Following the behavioral assessments, the rats were decapitated, and their brains were carefully extracted from the skull. The hippocampus was then quickly separated from the brain for biochemical assessments. Additionally, interleukin (IL)-6 and tumor necrosis factor alpha (TNF-α) were measured using ELISA kits, and the protein expression of brain-derived neurotrophic factor (BDNF) was evaluated by western blot.

Results: The data indicated that fingolimod significantly improved scopolamine-induced learning and memory impairments in the Barnes maze and shuttle box tests ($p < 0.05$). Furthermore, it reduced IL-6 and TNF-α levels ($p < 0.05$) in the hippocampus. Fingolimod also mitigated the scopolamine-induced downregulation of BDNF in the hippocampus ($p < 0.05$).

Conclusion: The present study highlights the neuroprotective effects of fingolimod, noting that it improves learning and memory impairments, and decreased IL-6, TNF-α, and increased BDNF in the hippocampus. We can conclude that the effects of fingolimod on memory function in the animal model of dementia is partly related to its multiple effects on the neuroinflammation and synaptic plasticity in the hippocampus.

Keywords: Fingolimod ،memory ،dementia

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Abstract: A-10-2844-1

Extraction of polyphenolic extract from propolis and investigation of its antioxidant properties

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Background: Over 60% of FDA-approved drugs in the areas of infectious diseases, oncology, and central nervous system disorders are derived from natural sources. Among these, natural small molecules like polyphenols play a crucial role. These molecules are vital for the development of innovative drugs due to their functional groups that interact well with biological components and macromolecules (particularly proteins), as well as their structural diversity and complexity. Polyphenols exhibit antibiotic, antioxidant, antiviral, anticancer, and antidiabetic properties. Propolis serves as an excellent source of polyphenols and possesses numerous medicinal benefits.
Methods: In this study, polyphenols were extracted using ethanol, followed by refluxing with water to extract more polar polyphenols. Six different methods, including variations in reaction temperature, solvent percentage and ratio, and sonication, were employed to optimize the extraction of polyphenols from propolis. Extraction efficiency, solubility of polyphenols in water, antioxidant properties, total phenol content, and flavonoid levels were measured.
Results: The extraction yield ranged from 3.6% to 7.2%. The lowest yield was observed with the extraction method using 80% ethanol at room temperature, while the highest total phenol content (14.42 ± 1.89 mg gallic acid/g) and flavonoid content (2.71 ± 0.17 mg myricetin/g) were obtained from extraction with 70% ethanol at 60 °C. Polyphenolic extracts demonstrated significant solubility in water.
Conclusion: The highest extraction efficiency for antioxidant properties, total phenol, and flavonoid content was achieved with the extraction using 70% ethanol at 60 °C.

Keywords: propolis, polyphenols, antioxidants

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Abstract: A-10-2851-2

Evaluation of antioxidant activity and protective effect of Rhus coriaria fruit aqueous extract on fibroblast cell against H2O2

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Background: Rhus coriaria exhibits antioxidant properties, yet its capacity to protect fibroblast cells from oxidative damage caused by H2O2 remains unclear. This study explored the antioxidant and cytoprotective effects of aqueous extracts from Rhus coriaria fruit on cultured human fibroblasts subjected to hydrogen peroxide (H2O2)-induced oxidative injury.
Methods: To prepare the aqueous extract of sumac, Rhus coriaria fruits were first obtained and authenticated by a botanist, then thoroughly washed, dried, and ground. One hundred grams of this powder were mixed with one liter of water and gently simmered for 10 minutes. After cooling, the mixture was filtered and dried using a spray dryer. Fibroblast cells, acquired from the Pasteur Institute, were cultured in 96-well plates in DMEM medium supplemented with 10% FBS and incubated at 37°C with 5% CO2. The aqueous extract of sumac was added to the culture medium at concentrations of 5.0, 10, 25, 50, 100, and 200 µg/ml, and the cells were incubated for 24 and 48 hours under these conditions. Cell viability was assessed using the MTT assay. Additionally, to evaluate the antioxidant activity of the extract, cells were exposed to various concentrations of H2O2, and its effect on cell survival was measured using the MTT assay. The antioxidant activity was also assessed using DPPH and ABTS assays.
Results: Aqueous extracts of Rhus coriaria fruit demonstrate significant antioxidant effects and a strong ability to inhibit oxidative damage-induced cytotoxicity in human fibroblasts.
Conclusion: Further in vivo research is necessary to translate these findings into therapeutic strategies for managing diseases characterized by heightened oxidative stress.

Keywords: Rhus-coriaria, Sumac, Antioxidant Properties, Human Fibroblasts

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2484-2

Association of 3: c.28+137C>G polymorphism (rs964372) in MT1B gene with risk of Breast Cancer: A Case-Control Study

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Background: Breast cancer is one of the most common malignancies affecting women worldwide. As research continues to discover genetic factors that contribute to risk of breast cancer, the importance of specific genetic polymorphisms has become a main point. One of the less known polymorphisms that has an association with some diseases and cancer is an intronic polymorphism 3: c.28+137C>G polymorphism (rs964372) in MT1B gene, which has been studied for its possible association with risk of breast cancer. This paper presents a study investigating whether the 3: c.28+137C>G polymorphism (rs964372) is associated with breast cancer susceptibility.

Methods: Our research analyzed two groups: 100 samples from individuals diagnosed with breast cancer and 100 healthy control samples. We applied the Tetra-ARMS PCR method to detect the presence of the 3:c.28+137C>G polymorphism (rs964372). This technique is known for its efficiency and accuracy in detecting specific genetic variants, allowing reliable comparison between the two groups.

Results: Data analysis revealed that the CC allele and AA allele had the highest and the lowest frequency, respectively (p value>0.05). In addition, rs964372 polymorphism of MT1B gene did not demonstrate a significant association with risk of breast cancer. This finding suggests that, contrary to some hypotheses, this particular genetic polymorphism may not be a risk factor for breast cancer. However, we recommend reevaluation of these results in more diverse and larger ethnic populations and statistical groups as well as the other polymorphisms in MT1B gene.

Conclusion: Our investigation showed that the rs964372 polymorphism of the MT1B gene has no significant association with risk of breast cancer. These findings highlight the importance of continuous research to identify genetic factors that actually influence breast cancer development. Understanding these associations is crucial for advancing personalized medicine and improving prevention and therapeutic strategies.

Keywords: Breast Cancer, MT1B Gene, genetic polymorphism, rs964372, Tetra-ARMS PCR

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Abstract: A-10-2491-1

Evaluation the efficacy of pH-sensitive RGD-modified nanoliposomes containing berberine on DU-145 human prostate cancer cell line

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Background: Prostate cancer remains a significant health concern, ranking as the third leading cause of cancer-related mortality among American men. Despite advancements in cellular and molecular research that have led to the development of novel biomarkers and therapeutic targets, effective treatment strategies continue to be elusive. Nanotechnology, particularly nanoparticles (NPs), has emerged as a promising framework for cancer therapy. Nanoliposomes, a versatile drug delivery system, offer potential enhancements in target-specific delivery, circulation longevity, intracellular influx, and stimuli sensitivity. The acidic tumor microenvironment presents a viable target for pH-sensitive liposomes, which can be further improved by incorporating specific targeting peptides such as RGD. This study investigates the potential of Berberine, a natural compound with reported anti-cancer properties, delivered via pH-sensitive, RGD-modified nanoliposomes for targeted prostate cancer treatment.

Methods: The anti-cancer efficacy of pH-sensitive nanoliposomes surface-modified with RGD peptide and encapsulating Berberine was evaluated against the DU-145 prostate cancer cell line. Cell viability was assessed using the MTT assay, while apoptosis was quantified through Annexin V/PI staining and flow cytometry analysis.

Results: pH-sensitive nanoliposomes showed optimal drug release at pH 6.5, simulating the acidic tumor microenvironment. RGD-modified, Berberine-loaded pH-sensitive nanoliposomes (pH-Sensitive-Lip-Ber-RGD) demonstrated superior cytotoxicity compared to non-targeted formulations across all tested concentrations.

Conclusion: The targeted drug delivery system consisting of pH-sensitive, RGD-modified nanoliposomes encapsulating Berberine significantly improved cytotoxicity in prostate cancer cells compared to non-targeting nanoparticles. These findings indicate that this novel formulation may provide a promising strategy for targeted prostate cancer therapy, warranting further exploration in preclinical and clinical settings.

Keywords: Prostate cancer, nanoliposomes, pH-sensitive, RGD peptide, Berberine, targeted drug delivery

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2912-2

BDNF as a biomarker of response to cognitive behavioral therapy in patients with major depressive disorder

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Background: Major depressive disorder (MDD) is a debilitating condition among psychiatric illnesses. Brain-derived neurotrophic factor (BDNF) has been proposed as a biomarker for treatment response. In the present study, changes in serum BDNF were examined as a biomarker of response to cognitive-behavioral therapy (CBT) in patients with major depressive disorder.

Methods: Forty patients suffering from depression (based on DSM-V criteria) were identified and assigned to CBT groups (90-minute sessions, once a week, for 12 weeks) (N=40). The Beck Depression Inventory-II (BDI-II) score and serum BDNF concentration were measured before and after treatment. The data were analyzed at a significance level of $P \leq 0.05$ using Graphpad Prism 9 statistical software.

Results: The average age of female patients was (31.24 ± 3.6) and male patients (29.45 ± 4.3). During treatment with the CBT method, serum BDNF concentration increased (from 1.13 ± 0.71 to 3.72 ± 0.71). The BDI-II score decreased significantly during CBT treatment (from 26.8 ± 0.6 to 9.5 ± 0.8).

Conclusion: Serum BDNF increased and BDI-II score decreased in MDD patients treated with CBT. Therefore, CBT appears to be an effective method for treating MDD patients. Serum BDNF is a suitable biomarker for CBT treatment response. It is recommended to conduct a study with a larger sample size and a longer research duration.

Keywords: BDNF, CBT, MDD

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Abstract: A-10-2991-1

Investigation of the protein-protein network of colorectal cancer metastasis to human Hepatocellular carcinoma (HCC)

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Background: Current methods for diagnosing colon cancer and its liver metastasis rely on imaging techniques such as PET scans and invasive procedures like biopsies. These traditional approaches often result in late diagnoses, leading to limited treatment options and impeding early intervention for liver metastases. This study aims to compare tissue-specific protein biomarkers of clonal liver metastasis using omics sciences, particularly proteomics, to identify a biomarker panel for early detection.

Methods: This study included 10 female patients, aged 45 to 55 years, diagnosed with colon cancer and liver metastasis. During surgery, a 150 mg sample of clonal metastatic tumor tissue was collected from the liver for pathological analysis. Proteins were extracted using the Trizol technique. The ITARQ technique and R software, along with gene ontology studies, were employed to compare the proteome expression profile of clonal metastatic liver tumor tissue with its local model, leading to the identification of a specific biomarker panel for liver metastasis.

Results: Proteome analysis revealed that all key proteins identified play crucial roles in cell proliferation and invasion pathways. Several of these proteins have been recognized as promoters of carcinogenesis pathways. The study identified a panel of 23 key proteins that collectively serve as a biomarker panel for the early diagnosis of colon cancer metastasis.

Conclusion: The key proteins identified through proteome analysis are critical in pathways related to cell proliferation and invasion, which underscore their potential as early diagnostic biomarkers for liver metastasis in colon cancer patients.

Keywords: Colon Cancer, Liver Metastasis, Proteomics, Biomarker Panel, Early Diagnosis, Computational Biology

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Abstract: A-10-2861-3

Prevalence of gastrointestinal parasites among herd dogs in Chaharmahal and Bakhtiari

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Background: Intestinal parasites pose a significant health risk for dogs, particularly those in rural and nomadic regions. These parasites can lead to various health issues, including malnutrition, anemia, and gastrointestinal disorders. This study aims to investigate the prevalence of intestinal parasites in herd dogs from Chaharmahal and Bakhtiari province in Iran. Understanding the prevalence and types of parasites present can aid in developing effective control and treatment strategies to enhance the health and productivity of these working dogs.

Methods: Samples of dog feces were collected from herdsmen and nomads across 9 regions of Chaharmahal and Bakhtiari provinces. This comprehensive sampling method provided a representative overview of intestinal parasite prevalence in herding dogs. The findings were compared with 36 filtered articles from PubMed, ScienceDirect, Iranpaper, and Google Scholar, focusing on intestinal parasites, herd dogs, and prevalence. The combination of field study and literature review strengthens the validity and generalizability of our conclusions regarding gastrointestinal health issues in rural canine populations.

Results: Analysis of feces samples from the sampled dogs showed a wide range of gastrointestinal parasites. The most common parasites identified were Ancylostoma spp. (23.6%), followed by Toxocara canis (5.5%), Trichuris vulpis (4.8%), and Giardia spp. (12.2%). These findings emphasize the significant burden of gastrointestinal parasites in the study population. Notable, the prevalence of Ancylostoma species. It was significantly lower in owned dogs compared to stray dogs, highlighting the protective role of responsible ownership against parasitic infections.

Conclusion: In conclusion, this study reveals high prevalence of intestinal parasites in herd dogs in Chaharmahal and Bakhtiari province, emphasizing need for targeted control measures and improved veterinary care access.

Keywords: intestinal parasites, herd dog, Chaharmahal and Bakhtiari

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2887-2

Comparison of serum levels of inflammatory factors and vitamin B9, B12 and D levels in patients with Obsessive-Compulsive disorder (OCD) and without OCD

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Background: The main mechanisms involved in Obsessive-Compulsive Disorder (OCD) are still unclear. However, immune system disorders are one of the proposed mechanisms in the pathophysiology of OCD. Considering the potential role of vitamins in regulating levels of inflammatory markers, this study examined the levels of IL-1, TNF-α, hs-CRP, and vitamins B9, B12, and D in patients with OCD and healthy individuals.
Methods: The research included 40 individuals diagnosed with and an equal number of healthy volunteers serving as control subjects. The concentrations of IL-1, TNF-α, vitamin B9, vitamin B12, and vitamin D in the blood were measured using Enzyme-Linked Immunosorbent Assay (ELISA). The lipid profile, hematological indices, and hs-CRP were evaluated using standard procedures.
Results: The concentration of IL-1ß in the blood of individuals with OCD was significantly higher compared to the control group. Furthermore, the serum levels of TNF-α and hs-CRP were higher in OCD patients than controls. The examination of serum levels of vitamins D, B12, and folate using the ELISA method revealed that the level of vitamin D in serum samples of individuals with OCD was significantly lower compared to those without the disorder. This was while the level of vitamin B12 among individuals with OCD did not statistically differ from those without obsessions. Similarly, no difference was observed in serum vitamin B9 levels between cases and controls. Vitamin D showed a significant negative correlation with both IL-1ß and TNF-α values.
Conclusion: Based on the obtained data, it seems that inflammatory cytokines and the indicated vitamins may play a significant part in the development of OCD. Additionally, the analysis of these markers might potentially be utilized as indicators to anticipate the occurrence of OCD. Nevertheless, more research is advised to get more definitive findings.

Keywords: Obsessive-Compulsive Disorder, Inflammatory cytokines, Inflammation Mediators, Vitamin D, Vitamin B12, Vitamin B9

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Acta Biochimica Iranica

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Abstract: A-10-2904-1

Role of STAT3 signaling pathway in Lung cancer: A Systematic Review

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Background: Signal transduction and transcription activator 3 (STAT3) as an oncogene plays a role in the initiation and progression of various cancers. Accumulated studies show that STAT3 is highly expressed in metastatic carcinomas such as lung cancer. We conducted a systematic review to identify the relationship between STAT3 expression and lung cancer.

Methods: We searched the keywords STAT3 and lung cancer from several databases including PubMed, Scopus, and Google Scholar from 2016 to 2024. The inclusion criteria included studies conducted in vitro, in vivo, and in clinical conditions that evaluated the involvement of STAT3 in lung cancer. Data extraction investigated the therapeutic implications of STAT3 and the pathways by which STAT3 affects lung cancer.

Results: The findings of 16 reviewed articles show that STAT3 activation in lung cancer tissues and cell lines is associated with increased tumor cell proliferation, invasion, survival, and resistance to chemotherapy. Therapeutic Interventions Such as RNAi and small molecule inhibitors targeting STAT3 have shown encouraging results in preclinical studies, but their efficacy has not yet been fully confirmed in clinical settings.

Conclusion: In most lung cancers, high STAT3 expression is associated with a lower survival rate. Preclinical studies showed significant effectiveness of drugs targeting the STAT3 signaling pathway in treating lung cancer. Therefore, this pathway is a potential therapeutic target in lung cancer.

Keywords: Stat3, Lung cancer, Signaling pathway, Systematic review

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Abstract: A-10-2894-1

Evaluation of Nano Taurin effect of drug resistant reduce on the MKN45 gastric cancer cell line

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Background: The drug resistance of cancer cells, on the one hand, due to drug limitations, and on the other hand, consumption without considering the effect and effective dose, the important issue of anticancer drugs today is to find new anticancer substances and the possibility of their targeted transfer to cancer cells. It is an important strategy in controlling cancer. Currently, the role of taurine is considered more important when human health is at risk. Functions and effects of taurine including antioxidant effect, fat secretion, growth, differentiation and protection of nerve cells, functions related to calcium and, liver protection effect, strengthening of taurine Safety, whitening and anti-cancer effects.

Methods: For this purpose, nano iron oxide was synthesized by hydrothermal method and its effect on MKN45 cancer cell was confirmed by spectroscopic method and its inhibition rate was evaluated by MTT method and the expression of MDR and Wnt4 genes was measured by real time PCR method.

Results: The results showed that nano iron oxide was prepared, then it was made by hydrothermal method at a temperature of 200 degrees in a reactor inside an incubator. And the XRD spectrum that showed the presence of Iron, Oxygen,N and Hydrogen in the Nano complex was another confirmation of the synthesis of nano taurine. The size of the synthesized nanoparticles was less than 60 nm in SEM imaging. The result of the MTT test showed that the IC50 for taurine was 1328 and for nano-taurine was 428 µg/ml for the drug-resistant cell line MKN45. Real Time PCR was used to evaluate the mechanism of its effect.

Conclusion: The results showed that the expression of MDR4 gene decreased under the treatment of nano taurine and the relative expression of Wnt4 increased, both of which indicated the failure of rowing resistance in MKN45 cell line.

Keywords: taurine, nano taurine, Canser, drug resistance, MKN45 cell line

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Abstract: A-10-2359-2

Prognostic Significance and Therapeutic Potential of Long Noncoding RNA GAS5 in Hepatocellular Carcinoma: A Systematic Review

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Background: Hepatocellular carcinoma is a major cancer mortality cause, usually diagnosed late with few treatment options. Recent studies show long noncoding RNA GAS5 is vital in HCC progression, drug resistance, and prognosis. This review summarizes evidence on GAS5's impact on tumor behavior, chemoresistance, and responses to sorafenib and cisplatin, and assesses its prognostic value and therapeutic potential.

Methods: A comprehensive PubMed, Google Scholar, and Scopus search was conducted to find research on GAS5 expression in HCC. Investigations of GAS5 interactions with microRNAs (e.g., miR-21, miR-126-3p, miR-135b, miR-222), drug sensitivity, and clinical outcomes were examined. Analysis was performed on research design, GAS5 and associated microRNA measurement methodologies, treatment response, and survival.

Results: A total of 15 reviewed papers showed that GAS5 was frequently downregulated in HCC tissues, which was associated with a poor prognosis and increased tumor aggressiveness and drug resistance. GAS5 acts as a tumor suppressor that sponges several microRNAs, influencing main pathways such as PTEN signaling and various resistance mechanisms. Overexpression of GAS5 increased sensitivity to chemotherapeutic agents such as cisplatin and sorafenib. More importantly, GAS5 has also been shown to enhance radiosensitivity, overcome sorafenib resistance, and inhibit tumorigenesis by interfering with several signaling pathways. Moreover, genetic variants in the promoter region of GAS5 have also been associated with clinical outcomes, thereby reinforcing its prognostic significance.

Conclusion: GAS5 has emerged as a highly promising biomarker and therapeutic target, serving as a critical factor in the development of tumors and the development of chemoresistance in HCC. GAS5 has the potential to improve the efficacy of treatment and result in improved outcomes, as this review has identified. Additional investigations will be necessary to examine the clinical utility of GAS5 as a predictive biomarker for personalized therapy and patient stratification.

Keywords: Hepatocellular carcinoma, GAS5, Drug resistance, long noncoding RNA, MicroRNAs

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Abstract: A-10-3095-1

Canertinib as an AKT1 Inhibitor: A Promising Therapeutic Strategy for Endometriosis in Light of Cancer Research

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Background: Endometriosis is a chronic, estrogen-dependent condition characterized by the presence of endometrial-like tissue outside the uterus, leading to symptoms such as pelvic pain and infertility. Recent studies suggest a potential link between endometriosis and hormone-related cancers, particularly breast cancer, as both conditions are influenced by hormonal factors. The chronic inflammation associated with endometriosis may increase the risk of developing malignancies, including breast cancer.
Methods: Using the Gene Expression Omnibus (GEO) dataset, significant changes in the pattern of gene expression associated with endometriosis were identified. RAC-alpha serine/threonine-protein kinase (AKT1) was identified as a hub gene with the highest degree of connectivity using STRING and Cytoscape, highlighting it as a key participant in endometriosis-associated pathways. Notably, STRING analysis indicates that AKT1 also serves as a hub gene not only in breast but also in lung cancer, corroborated by existing literature and GeneCard database.
Results: Based on the DrugBank database, we identified Canertinib, which inhibits AKT1 and has demonstrated efficacy in both breast and lung cancers. Additionally, articles and the GeneCards database corroborate our findings regarding the role of this drug in these malignancies.
Conclusion: Our research highlights the promise of targeting AKT1 as a therapeutic approach for endometriosis, given its recognized involvement in breast and lung cancers. The identification of Canertinib, which effectively inhibits AKT1 and demonstrates efficacy against these cancers, presents a promising therapeutic alternative. Additional studies into the use of Canertinib for endometriosis are necessary, potentially providing renewed hope for patients dealing with this challenging condition.

Keywords: Endometriosis, AKT1, Canertinib, Breast Cancer, Lung Cancer

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Abstract: A-10-3132-1

Determining the genotype and drawing the phylogenic tree of Tilleria species in the cows of Marivan City

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Background: Theileriosis is considered one of the most important and dangerous diseases in tropical and subtropical regions, which causes many casualties and economic losses to the animal husbandry industry every year. Theileriosis, a disease caused by the Theilaria protozoan, appears with different symptoms such as fever, anorexia, depression, anemia, enlarged lymph nodes, decreased milk production, jaundice, neurological and skin disorders, and causes major damages. to the country's livestock industry. Therefore, the purpose of this study was to determine the genotype and draw the phylogenic tree of Tilleria species in the cows of Marivan city (west of Iran).

Methods: For this purpose, in order to conduct the present study, blood samples were taken from the cows of Marivan city and the samples were sent to the microbiology laboratory following the cold transfer chain. Then, the molecular identity of the investigated microorganisms was determined by extracting DNA and using Multiplex Nested PCR method. Then the data were statistically analyzed using SPSS statistical software and chi-square analysis method.

Results: The results obtained in the present study indicated that 10% of the studied cows were infected with Theilaria annulata. Also, the level of Theilaria annulata infection in female cows was significantly higher than that of male cows. Age was another important factor in the rate of infection with Theilaria annulata, and the rate of infection with this parasite was higher in old cows than in young cows.

Conclusion: According to the results obtained in this study, the sensitivity of the PCR technique in the detection of Theileria annulata is very high compared to the microscopic method. Considering the prevalence of 10%, there is a need for epidemiological studies and control measures.

Keywords: Theileriosis ،Theilaria annulata ،PCR ،Marivan

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Abstract: A-10-2957-1

Nano-niosomal formulation of Spirulina platensis extract as a Potential Product for Hyperpigmentation

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Background: Hyperpigmentation of the face and neck is a common concern, particularly among middle-aged women. This condition can be attributed to both endogenous (hormonal) and exogenous factors, including cosmetics, exposure to sunlight, and other environmental factors. Addressing hyperpigmentation is a significant aspect of skincare and beauty, and researchers have been exploring various potential solutions. Niosomes offer unique advantages such as better skin penetration potential, stable transport properties, higher stability, and lower cost, making them an attractive option for skincare formulations. This study aimed at the potential of spirulina platensis extracts nanonisome in addressing hyperpigmentation.

Methods: The nanonisomes were prepared by mixing lecithin, cholesterol, and tween 80 in a specific ratio in 10 ml of ethanol. Subsequently, the water is evaporated during the rotary dehydration process, resulting in the formation of a thin layer. Vortexing different concentrations of spirulina is performed three times for one minute each, and the dissolution results are evaluated by rotary evaporation at a temperature of 60 C for 20 minutes. The physicochemical properties of nanosystems in terms of size, zeta potential, and drug release, were characterized using different methods such as dynamic light scattering (DLS) and UV-visible spectrophotometry. Finally, the melanogenic protein expression of tyrosinase (TYR) was examined to investigate the anti-hyperpigmentation potential of nanoniosome.

Results: According to the findings, the nanoniosomalformulation of spirulina platensis was suitable in terms of size, zeta potential, and drug release, as well as downregulation of tyrosinase gene expression.

Conclusion: As research in this field progresses, spirulina nanonisomes can revolutionize the approach to treating hyperpigmentation, offering individuals renewed confidence in their skin's appearance.

Keywords: Nanoniosom, hyperpigmentation, spirulina platensis

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Abstract: A-10-3133-1

Performance of Artificial Neural Networks to Evaluate the Reciprocal Relationships between Carbohydrate and Lipid Metabolism Parameters

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Background: This study aimed to evaluate the significance of artificial neural network (ANN) for revealing the complicated relationships between carbohydrate and lipid metabolism according to the related parameters in human plasma.
Methods: A total of 124 human plasma samples were analyzed by standard assay methods for biochemical indices. To design ANN models, 11 parameters were selected as independent variables and hyperbolic tangent and identity activation functions were selected in the hidden and output layers, respectively. Moreover, rescaling of the independent and dependent parameters was performed using a standardized method.
Results: Our designed multilayer perceptron (MLP) demonstrated an acceptable sum of squares error and relative error in training and testing steps. The predicted by observed charts for parameters showed a positive linear correlation for total cholesterol, fasting blood glucose (FBS), HDL-cholesterol and LDL-cholesterol. Our ANN model effectively identified the most important markers of carbohydrate and lipid metabolism and provided valuable insights into the biochemical factors that influence metabolic reactions.
Conclusion: ANNs are valuable tools for solving problems by creating mathematical models through a vast range of analyses. This study successfully designed accurate ANN models to identify key biochemical parameters in carbohydrate and lipid metabolism and therefore, finally provided approximate solutions for highly complex problems in biochemistry.

Keywords: Artificial Neural Network, Carbohydrate Metabolism, Lipid Metabolism, Plasma.

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Abstract: A-10-3133-2

Application of Feedforward Multilayer Perceptron Models to Determine the Oxidative Conditions in Human Plasma

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Background: We conducted a comprehensive study to evaluate a mathematical approach for predicting the antioxidant power of plasma and to rank the importance of various biochemical parameters in human plasma.
Methods: In this experimental study, we analyzed biochemical parameters in 165 blood samples of healthy donors in parallel to demographic indices including age, weight, and gender. The parameters were albumin, creatinine, fasting blood sugar (FBS), triglycerides, and uric acid. To assess oxidative stress, we measured the ferric reducing ability of plasma (FRAP) and the carbonyl content of plasma proteins (PCO). We developed artificial neural networks (ANN) using a feedforward multilayer architecture. The ANN models were developed by IBM SPSS Statistics 20.
Results: Our designed ANN model demonstrated a statistically significant positive correlation between the predicted and observed FRAP levels, with an R^2 value of 0.912. The high correlation indicated that our model accurately predicted the antioxidant power of plasma based on the biochemical parameters. By pinpointing the most critical markers, the designed ANN model can streamline clinical procedures and make diagnosis faster and more cost-effective.
Conclusion: The ability of ANN models to accurately predict the most important markers can lead to improved patient outcomes and more targeted therapeutic interventions. Moreover, our study highlighted the potential of advanced mathematical models in clinical research to enhance our understanding of complex biochemical processes and to improve healthcare measures.

Keywords: Feedforward Multilayer Perceptron, Oxidative Stress, Plasma.

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Abstract: A-10-2614-1

Therapeutic Potential of Metformin in Down-Regulation of Intrauterine Adhesions

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Background: Intrauterine adhesion bands (IUABs), or Asherman syndrome (AS), are often distinguished by scar tissue within the uterine cavity, usually caused by infectious or mechanical damage to the endometrium. This situation can easily trigger abnormal menstrual bleeding and infertility. Ongoing cures are still invasive and not consistently operational. Metformin, which is typically consumed for type 2 diabetes has shown great fibroses-mitigating effects. This research probes metformin's potency in preventing IUAB formation through a rat model.

Methods: Female Wistar rats were used to make an IUAB model by means of mechanical uterine injury. The rats were separated into three groups: sham, IUAB control, and metformin treatment. Metformin was administered orally at a dose of 100 mg/kg/day for 10 days. The severity of adhesion was evaluated, and histological analysis was conducted with hematoxylin and eosin (H&E) and Masson's trichrome staining. Inflammatory cytokines (IL-1, IL-6, and TNF-α) were also measured using ELISA.

Results: Metformin could considerably diminish the formation and severity of IUABs in comparison with the control group. Histological analysis also revealed less infiltration and fibrosis of inflammatory cells in the metformin-treated group. Moreover, metformin lowered the levels of pro-inflammatory cytokines IL-1, IL-6, and TNF-α in adhesive tissues.

Conclusion: The preventive effects of metformin in the formation of intrauterine adhesion bands are apparent in the rat model through its anti-inflammatory and anti-fibrotic characteristics. These results put metformin forward as a potential non-invasive cure for IUABs, which still demands more medical investigation.

Keywords: Intrauterine adhesion bands, Asherman syndrome, Metformin, Fibrosis, Inflammation

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3130-1

Evaluation the Anticancer Effect of Sumac (Rhus coriaria) Aqueous Extract and Lactobacillus acidophilus on Gastric Cancer Cells

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Background: Gastric cancer is one of the most common malignancies and the leading cause of cancer-related deaths worldwide. Medical plants and probiotics have drawn the attention of researchers due to their numerous therapeutic effects. Some plant extracts, such as sumac (Rhus coriaria), have anticancer properties and positive effects against cancer progression. Lactobacillus acidophilus is an important probiotic bacterium that provides health benefits to the host by stimulating the immune system and producing anticancer compounds. This study aimed to evaluate the anticancer activity of sumac (Rhus coriaria) aqueous extract and L. acidophilus individually and together on gastric AGS cells.

Methods: Initially, sumac extract was prepared by spray drying method and L. acidophilus bacteria was obtained from the Pasteur Institute. Then, through MTT method, we evaluated the effects of different concentrations of sumac extract and L. acidophilus bacteria, individually and together, on the viability of gastric cancer cells. Subsequently, the degree of apoptosis that occurred in AGS cells was examined using flow cytometry method, after treatment with IC50 concentrations of sumac extract and L. acidophilus, either individually or together.

Results: Sumac aqueous extract and L. acidophilus bacteria, either individually or together, significantly reduced AGS cells viability and increased their apoptosis. Furthermore, L. acidophilus strains and sumac extract showed synergistic effects in inducing apoptosis and death of AGS cells. The calculated IC50 for the sumac extract alone was 250 µg/ml, which decreased to 92.07 µg/ml after combination with L. acidophilus.

Conclusion: Our findings demonstrate that sumac extract and L. acidophilus strains have anticancer and apoptosis-inducing effects on gastric cancer cells, individually. Moreover, they have synergistic effects when used together at low concentrations. These results suggest that, with further studies, we can use the combination of sumac aqueous extract and L. acidophilus strains as a biological product for cancer treatment.

Keywords: Rhus coriaria, Sumac, Lactobacillus acidophilus bacteria, Gastric cancer

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Abstract: A-10-3138-1

HSP27: A missing element in drug resistance in cancers

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Background: HSP27, a small heat shock protein, is crucial in personalized medicine, especially in cancer therapy. Its versatile properties make it a promising target for enhancing treatment effectiveness and reducing side effects. Despite advancements in treatment modalities like chemotherapy, radiotherapy, surgery, and immunotherapy, cancer remains a primary global mortality cause. Drug resistance within tumors can hinder desired responses, making it essential to investigate and combat it. HSP27's expression levels can dictate cellular susceptibility or resistance to various chemotherapeutic agents and targeted treatments, making it a pivotal player in cancer therapy.
Methods: This systematic review was conducted to outline comprehensive studies published in PubMed, Scopus, and Google Scholar databases from 2015 to 2024 by using keywords such as “HSP27”, “drug resistance”, “cancer”, “pharmacogenetic” and related combinations, 52 articles were screened and 11 were included.
Results: The HSP27 molecule is crucial in drug resistance and sensitivity mechanisms in cancers. It is overexpressed in tumors, providing protection against drugs like Doxorubicin by inhibiting senescence through p53 mediation. In oncogene-addicted cancer cells, suppressing HSP27 can shift target factors from cytostatic to cytotoxic, enhancing apoptosis and drug efficacy. Reducing HSP27 in colon cancer cells increases sensitivity to 5-Fluorouracil and Vincristine, promoting apoptosis and tumor growth inhibition. Inhibiting HSP27, particularly through phosphorylation, has shown potential in enhancing radiotherapy efficacy. HSP27 also acts as a negative regulator of apoptosis in glioblastoma, suggesting its modulation could improve treatment outcomes.
Conclusion: In summary, HSP27 is crucial for drug resistance development, but its modulation can enhance drug sensitivity. It can strengthen cancer therapies and protect against treatment-related toxicity, but overexpression can complicate treatment strategies, necessitating precise examination in personalized medical approaches.

Keywords: HSP27, Pharmacogenetic, Cancer, Drug resistance

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Abstract: A-10-2883-1

Investigation of the synergistic effect of microgravity and Hydroxyurea on the expression of PRKCA and HDAC1 genes in the K562 chronic myeloid leukemia cell line

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Background: Simulated microgravity affects cell morphology, proliferation, differentiation and gene expression. This study aimed to investigate the effects of microgravity and Hydroxyurea on HDAC1 and PRKCA gene expression in the K562 cell line. These genes play important roles in cancer treatment; PRKCA are known to be involved in diverse cellular signaling pathways and HDAC1 play a key role in the regulation of gene expression.
Methods: The two-dimensional clinostat was applied for simulating microgravity. Quantitative PCR (qPCR) was utilized in this research.
Results: Our results showed that Hydroxyurea treatment decrease PRCKA and HDAC1 genes expression in microgravity conditions compared to normal gravity. This study indicated that simulated microgravity conditions increase the cytotoxic effects of Hydroxyurea in the K562 cell line.
Conclusion: These methods imply that microgravity may alter cancer cells reaction to medication, maybe by influencing important signaling pathways and histone deacetylation. More study is needed to completely understand the mechanisms which establish cancer treatment.

Keywords: CML ،Microgravity ،Hydroxyurea ،HDAC1 gene ،PRKCA gene ،Cancer ،K562

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Abstract: A-10-3142-1

The Relationship between Type 2 Diabetes and Prostate Cancer Incidence: A Study on Patients in Isfahan Province (2018-2024)

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Background: Prostate cancer is the second most common cancer in men and is one of the leading causes of cancer-related mortality worldwide. Various studies have indicated that type 2 diabetes may have a protective effect against the incidence of prostate cancer. This is likely due to hormonal and metabolic changes associated with diabetes. Understanding the mechanisms that may reduce the incidence of prostate cancer in individuals with type 2 diabetes can aid in the prevention and better management of this cancer. In this study, we investigated the levels of prostate-specific antigen (PSA) and insulin-like growth factor (IGF-1) in diabetic patients and healthy individuals.

Methods: This study was conducted on 50 diabetic patients and 50 healthy individuals who referred to Omid Hospital and Al-Zahra Diabetes Clinic in Isfahan province. Blood samples were collected from both groups, and serum levels of IGF-1 and PSA were measured using standard laboratory methods. The data were statistically analyzed using one-way analysis of variance (ANOVA). Results are presented as mean ± standard deviation, and a significance level of $P < 0.05$ was considered at all stages.

Results: The mean PSA level in diabetic patients was 1.5 ± 0.3, which was significantly lower compared to 1.9 ± 0.77 in healthy individuals ($P = 0.008$). The IGF-1 level in diabetic patients was 149 ± 38.2, while in healthy individuals it was 166 ± 51.3. Although the IGF-1 level was lower in diabetic patients, this difference was not statistically significant ($P = 0.06$)

Conclusion: This study demonstrated that PSA levels in diabetic patients were significantly lower than those in healthy individuals, which may indicate a protective role of type 2 diabetes in reducing the risk of prostate cancer. However, the IGF-1 level in diabetic patients was also lower, but this reduction was not statistically significant.

Keywords: Prostate Cancer, Type 2 Diabetes, PSA (Prostate-Specific Antigen), IGF-1 (Insulin-like Growth Factor 1)

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Abstract: A-10-3118-1

Inverse correlation between IGF-1 levels and fasting blood sugar in patients with type 2 diabetes undergoing therapy

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Background: Type 2 diabetes is considered a chronic disease depending on genetic factors combined with environmental ones, which contribute to the appearance and development of this disease. Diabetes is characterized by metabolic disorders such as hyperglycemia and insulin resistance. Among growth factors, IGF-1 (Insulin-like Growth Factor 1) has structural homology with insulin, which allows it to bind to insulin receptors. Because of this structural homology, IGF-1 may be implicated in the maintenance of blood glucose. Thus, the aim of this study was to investigate the levels of IGF-1 and FBS (fasting blood sugar) diseased conditions such as type 2 diabetes undergoing therapies in northern Iran.

Methods: For this purpose, 30 patients with type 2 diabetes who were referred to the Diabetes Research Center in Sari City were studied. FBS assay kits by Delta Derman and IGF-1 assay kits by Diametra were utilized for the measurement of FBS and IGF-1 levels of the patients' blood serum, respectively.

Results: Comparison of mean data showed that the reduction in fasting blood sugar was directly proportional to an increase in IGF-1 levels in treated patients.

Conclusion: These findings only highlight how much IGF-1 could be of real significance in the management of diabetes in addition to conventional treatment modalities. Hence, knowledge of what triggers the expression of IGF-1 could be an important step in the future management of type 2 diabetes.

Keywords: Type 2 Diabetes, IGF-1, FBS

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Abstract: A-10-2863-1

The Association Between MC4R Gene Polymorphisms and Type 2 Diabetes Mellitus: A Systematic Review

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Background: The melanocortin 4 receptor (MC4R) gene encodes a G-protein-coupled receptor involved in the regulation of energy balance and metabolism. The protein product of this gene interacts with adrenocorticotropic hormone, playing a key role in appetite control and energy homeostasis. MC4R is an intron-less gene, and mutations in this gene have been implicated in the development of autosomal dominant obesity. Additionally, there is growing evidence linking MC4R polymorphisms to Type 2 Diabetes Mellitus (T2DM), a complex metabolic disorder primarily characterized by insulin receptor resistance and hyper-insulinemia. Unlike other forms of diabetes, T2DM is frequently associated with obesity but seldom with ketosis. Several studies have explored the relationship between MC4R polymorphisms and T2DM. However, no comprehensive review has been conducted to summarize the available evidence. This systematic review aimed to evaluate the association between MC4R gene polymorphisms and the risk of T2DM, considering the contradictory findings in the current literature.
Methods: A systematic literature search was performed using the keywords "MC4R," "polymorphism," and "Type 2 diabetes" or "T2DM" in PubMed, Google Scholar, and Web of Science databases. A total of 458 articles were initially identified, of which 10 met the inclusion criteria for further analysis following screening.
Results: The study included data from 15,595 confirmed T2DM patients (mean age: 59 years; men: 71.8%, women: 28.2%). Polymorphisms rs12970134 and rs2229616 were associated with an increased risk of T2DM, while rs17782313 and rs663129 were found to decrease the risk.
Conclusion: This review highlights the potential role of MC4R gene polymorphisms in the development of T2DM. While certain polymorphisms appear to increase risk, others may confer protective effects. Further research is needed to elucidate the underlying mechanisms of these associations.

Keywords: MC4R, polymorphism, T2DM, Diabetes

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Abstract: A-10-2517-2

A study examining both qualitative and quantitative approaches for assessing troponin I levels across three diagnostic and treatment facilities in Guilan province

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Background: Myocardial infarction (MI) represents the foremost cause of death and illness globally. Timely identification of MI is crucial for effective intervention. Cardiac troponin (cTn) serves as a regulatory protein within the myofibrillar thin filament of striated muscle, playing a crucial role in the regulation of excitation-contraction coupling in cardiac tissue. Cardiac troponin I (cTnI) is commonly employed in emergency departments as the primary biomarker for diagnosing acute myocardial infarction (MI).This study seeks to evaluate the sensitivity and specificity of a qualitative troponin I kit in comparison to the quantitative laboratory test for troponin I, with the goal of advancing MI diagnostic accuracy.

Methods: In this research, carried out at Some Sera Hospital, a total of 40 patients suspected of experiencing a heart attack were evaluated. These patients underwent a cardiac troponin I (cTnI) test using the Troponin alpha rapid test kit manufactured in the United States. Subsequently, the serum samples from the patients were dispatched to a private laboratory employing the Continuous Flow Analysis method, as well as to the laboratory of a cardiac specialist hospital utilizing immunoassay techniques for quantitative analysis. Quantitative findings were presented in both affirmative and negative contexts, utilizing a designated cutoff point. The outcomes derived from the qualitative approach were assessed in conjunction with those from the quantitative method, which was deemed to provide a more precise evaluation. Additionally, sensitivity, specificity, positive predictive value, and negative predictive value were computed for the qualitative method.

Results: The findings indicate that the qualitative method demonstrated a sensitivity of 95.5%, a specificity of 11.1%, a positive predictive value of 56.8%, and a negative predictive value of 66.7%, as derived from the quantitative method's data.

Conclusion: While the qualitative method demonstrates a high sensitivity in detecting individuals experiencing a MI, it has low predictive values.

Keywords: troponin I, sensitivity, specificity, qualitative analysis, quantitative assessment, myocardial infarction

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Abstract: A-10-3140-1

Comparison of atomic absorption of zinc, iron, copper, manganese, cadmium and arsenic elements in people infected with Giardia lamblia, Blastocystis hominis and healthy people.

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Background: Giardia lamblia and Blastocystis hominis are prevalent intestinal parasites that contribute to gastrointestinal disturbances, particularly in vulnerable populations such as children and international travelers. Giardia can lead to severe symptoms, including diarrhea and malabsorption, while Blastocystis is often associated with digestive issues but its pathogenic role remains unclear. Both parasites may disrupt essential micronutrient metabolism, particularly zinc and iron, which are crucial for various biological processes.
Methods: The following keywords were utilized for the literature search: "Giardia lamblia","Blastocystis hominis", " Rare elements" and the relationship between them. A comprehensive search was conducted using multiple databases, including: PubMed, Web of Science, and Google Scholar. Inclusion criteria for the systematic review were: 1. Peer-reviewed articles focusing on the relationship between Giardia lamblia or Blastocystis hominis and Rare elements. 2. Studies involving human subjects, particularly children, and individuals in developing countries. 3. Articles published in English. Exclusion criteria included: 1. Studies not focused on Giardia or Blastocystis. 2. Articles that did not provide data on Rare elements levels or health outcomes. 3. Duplicate publications.
Results: The search was conducted using multiple databases and a time frame of January 2016 to December 2023. Out of 150 articles, 45 were included, providing relevant findings on the impact of these parasites on micronutrient metabolism. The review synthesized the findings to highlight the associations between these intestinal parasites and essential micronutrient metabolism. Consultation given the implications of Giardia and Blastocystis infections on nutrient absorption and overall health, it is crucial for healthcare providers to consider screening for these parasites in symptomatic patients, particularly in high-risk groups. Nutritional interventions focusing on replenishing zinc and iron levels may be beneficial.
Conclusion: Further research is needed to elucidate the mechanisms by which these parasites affect micronutrient metabolism and to explore potential therapeutic strategies.

Keywords: Giardia lamblia‹Blastocystis hominis‹rare elements

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Abstract: A-10-3126-1

Hearing loss and COVID-19 infection: A Systematic review study

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Background: The COVID-19 virus affects multiple organ systems, including the gastrointestinal, urinary, and auditory systems. The question is whether COVID-19 increases the incidence of ear infections and hearing loss. Studies have explored this issue, yielding mixed outcomes. This systematic review assessed the impact of COVID-19 on hearing loss and auditory disorders.

Methods: The impact of COVID-19 on hearing loss in infants and adults was assessed through searching scientific databases (Scopus, Web of Science, PubMed, and Science Direct) for articles from January 2019 to September 2024. Keywords included “COVID-19”, “SARS-CoV-2”, “SARS-CoV-2 infection”, “COVID-19 Pandemic”, “Hearing loss”, “Congenital hearing loss”, “Late-onset hearing”, “Infant hearing loss”, “Unilateral hearing loss”, “Otitis media” and “Middle ear effusion”. Eligible studies involved COVID-19 patients, focused on hearing loss, and utilizing observational or interventional designs. Based on the inclusion criteria data were extracted on study characteristics and outcomes.

Results: Out of 973 articles, 958 were excluded, resulting in 15 studies. Exposure to COVID-19 during pregnancy may cause minor hearing abnormalities in newborns. Still, it does not lead to congenital or late-onset hearing disorders. Among infants exposed to COVID-19, no significant differences were observed in brainstem auditory evoked response, auditory steady-state response, or acute vestibular cochlear dysfunction. In adults, a significant increase was seen in the incidence of middle ear effusion, otitis media with effusion, and sudden sensorineural hearing loss. Long-term exposure did not result in permanent hearing loss or deafness.

Conclusion: In the short term, COVID-19 may lead to middle ear infections and temporary hearing issues. Hearing loss or deafness in infants and adults exposed to COVID-19 did not significantly differ from those not exposed. These findings should be validated by future studies across different region and populations.

Keywords: Hearing loss, Deafness, COVID-19, sars-cov-2.

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Abstract: A-10-3143-1

Frequencies and Clinical Significance of Helios and Neuropilin-1 in Patients with Parkinson disease

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Backgrounds: Parkinson disease (PD) is the second most common progressive neurodegenerative disease with various clinical symptoms such as tremor, bradykinesia and cognitive dysfunction. Immunologic and biochemical pathways have a pivotal role in PD pathophysiology. We aimed to evaluate the circulatory frequency of T regulatory cells (Tregs) expressing Helios and Neuropilin-1 (NRP-1) in PD.

Methods: In this case-control study, 83 patients with PD and 83 healthy controls were enrolled. The modified Hoehn and Yahr (H and Y) were used to determine the severity of PD. Flow cytometry was used to evaluate the circulatory frequency of CD4+CD25+Foxp3+Tregs expressing and Helios and NRP-1 in all participants. Also, correlation of H and Y with such frequencies was evaluated.

Results: Our findings showed that frequency of CD4+CD25+Foxp3+Tregs expressing NRP-1 (P=0.04) and Helios (P=0.01) in patients with PD was significantly higher than those in healthy subjects. The frequency of Tregs expressing Helios and NRP-1 showed a negative correlation with H and Y criteria and disease duration.

Conclusion: Our study showed that the frequency of Tregs expressing Helios and NRP-1 may be important prognostic biomarkers of PD.

Keywords: Parkinson disease, Helios, Neuropilin-1

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Abstract: A-10-3121-1

The Role of circRNAs as Biomarkers or Therapeutic Options in Diabetic Foot Ulcers: A Systematic Review of Current Evidence

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Background: Diabetic foot ulcers (DFUs) affect approximately 25% of individuals with diabetes, leading to severe health risks, including complications and potential amputations. Recent studies highlight the involvement of circular RNAs (circRNAs)—a class of long non-coding RNAs that function as miRNA sponges and interact with RNA-binding proteins—in the pathophysiology of DFUs. Monitoring circRNA levels may serve as valuable biomarkers for assessing DFU complications and identifying them as valuable therapeutic targets.

Methods: A systematic search was performed across several online databases, including MEDLINE, EMBASE, ISI Web of Science, and Google Scholar, utilizing both non-Mesh and MeSH terms. The search process was overseen by three independent researchers, with a fourth available for conflict resolution. Only studies adhering to the search criteria and published in English were included.

Results: Overall, 20 studies were included in the review. The analysis identified several circRNAs with potential as biomarkers for DFUs. For instance, decreased levels of circ-Snhg11, circ-Erbb2ip, and circ-ITCH were recorded, alongside significantly reduced expression of FBXO7, ATM, and LMBRD1 circRNAs. Conversely, has-circ-0084443 exhibited a marked elevation in DFU tissue samples. Other circRNAs, including has-circ-0049271, has-circ-0074559, and Circ-0089761, emerged as potential diagnostic biomarkers. Additionally, Mmu-circ-0000250 and others, such as circ-Klhl8 and circ-Astn1, showed therapeutic promise, with involvement in angiogenesis and infectious inflammation linked to DFU.

Conclusion: circRNAs demonstrate potential as both biomarkers and therapeutic targets for diabetic foot ulcers due to their unique structural properties and roles in pertinent molecular pathways. Further research is essential to elucidate their functions and to establish effective biomarkers and treatment strategies for this condition.

Keywords: circular RNA, Diabetes Mellitus, Diabetic foot ulcer, biomarker, treatment

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Abstract: A-10-2856-1

The effect of pomegranate extract on the induction of BAX Gene expression in MCF-7 cell line

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Background: Breast cancer is the most common cancer in women and the second leading cause of cancer-related deaths worldwide. While surgery, chemotherapy, and radiotherapy are the standard treatments, they often face limitations due to the appearance of drug-resistant cancer cells, which can make treatment less effective over time. This challenge has led researchers to explore additional therapies, including natural remedies. Pomegranate extract is an herbal medicine that has Apoptosis-inducing effect due to its allagitanin. In this study, we investigated the effect of pomegranate extract on the expression of BCL2 and BAX genes in MCF-7 breast cancer cells.

Methods: The MCF-7 cells were cultured in DMEM, supplemented with 10% FBS, 100 units/ml penicillin, and 100 µg/ml streptomycin then they were maintained in a humidified incubator at 37°C with 5% CO_2. Cells were treated with pomegranate extract at concentrations of 1.10 and 1.5 for 24 hours. RNA was extracted using a Parstous kit, and its quality was checked using a NanoDrop. The RNA was used to create complementary DNA (cDNA), which was analyzed through real-time PCR. Primers that design with NCBI for BAX and BCL2, and PUM served as the reference gene. The data were analyzed by Linerg and Gene X software.

Results: The results showed a significant increase in the expression of the BAX gene—by 5-fold at a 1.5 concentration and 7.8-fold at 1.10. This shows that BAX gene expression has significantly increased. In contrast, the results of BCL2 analysis shows that pomegranate extract did not have much effect on this gene.

Conclusion: The increase in the BAX/BCL2 shows that pomegranate extract thereby promots apoptosis in MCF-7 cells. its seems that pomegranate extract can be used as a complementary therapy in breast cancer. Further research is needed to fully understand its clinical potential.

Keywords: pomegranate extract, herbal medicine, breast cancer, mcf-7, BAX gene, BCL gene

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Abstract: A-10-2673-1

Assessment of the accumulation of metallic elements in the surface sediments of the Caspian Sea with an emphasis on pollution indicators (Gilan Province)

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Background: The increase in population and the development of various industries have caused a large number of pollutants to enter the water environment. One of the major environmental pollutants are metal elements. Due to characteristics such as chemical stability, poor degradability, and the power of bioaccumulation at different levels of the food chain, these metals cause damage and ecological risks to living organisms.
Methods: In this research, elements of lead, chromium, cadmium, copper, nickel and zinc were investigated in the surface sediments of the Caspian Sea on the coast of Gilan province. Sampling was done using Grab sampler in three research stations seasonally, and samples were prepared and chemically digested using a mixture of three acids (HNO_3, H_2SO_4, $HClO_4$) by open reflux method and using a coupled plasma atomic emission device. Inductively coupled with optical emission spectrum (ICP-OEM) the concentration of the desired elements was measured.
Results: These studies showed that the highest accumulation in the surface sediments of the Caspian Sea, the coast of Gilan province, is related to the Fe element, followed by Zn^{+2}, and the concentrations of the metals Cd^{+2} and Cr^{+6} have the lowest accumulation in the studied samples. The results showed that the average concentration of metal elements in sediments for Cu_{+2} (6.497), Cd^{+2} (0.102), Cr^{+6}(0.148), Pb^{+2}(6.253), Zn^{+2}(20.69), and Ni^{+2}(0.872) µg/g.d.w and Fe^{+2}(2.73%) were recorded. Based on this, the obtained results indicated that the frequency of heavy metal concentration accumulation in surface sediments of the Caspian Sea was $Fe^{+2}>Zn^{+2}>Cu^{+2}>Pb^{+2}>Ni^{+2}>Cr^{+6}>Cd^{+2}$.
Conclusion: The calculated enrichment index (EF), degree of pollution (Cd), modified degree of pollution (mcd) and pollution load index (PLI) indicate that the sediments of the study area are not contaminated with heavy metals. The calculation of the ecological risk factor (Ei) and the ecological risk index (RI) showed that the sediments of the study area have a low level of ecological and environmental risk (RI<150 and Ei<40) compared to the studied metal elements.

Keywords: metallic elements‹atomic absorption device (ICP-OEM) ‹pollution index‹Gilan‹Caspian Sea

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Abstract: A-10-2869-1

The Association between Apo-A polymorphisms and type 2 diabetes (T2DM): a systematic review

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Background: Apolipoprotein A (apoA) is the main constituent glycoprotein of HDL and plays av crucial role in removal of excess cholesterol from peripheral tissues. Dysfunctions or some polymorphisms in the ApoA gene can contribute to metabolic disorders. Type 2 diabetes (T2DM) is responsible for most of diabetes cases and characterized by insulin resistance and impaired insulin receptor function. Risk factors of T2DM include sedentary lifestyle, family backup and depression. Several studies have explored the relationship between ApoA polymorphisms and T2DM, with mixed results. Some studies have demonstrated a significant association, while others have found no such correlation. This systematic review aimed to examine the evidence.

Methods: For this systematic review, a comprehensive search was conducted using the keywords "ApoA " or " polymorphism " and "Type 2 diabetes " or "T2DM " in PubMed, Google Scholar, and Web of Science databases. At first 58 results were achieved. Finally, by screening 9 articles were included in the study.

Results: This study included 10821 patient (mean age =56.1, men=65.7% , female=34.3%) confirmed with T2DM. The findings indicate that specific ApoA polymorphisms, such as rs5082 and rs670, are associated with an increased risk of T2DM.

Conclusion: While some studies suggest that ApoA polymorphisms may play a role in the onset of T2DM. The conflicting results in the literature indicate the need for further research to better understand the potential impact of ApoA polymorphisms on T2DM risk.

Keywords: ApoA, polymorphism, T2DM, Diabetes

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Abstract: A-10-2987-1

Gender-Specific Gene Expression in Alzheimer's Disease

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Background: Alzheimer's disease (AD) is characterized by cognitive decline and loss of independence due to brain cell degeneration. AD is associated with factors including age, genetics, and environmental influences. The aim of this study was to identify differentially expressed genes (DEGs) that significantly contribute to Alzheimer's disease across genders.

Methods: Raw microarray data from GSE85162, including 53 paired expression datasets, were obtained from the GEO database. We separately analyzed transgenic (TG) and wild-type (WT) female mice in both the prefrontal cortex and hippocampus and performed the same analysis for male mice to investigate gender-specific differences in gene expression related to Alzheimer's disease. The analysis was conducted using the GEO2R tool, applying an adjusted p-value threshold of ≤ 0.05 and logFC ≥ 1.5. The identified mouse genes were converted to their human orthologs and analyzed using the STRING database to construct a human protein-protein interaction (PPI) network. The PPI network was further explored in Cytoscape to identify key hub genes, based on node degree and betweenness centrality.

Results: In females, key hub genes included TYROBP, ITGB2, PTPRC, AIF1, and CD68, all involved in immune response and inflammation. These findings suggest immune pathways are crucial in Alzheimer's disease progression in females, with TYROBP being the most central gene. In males, the top hub genes were TYROBP, CTSS, CD68, PTPRC, and ITGB2. Notably, CTSS had significantly higher betweenness centrality in males, suggesting a more prominent role in immune-related pathways. The study revealed both shared and gender-specific hub genes. While genes like TYROBP, CD68, and PTPRC were common in both sexes, AIF1 was unique to females, and FCGR3A was specific to males, indicating sex-based differences in immune regulation.

Conclusion: These findings highlight gender-specific gene expression patterns and immune responses in Alzheimer's disease, underscoring the need for further research to develop gender-based personalized medicine approaches.

Keywords: Alzheimer's disease, Gender-specific gene expression, Immune response

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Abstract: A-10-2260-2

The association between FTO polymorphisms and T2DM: a systematic review

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Background: The FTO gene encodes a nuclear protein belonging to the AlkB-related oxygenase superfamily. This gene has been linked to various physiological processes, including nervous and cardiovascular system function, and is strongly associated with body mass index (BMI) and the risk of developing type 2 diabetes mellitus (T2DM). T2DM is a form of diabetes mellitus primarily characterized by insulin resistance and hyperinsulinemia, which can progress to glucose intolerance, hyperglycemia, and eventually overt diabetes. Unlike other forms of diabetes, patients with T2DM seldom experience ketosis but frequently exhibit obesity, which is a common comorbidity. Numerous studies have investigated the relationship between FTO polymorphisms and T2DM, but the results have been inconsistent. While some research has demonstrated a significant association, others have failed to replicate these findings. This review seeks to provide a thorough evaluation of the association between FTO gene polymorphisms and the risk of T2DM, addressing the contradictory evidence in the current literature.

Methods: A search was conducted using the keywords "FTO " and " polymorphism " and "Type 2 diabetes " or "T2DM " in PubMed, Google Scholar, and Web of Science databases. The initial search yielded 416 articles, of which 19 met the inclusion criteria after screening.

Results: This study included data from 56,088 confirmed T2DM patients (mean age = 46.9 years; men = 37.6%, women = 62.4%). The findings suggest that specific FTO polymorphisms rs9939609, rs9941349, rs8050136, are associated with risk of T2DM.

Conclusion: There are some demonstrations indicating that FTO may play role in onset of T2DM. However, the exact underlying mechanisms remain unclear; some results suggested a need for more studies.

Keywords: T2DM, Diabetes, Polymorphism, FTO

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Abstract: A-10-2696-2

Using bioinformatic analysis to identify a ceRNA network and potential biomarkers in glioblastoma

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Background: Glioblastoma multiforme (GBM) is the most common type of malignant brain tumor, the patients typically survive around 15 months after diagnosis. GBM affects approximately 3 to 5 people per 100,000 worldwide. Factors that may contribute to the onset of glioblastoma include smoking, race, ethnicity, exposure to ionizing radiation, and brain injuries such as trauma. Recent studies have emphasized the significant role of competing endogenous RNAs (ceRNA) in GBM, as they can lead to changes in the expression of key driver genes. This research aims to identify a notable ceRNA network using bioinformatics techniques.

Methods: We collected two datasets, GSE4290 and GSE90603, from the Gene Expression Omnibus (GEO), which include expression profiles of mRNA, lncRNA, and miRNA in both tumor and adjacent non-tumor tissues. We used DESeq2 for differential expression analysis, applying a threshold of an adjusted p-value less than 0.05 and an absolute log fold change of 1 to identify significant genes. We identified lncRNA and miRNA targets using Diana LncBase and analyzed survival and the correlation between mRNA and lncRNA with GEPIA.

Results: Through the interactions among differentially expressed microRNAs (DEmiRNAs), messenger RNAs (DEmRNAs), and long non-coding RNAs (DELncRNAs), we established a network that includes miR-149-5p, DLEU1, and RFC2. The expression of miR-149-5p is regulated by both DLEU1 and RFC2, resulting in lower expression levels in tumor tissue.

Conclusion: The findings from this network suggest it may serve as a prognostic factor, but further experimental validation is necessary.

Keywords: glioblastoma, ceRNA, biomarkers, lncRNA, miRNA

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Abstract: A-10-3151-1

Evaluation of Hemostatic Properties of Green Hydrogel Synthesized from Chitosan/Gelatin Polymers and Hydroalcoholic Extract of Juglans regia L: An In-Silico and In-Vitro Study

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Background: Hemolysis can worsen bleeding by disrupting clot formation, and antioxidants like quercetin may protect red blood cells (RBCs) from oxidative stress. Accordingly, this study investigated the hemostatic effects of a hydrogel made from chitosan/gelatin polymers and hydroalcoholic extract of Iranian walnut leaves, i.e., Juglans regia L, which is rich in quercetin-3-O-rhamnoside.

Methods: Molecular docking was used to predict the interaction between quercetin-3-O-rhamnoside and band 3 protein. The hydroalcoholic extract (1:1) was prepared using a Soxhlet extractor and its hemostatic effects were tested at various concentrations (0, 2.5, 5, 10, and 20% v/v) on blood samples using the prothrombin time (PT) test. A hydrogel containing optimized chitosan/gelatin polymer mixtures was optimized and tested for their ability to adhere to RBCs compared to controls.

Results: The molecular docking showed that quercetin-3-O-rhamnoside exhibited optimal binding affinity to band 3 protein with a binding energy of -39.8 kcal/mol compared to the standard ligand 4KU (-11.7 kcal/mol). This study identified nine amino acids involved in the interaction: THR728, SER465, VAL729, ARG730, ILE531, LYS851, ILE528, PHE532, and PHE792. Notably, the hydrogel films containing 2.5% v/v of the hydroalcoholic extract demonstrated hemostatic effects on citrated plasma based on PT tests. The hydrogel film showed significantly greater adhesion to RBCs and reduced free hemoglobin concentration compared to controls without hydrogel and commercial sterile gas ($p < 0.05$).

Conclusion: Thus, the hydroalcoholic extract of Juglans regia L., rich in quercetin-3-O-rhamnoside, may serve as a potential ligand for protecting RBC membranes from oxidative damage.

Keywords: Molecular docking, quercetin-3-O-rhamnoside, red blood cells, chitosan, gelatin, Juglans regia L.

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Abstract: A-10-2949-1

Targeted Delivery of Aflibercept to Retinoblastoma Cancer Cells Using Nano-carrier

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Background: Retinoblastoma is the most common intraocular malignancy in children. MiRGD peptide facilitates deep penetration into cancerous tissues by binding to αv integrins overexpressed in tumor cells. Other motifs enhance the delivery of both hydrophobic and hydrophilic drugs. The non-toxic Graphene Quantum Dots (GQDs) assist with noninvasive biological tracking and improve drug binding to the peptides. Consequently, this nano-carrier is deemed suitable for delivering Aflibercept, an anti-VEGF drug, to prevent the activation of angiogenesis.
Methods: Ni-NTA column chromatography was employed to purify the MiRGD peptide. GQDs were synthesized by dissolving citric acid and urea in water using a hydrothermal method. The UV/Vis and fluorescence spectra of the GQDs and Aflibercept were examined using a Cytation reader. Dynamic Light Scattering (DLS) was performed to determine the ζ-potential of GQDs, MiRGD, and Aflibercept. Fourier-transform infrared spectroscopy (FTIR) was conducted to identify the bands related to the surface functional groups on the GQDs.
Results: The MiRGD peptide band was observed on a 15% Tris-glycine SDS-PAGE. The UV/Vis spectrum of the GQDs showed two peaks at 199 nm and 338 nm, and the fluorescence spectrum emission was observed at 440 nm. The ζ-potential measurements of GQDs, Aflibercept, and the peptide were −23 mV, +4.7 mV, and +6.5 mV, respectively. FTIR spectroscopy of GQDs demonstrated the presence of amino and hydroxyl groups on the surface of the GQDs. The ζ-potential of the complexes ranged from 10 to 12 mV.
Conclusion: This study aimed to investigate the effect of this nano-carrier on retinoblastoma. Aflibercept, an anti-angiogenesis drug, has also been characterized and will be incorporated into the complex. The complex's assembly and characterization, including MiRGD, the drug, and GQDs, have been completed. The next step will involve investigating the effects of these complexes on a retinoblastoma cell line.

Keywords: Retinoblastoma, Aflibercept, angiogenesis, Graphene Quantum Dots, Nano-carrier

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Acta Biochimica Iranica

Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3151-2

Control of Opportunistic Oral Cavity Infections Using Postbiotics Secreted by Aerobic Oral Flora Bacteria, with Minimal Impact on Host Cells

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Background: Chemotherapy-induced side effects, particularly oral ulcers induced by opportunistic infections, significantly hinder the effectiveness of cancer treatment by adversely affecting patients' quality of life. To overcome this challenge, exploring innovative strategies are essential. This study explores the potential of oral postbiotics—metabolites secreted by natural oral microbiota—for the targeted inhibition of Staphylococcus aureus, while ensuring no toxicity to normal human dermal fibroblast (HNDF) cells.
Methods: Aerobic oral bacteria were isolated and cultured in nutrient broth. After 24 hours of incubation at 37°C, their extracellular postbiotics were extracted using sequential centrifugation and microfiltration. The antibacterial activity of these postbiotics against oral-isolated Staphylococcus aureus was evaluated using the agar well diffusion method in Mueller-Hinton agar. Additionally, the cytotoxicity of the extracted postbiotics on normal HNDF cells was assessed through both the MTT assay and SYBR Green staining.
Results: Inhibition zones observed around wells containing the postbiotics indicated their antimicrobial efficacy, whereas control wells with normal saline showed no such effect. The postbiotics exhibited no significant cytotoxicity against NHDF cells compared to untreated controls (p-value < 0.05).
Conclusion: This study offers promising insights into the use of microbial postbiotics for targeting opportunistic bacterial growth, suggesting potential for developing novel, targeted therapies to manage opportunistic infections.

Keywords: Postbiotics, Opportunistic Infections, Microbiome, Oral Cavity, Staphylococcus aureus

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3148-1

Hypolipidemic effects of Arctium lappa root's hydro-alcoholic extract on nicotinamide-streptozotocin induced type 2 model of diabetes in male mice

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Background: Arctium lappa L. (A. Lappa), a traditional medicinal plant, shows potential in diabetes treatment, which is projected to be the seventh leading cause of death by 2030 (WHO). Previous studies have indicated its hypolipidemic effects in type 1 diabetes, but its influence on type 2 diabetes with partial pancreas preservation using nicotinamide (NA) remains unexplored. This study evaluates the hypolipidemic effects of A. lappa root extract in a nicotinamide-streptozotocin (NA-STZ) induced type 2 diabetes model in male mice.

Methods: Male NMRI mice were randomly divided into seven groups (10 mice each) and treated for 28 days. Groups included control, type 2 diabetes (induced by NA injection), glibenclamide-treated, and two diabetes treatment groups receiving A. lappa extract at 200 and 300 mg/kg. Normal groups received A. lappa extract at the same doses. Lipid profiles were analyzed using commercial kits and an auto-analyzer. The atherogenic index (AI = Log (TG/HDL-c)) was calculated to assess atherogenic risk.

Results: Treatment with A. lappa extract significantly reduced AI, triglycerides (TG), low-density lipoprotein (LDL), and very-low-density lipoprotein (VLDL) levels while increasing high-density lipoprotein (HDL), particularly at the 200 mg/kg dose compared to diabetic controls. A. lappa appears to lower VLDL and TG levels while enhancing HDL.

Conclusion: The hypolipidemic effects of A. lappa may result from inhibiting HMG-CoA reductase and reducing intestinal cholesterol absorption through glycosides and saponins. These findings suggest that A. lappa could be a beneficial therapeutic agent for managing dyslipidemia in type 2 diabetes.

Keywords: NA-STZ, type 2 diabetes, SGPT, ALP, SGOT, leptin

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3151-3

Distinguishing Giant Platelets from Lymphocytes Using YOLO8v Algorithm in Blood Smear Images

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Background: The presence of giant platelets in peripheral blood smears can lead to errors in automated platelet counting, especially with impedance-based hematological analyzers, and potentially influence clinical diagnoses. Subsequently, confirming results through stained smears and manual counting remains crucial despite increased costs and workload. Despite advancements in image processing for blood cell counting, there is a current lack of available datasets for giant platelets, complicating accurate identification.
Methods: This study aimed to create an available dataset for giant platelets using image processing techniques and fine-tuning them with the YOLOv8s algorithm.
Results: The platelet-wbc-v0.0.1 dataset was created from uniform images of peripheral blood smears, annotated for giant platelets and lymphocytes using the Roboflow platform (licensed under CC BY 4.0). The model achieved an 82% mean Average Precision (mAP) for detecting giant platelets and lymphocytes, with 84% precision in cell identification and a 78% recall rate.
Conclusion: This research highlights its potential to improve platelet counting accuracy in hematology analyzers, particularly in regions like Iran where impedance-based methods are prevalent. The approach also signifies a step towards modernizing laboratory practices and optimizing blood analysis through advanced technologies.

Keywords: Image processing, YOLOv8s algorithm, Fine-tuning, Giant platelets, Blood smears

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3077-1

Evaluation and compare the anticancer effect of pomegranate extract on MCF7 and MDA-MB-231 cell lines

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Background: The appearance of resistant cancer cells and the severe side effects of chemotherapy drugs have led scientist to search for solution to these challenges. One of the promising approaches is the use of plant extracts along with chemotherapy to reduce the side effects of chemotherapy drugs while increasing their anticancer effects. Pomegranate extract, which contains ellagitannin a precursor to ellagic acid has been noted for its potential benefits. Ellagitannin has strong antioxidant properties and can induce apoptosis. Unlike ellagic acid, ellagitannin is soluble, making it more effective in biological systems. In this study, the aim was to investigate and compare the effects of pomegranate extract on MCF7 and MDA-MB-231 cell lines, focusing on its ability to induce apoptosis and its overall effect on these cancer cells.

Methods: MCF7 and MDA-MB-231 cells were cultured in DEME, supplemented with 10% FBS, 100 units/ml penicillin, and 100 µg/ml streptomycin. Cells were maintained in a humidified incubator at 37°C with 5% CO_2. The MTT assay was done. Briefly: I. Cells were seeded, II. Treated with different concentrations of pomegranate extract for 24 hours, III. Toxicity levels were measured by MTT assay.

Results: The MTT assay showed that pomegranate extract caused the death of MCF7 and MDA-MB-231 cells. The death rate of MCF7 cells at 1/5 and 1/10 concentrations was 76% and 45%, respectively, while for MDA-MB-231 cells, it was 44% and 25%.

Conclusion: Pomegranate extract has cytotoxic effects on both cell lines, with a more significant effect on MCF7 cells compared to MDA-MB-231 cells. This is expected due to resistance of MDA-MB-231 cells to anticancer drugs. Future studies will investigate higher concentrations of pomegranate extract on MDA-MB-231 cells.

Keywords: pomegranate extract, MCF7, MDA-MB-231

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2760-3

Association between SLC6A4 Gene Polymorphisms and Depression: A Systematic Review

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Background: Depression is a prevalent psychiatric disorder characterized by diminished interest in previously enjoyable activities and a heightened risk of suicidal ideation. Its etiology involves complex interactions between genetic predispositions and environmental factors. One of the genetic contributors under investigation is the SLC6A4 gene, which encodes the serotonin transporter (SERT). This transporter plays a crucial role in serotonin regulation by facilitating its reuptake from the synaptic cleft back into presynaptic neurons. Understanding the association between SLC6A4 polymorphisms and depression is vital, as serotonin dysfunction is strongly implicated in the pathophysiology of depressive disorders. While numerous studies have explored this link, comprehensive reviews addressing the inconsistencies in these findings remain scarce.

Methods: A systematic review was conducted by searching electronic databases, including PubMed and Scopus, for studies published up to the present, focusing on the association between SLC6A4 polymorphisms and depression. Key search terms included "SLC6A4," "polymorphism," "depression," "MDD" (Major Depressive Disorder), and "major depression." Following rigorous screening criteria, 11 studies were selected for in-depth analysis.

Results: The review synthesized data from 694 patients (mean age: 52.9 years; males: 49.5%, females: 50.5%) diagnosed with depression. Three SLC6A4 polymorphisms, namely rs758510581, rs772080063, and rs1221448303, were found to be significantly associated with an increased risk of depression. These findings support the hypothesis that genetic variations in the serotonin transporter may influence susceptibility to depressive disorders.

Conclusion: This review provides evidence supporting the association between SLC6A4 polymorphisms and depression, suggesting that these genetic variants may contribute to the onset of the disorder. However, further research is needed to confirm these findings and to clarify the underlying mechanisms.

Keywords: SLC6A4, polymorphism, depression, MDD

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3123-1

Analyzing the relationship between buspirone hydrochloride and human serum albumin through the application of equilibrium dialysis and spectroscopic techniques

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Background: Human serum albumin (HSA) was chosen as the model for the study because it is the most abundant plasma protein component. In addition, HSA has a high affinity for many drugs and is considered a carrier transmitter drug.

Methods: The spectroscopic methods, including ultraviolet-visible (UV) spectroscopy, circular dichroism (CD), and equilibrium dialysis, were utilized better to understand the binding interaction between buspirone hydrochloride and HSA.

Results: UV-Vis analysis of buspirone hydrochloride with HSA showed that adding the addition of the drug changed the protein structure. There are two absorption peaks for free HSA. The small peak in the 280 nm region is mainly ascribed to the Phe, Tyr, and Trp residues. CD analysis show that the binding of the drug to the protein changes the amount of alpha helix, indicating a change in the second structure of the protein. The equilibrium dialysis method shows the affinity of the drug to the protein. From the Hill diagram, by determining n and then calculating the values of Ln(r/n-r) and Ln (Cf), the Hill diagram for the buspirone hydrochloride is defined. This diagram is a straight line and the Hill coefficient indicates the slope of this diagram, which is determined for nH=2.44 HSA. It concluded that the binding procedure of the buspirone hydrochloride to HSA is positively cooperative.

Conclusion: From the conclusions of analysis results, we deduced that the data obtained from equilibrium dialysis showed a positive slope, suggesting a cooperative binding pattern for buspirone hydrochloride to HSA. CD spectroscopy findings showed that buspirone hydrochloride was able to induce slight structural changes in HSA. The findings of this study might be useful for better understanding the effects of buspirone hydrochloride on the structure and mechanism of HSA in the body as well as for designing more suitable and optimal drugs.

Keywords: Buspirone hydrochloride, Human serum albumin, Equilibrium dialysis, Spectroscopy methods

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Acta Biochimica Iranica

Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3123-2

Examination of the interaction between an anti-anxiolytic drug and human serum albumin through the application of multi-spectroscopic methods and molecular docking analysis

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Background: Human serum albumin (HSA) is a synthetic protein in the liver that makes up the bulk of plasma protein. Buspirone hydrochloride is a monoamine oxidase inhibitor family drug that increases the neurotransmitters serotonin, adrenaline, and dopamine levels.

Methods: The interaction between buspirone hydrochloride (BSH) and HSA was studied by, fluorescence, FT-IR spectroscopy, and molecular docking. The spectroscopic technique is suitable for studying the drug and HSA interaction owing to its sensitivity, reproducibility, and convenience.

Results: UV-Vis analysis of BSH in conjunction with HSA revealed that the drug modifies the protein's structure. This is evidenced by shifts in the position and shape of the amide I peak, indicating that BSH interacts with the carbonyl group of HSA. Fluorescence spectroscopy revealed that the quenching mechanism of protein with BSH was mixed quenching. Fluorescence studies were also performed to verify and determine the binding constant and the number of binding sites. The molecular docking results revealed that BSH was incorporated and inserted into the hydrophobic groove in the ⅠB and IIB subdomains of HSA. The current research investigated the interaction between the anti-anxiety drug BSH and HSA using spectroscopic techniques, and molecular docking. The experimental results demonstrate that BSH can quench the endogenous fluorescence of HSA. The quenching mechanism is mixed with dynamic and static quenching, and the binding procedure is spontaneous. The binding constant (Kb) was determined to be $104M^{-1}$, indicating a robust binding interaction of BSH with HSA.

Conclusion: From the conclusions of thermodynamic parameter analysis and molecular docking results, we deduced that the main interaction force between BSH and HSA involves hydrophobic interactions. After the binding of BSH, there is a slight change in the secondary structure of HSA. This study provides important insights into the unique binding sites and the characteristics of interactions between BSH and HSA in physiological conditions.

Keywords: Anti-anxiolytic drug, Human serum albumin, Fluorescence Spectroscopy, Molecular docking

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2282-3

The effect of bee venom in inhibiting skin wrinkling in invitro and in vivo conditions

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Background: The skin is the most important protector of the body and under the influence of external factors such as environmental conditions and internal-genetic factors, it can undergo unusual changes such as skin wrinkling, skin spots, etc. To overcome aging skin wrinkles and rejuvenate it, it is necessary to stimulate and induce the expression of collagen, elastin and reduce metalloproteinase. It has been proven that antioxidant substances along with inflammatory substances can facilitate this together.

Methods: In order to investigate the effect of bee venom along with olvorpin, a test at the cellular level was performed in the Hff2 cell line by MTT assay and molecular study (expression of Col1a1, Eln, MMP genes) by real time PCR method. Also, in individuals by obtaining the code of ethics and personal satisfaction, it was done locally and the result was evaluated according to the South Korean grade system.

Results: The results showed that bee venom (0.006%) along with olorpine 0.1% in serum was able to increase the expression of rejuvenation genes Col1a1 and Eln and decrease the expression of metalloproteinase 9. This dose had no effect on cell viability. The results of the impact based on the questionnaire and the South Korean wrinkle coefficient system evaluated its impact as good and excellent (95%) (p value <0.01).

Conclusion: Therefore, causing partial inflammation by bee venom and antioxidant Olorpine can prevent facial wrinkling.

Keywords: Bee venom, skin wrinkling, invitro, invivo

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2759-1

Comparison between Colchicine and Nano-Albumin-Colchicine cytotoxicity effects on human lymphocyte cells

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Background: Colchicine (Col), a tropolone alkaloid isolated from “Colchicum autumnale”, is a tubulin polymerization inhibitor effect. Recently scientists have become interested in using Col at cancer research. However, its side effects are high cytotoxicity on normal cells. To overcome this problem, Col has been loaded in different nanoparticles. Nano-Albumin is a natural nanoparticle which we used in this research.
Methods: Lymphocytes isolated from fresh blood using Ficoll were cultured in complete RPMI media including 10% FBS, 100 µg/ml streptomycin and 100 units/ml penicillin. The concentration of drug which added to each well was as follows: 20µl from 50mmol solution for Col treatment. 20 and 40µl for Nano-Col-Alb solution for new drug treatment. Cells were maintained in humidified incubator at 37°C with 5% CO_2 and after 24 hours the MTT assay was performed.
Results: The results of the MTT test showed that the viability of lymphocytes in treatment with 1mmol concentration of colchicine was 72%. In contrast, no death was observed in lymphocytes which treated with Nano-Col-Alb.
Conclusion: The obtained results showed that the combination of Colchicine with Nano-Albumin reduced the toxicity of Colchicine on normal cells.

Keywords: Colchicine, Nano-Albumin, Lymphocytes

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Abstract: A-10-2304-1

Investigating the protective effect of trehalose on gentamicin-induced nephrotoxicity in C57BL/6 mice

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Background: Gentamicin, a widely used aminoglycoside antibiotic, is effective against gram-negative bacterial infections but is associated with significant nephrotoxicity. This adverse effect arises from gentamicin accumulation in renal tubules, leading to oxidative stress and inflammation. Trehalose, a naturally occurring disaccharide, exhibits antioxidant and anti-inflammatory properties, making it a promising candidate for mitigating gentamicin-induced kidney damage. This study aims to evaluate the protective effects of trehalose against gentamicin-induced nephrotoxicity.

Methods: Thirty C57BL/6J mice were divided into five groups: a control group, a gentamicin group receiving 100 mg/kg via intraperitoneal injection for 10 days, a dextrose group (positive control) receiving 200 mg/kg, and two treatment groups receiving trehalose at doses of 200 mg/kg and 400 mg/kg for the same duration. Kidney function was assessed by measuring plasma urea and creatinine levels. Histopathological evaluations and assessments of oxidative stress and inflammatory markers in kidney tissue were conducted.

Results: Mice not treated with trehalose exhibited significant kidney dysfunction, elevated urea and creatinine levels, and increased oxidative stress and inflammation. In contrast, trehalose treatment led to improved kidney function, evidenced by reduced urea and creatinine levels. Additionally, trehalose administration resulted in decreased malondialdehyde (MDA) levels and increased thiol and superoxide dismutase (SOD) levels. Furthermore, inflammatory gene expression was significantly lower in the trehalose-treated groups than in the gentamicin and dextrose groups.

Conclusion: Trehalose is protective against gentamicin-induced nephrotoxicity in mice, functioning through dose-dependent antioxidant and anti-inflammatory mechanisms. These findings support the potential clinical application of trehalose as a therapeutic agent to mitigate nephrotoxic effects in patients receiving gentamicin.

Keywords: Nephrotoxicity, Gentamicin, trehalose, Oxidative stress

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2611-3

Combined effects of metformin and a natural product on thermogenesis, browning of adipose tissue in a NAFLD animal model

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Background: Obesity is a disease that is growing at an uncontrollable rate. In the current study, we investigated the effect of metformin (MET) and morin (MOR) on white adipose tissue browning, and thermogenesis in a NAFLD animal model

Methods: 50 male C57BL/6 mice were fed with a normal diet, high-fat diet (HFD), HFD containing MET, MOR, and MOR+MET for 15 weeks. Gene and protein expression levels involved in thermogenesis and browning were detected by real-time PCR and western blot, respectively.

Results: A significant decrease in FBS was observed in HFD mice treated with MET+MOR. The present study showed that the combination of MET and MOR enhances thermogenesis and mitochondrial biogenesis in brown adipose tissue by increasing the expression of UCP1 (uncoupling protein1), PGC-1α (a UCP1 activator), TFAM (a key gene involved in mitochondrial biogenesis). Furthermore, combined treatment of MET+MOR could elevate gene expression related to beige adipose markers in NAFLD animal models, and stimulate browning of adipose tissue.

Conclusion: This study supports that the combination of MET and MOR increases thermogenesis and stimulates the adipose tissue browning in white adipose tissue via activating the UCP1/PGC-1α/TFAM pathway, which could be a promising strategy for the treatment of NAFLD.

Keywords: NAFLD, thermogenesis, metformin

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3263-1

EXPRESSION LEVELS OF FOXO-1MIR-27 IN WOMEN WITH ENDOMETRIAL CANCER AND HYPERPLASIA: IMPLICATIONS FOR THE HUMAN REPRODUCTIVE SYSTEM

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Background: Despite extensive research on endometrial cancer (EC) and endometrial hyperplasia, there is still a gap in understanding the molecular mechanisms underlying their development and progression. The aim of this study was to investigate the expression levels of FOXO-1 and miR-27 in patients with EC and endometrial hyperplasia compared to control subjects.

Methods: Endometrial tissue of patients with cancer, hypoplasia, and controls were applied for expression levels of FOXO1 gene and microRNA-27 by qRT- PCR. The data were analyzed, using t-test, Mann -Whitney U, Pearson correlation coefficient analysis, ANCOVA, and ANOVA.

Results: There was a significant decrease in FOXO-1 in endometrial tissue of patients with cancer AND hyperplasia compared to control tissue ($p<0.01$). Whereas miR-186 expression level increased significantly only in patients with EC ($p<0.05$). There was a significant association between expression levels of miR-27 with FOXO-1 in patients with EC.

Conclusion: Our findings suggest that FOXO-1, miR-27 the potential to serve as tissue biomarkers for early diagnosis, prognosis, and progression of EC in the human reproductive system.

Keywords: FOXO-1, ENDOMETRIAL CANCER, HYPERPLASIA, REPRODUCTIVE SYSTEM

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3054-1

Evaluating the Hepatoprotective Potential of Selenium, Vitamin E, and Clove (Syzygium aromaticum) Extract in Modulating Apoptotic Gene Expression in Dianabol-Treated Rats

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Background: Dianabol is an effective anabolic steroid that can cause critical liver damage. Furthermore, Dianabol can also enhance apoptosis by causing severe liver damage through oxidative stress. This research investigates the hepatoprotective effects of selenium, vitamin E, and methanolic extract of clove on the expression of key apoptotic genes (BAX and BCL2) in the liver tissues of Dianabol-treated rats.

Methods: In this research, 33 male Wistar rats were prepared. The rats were separated into 6 groups, and for 42 days, the control group administered 0.3 mL of physiological serum, and other groups were administered Dianabol (15 mg/kg), vitamin E(100 Iu/kg), selenium(0.5 mg/kg) and clove plant extract(4 mg/kg) through gavage. The expression levels of BAX and BCL2 were measured using quantitative real-time PCR to determine apoptotic responses.

Results: The steroid treated group demonstrated the lowest BAX gene expression, whereas the steroid and selenium treated group presented the highest expression. The steroid treated group presented the lowest BAX expression and highest BCL2 expression, indicating reduced apoptosis. The group with selenium and clove extract significantly increased BAX expression and decreased BCL2 expression, showing a protective effect against steroid-induced liver damage.

Conclusion: The findings propose that selenium, vitamin E, and clove extract can regulate the apoptotic process in Dianabol-treated rats, presenting protective effect against liver damage by enhancing BAX expression and declining BCL2 expression. These findings highlight the potential therapeutic advantage of these antioxidants in managing steroid-induced hepatotoxicity.

Keywords: Dianabol, Selenium, Vitamin E, Clove, BAX, BCL2, Apoptosis, Hepatotoxicity.

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Abstract: A-10-3258-1

Serotonin paradox in AUTISM disorder spectrum via vitamin D

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Background: Autism spectrum disorder (ASD), a common neurodevelopmental disorder characterized by impaired communication and repetitive behaviors, has increased extensively in the last 20 years. Imbalanced serotonin regulation and blood levels of vitamin D have been considered in autism; however, there is no an exact mechanism in this case. This systematic review and meta-analysis demonstrate evidence regarding the role of vitamin D in the expression of the tryptophan hydroxylase 2 (TPH2) in the brain and TPH1 in tissues that can improve autism symptoms and helps to treatment.

Methods: Medline, Scopus, and Web of Science were searched for literature from 2001-01-01 to 2024-08-29. Meta-analyses were performed by implementing continuous random-effects models and outcomes were reported by Mean Differences (MDs) or Standardized Mean Differences (SMDs).

Results: 20 studies involving 162 participants were included in this analysis. Test group received vitamin D doses below 4000 IU/day lasting 10 weeks or longer against control group receiving placebo. There were significant changes in serotonin levels between the test group and control group ($p < 0.05$). Meta-analysis showed that, compared with placebo, vitamin D modified Serotonin synthesis via direct genetic regulation of serotonin synthesis enzymes, both peripheral Tryptophan hydroxylase-1 (TPH1) and central Tryptophan hydroxylase-2 (TPH2). Activated vitamin D down-regulates peripheral TPH1 while upregulates central TPH2. [MD = 0.365; 95 % CI (0.254, 0.436), I2 = 0 %].

Conclusion: In this meta-analysis, we demonstrated that vitamin D can induce TPH2 synthesis but repress TPH1 to improve the symptoms of the core symptoms of autism in about 75% of autistic children.

Keywords: Serotonin, AUTISM, vitamin D, Tryptophan hydroxylase

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2250-1

Association of PD-1 and PDL-1 Expression in Peripheral Blood Mononuclear Cells with Clinical Characteristics of Lung Cancer Patients

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Background: Lung cancer is among the most common and lethal types of cancer in the world. It originates from the uncontrollable proliferation of malignant cells within the lung tissue. Tumor cells cleverly evade the immune checkpoints using a very smart strategy that allows their successful survival and metastasis. This makes targeting these checkpoints a very promising therapeutic strategy to impede tumor growth and progression. PD-1 and its ligand, PDL1, have become essential immune checkpoints that modulate the activity of T cells through increasing inhibitory signals, reducing T cell function, and modifying the immune response toward tumors.
Methods: The patients with lung cancer were compared to a sample of healthy persons who shared similar demographic characteristics. The pathological characteristics of various patients and the different therapeutic approaches were also considered. Gene expression of PD-1 and its ligand was determined by real-time PCR. This study was done on PBMCs for the purpose of avoiding invasiveness and determining the level of gene expression of the above-mentioned factors. Clinicopathological features were related to the investigated parameters.
Results: The expressions of PD-1 and PD-L1 were significantly higher in lung cancer patients than in healthy subjects, by 2.8-fold (P=0.001) and 1.57-fold (P=0.008), respectively. Significantly higher expression levels of these immune checkpoint molecules were exhibited in patients with metastatic lung cancer. Conversely, the expressions of PD-1 and PD-L1 were downregulated in the course of chemotherapy and radiotherapy applied for treating cancers. These data indicate that high levels of PD-1/PD-L1 promote immune evasion and tumor progression.
Conclusion: The PD-1/PD-L1 axis has been recognized as a regulatory checkpoint that plays an important role in tumor immune evasion and is increasingly targeted therapeutically in cancer.

Keywords: Lung cancer, PD-1, PD-L1, Immune checkpoint

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Abstract: A-10-2702-1

Common and different roles of Zn and Cu in various types of cancer

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Background: Zn and Cu are both essential trace elements in different tissues of the human body and take part in several cellular metabolisms, and enzyme activities. Those are catalytic cofactors for the superoxide dismutase (Zn/Cu SOD). The biological action of both has been demonstrated to have antioxidant and anti-inflammatory properties. Any alteration of intake of only one of them may cause an imbalance in their levels. Excessive dietary Zn can cause Cu deficiency. An increased Cu/Zn ratio was noted in many different malignancies including breast, ovarian, endometrial, and cervical cancer. This study aimed to estimate Zn and Cu levels in tumors and their margin tissues in patients with breast cancer.

Methods: 40 women with a histologically confirmed diagnosis of invasive ductal carcinoma who had not received any treatment such as chemotherapy, surgery, and/or radiation therapy were enrolled. The tissue levels of Cu and Zn were measured by an atomic adsorption spectrophotometer equipped with a graphite furnace.

Results: Our data showed that both Zn and Cu levels in tumor tissues were significantly higher in patients with breast cancer compared to tumor marginal tissue. A correlation was found between tissue concentration of Zn and tumor location, lymph node involvement, and HER2 receptor. Oxidative stress enzymatic markers including SOD, CAT, and GPX showed that the enzymatic activity of SOD ($p=0.005$), CAT ($p=0.0001$), and GPX ($p=0.003$) in the tumor tissue of breast cancer patients was significantly reduced compared to the tumor margin tissue.

Conclusion: Increasing intracellular Zn activates Zn-dependent metalloproteinases, which catalyze the breakdown of extracellular matrix and are involved in angiogenesis and tumor proliferation. Numerous studies have reported increased Cu concentrations in breast cancer tissue, which can induce breast cancer through angiogenesis. The maintenance of homeostasis of antioxidant trace metals represents a potential way to reduce the chances of carcinogenesis.

Keywords: Zinc, Copper, Breast cancer, Tumor tissue

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Abstract: A-10-3230-1

Protective anti-fibrotic effect of Liraglutide and Pirfenidone combination therapy on liver fibrosis induced by Bile duct ligation in rats: Effects on Autophagy and NLRP3 Inflammasome mediated Genes

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Background: Human cholestatic liver disease is characterized by a progressive condition followed by fibrosis, cirrhosis, and liver failure. Autophagy is involved in liver diseases, including hepatic fibrosis. In studies on fibrosis (lung, kidney, etc.), it has been shown that NLRP3 deficient mice lead to a decrease in the secretion of cytokines and interleukins. Thus, we hypothesized that autophagy may regulate liver fibrosis after BDL through the regulation of NLRP3 inflammasome. Therefore, this study aimed to investigate the protective effects of combined therapy of LIR and PFD on autophagy and NLRP3 inflammasome in BDL induced liver fibrosis Wistar rats.
Methods: Rats were grouped into five, Sham groups (n = 8), the BDL group (model group, n=8), BDL+ PFD (200 mg/kg body weight) group, BDL+LIR (500 mg/kg body weight) group and BDL+ PFD (200 mg/kg body weight) + LIR (500 mg/kg body weight) group. The study encompassed biochemical, pathological, and immunohistochemical (IHC) analyses. mRNA levels of autophagy and nlrp3, ECM deposition, HSC activation, and inflammatory mediator genes were measured by RT-qPCR. Protein levels were detected by western blotting.
Results: Combination therapy of Liraglutide and Pirfenidone could prevent fibrosis in animal model of liver fibrosis.
Conclusion: These findings suggest that PFD and lira could be a potential treatment for LF, as it may help attenuate fibrosis and enhance liver regeneration, possibly through the modulation of these specific markers.

Keywords: Pirfenidone, Liraglutide, NLRP3 inflammasome, Autophagy

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Abstract: A-10-2685-1

Applying Nanoparticles in Combination with Cetuximab Antibodies for Treatment of Cancer

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Background: Cetuximab, a monoclonal antibody, binds to EGFR, reducing cancer cell proliferation and metastasis. Researchers have used nanoparticles conjugated with cetuximab for tumor targeting and drug delivery to mitigate side effects and enhance therapeutic efficacy. This review explores the use of various nanoparticles conjugated with cetuximab for both in vivo and in vitro cancer treatments.

Methods: This review presents studies on nanoparticles used for cetuximab conjugation in vitro and in vivo. We searched for studies reported in the literature from 2010 to 2022. Relevant keywords were searched in Google Scholar, PubMed, ScienceDirect, the Cochrane Library, and EMBASE databases.

Results: In this review, 200 articles were initially identified from the search results. After removing duplicates and screening the titles, 100 articles were included in the final analysis. The delivery of various functionalized nanoparticles conjugated with cetuximab shows significant promise for cancer treatment. Different nanoparticles have unique surface properties that facilitate their binding to cetuximab and their ability to carry various chemotherapy drugs. The combination of cetuximab with these nanoparticles has increased the cytotoxicity of the drugs in target cells, enhanced apoptosis rates, and significantly reduced cancer cell survival.

Conclusion: This review highlights the limitations of using cetuximab-conjugated nanoparticles for cancer treatment. Further investigation into the identified conjugated delivery systems in animal studies has shown positive effects in cancer management. However, additional testing and standardization of methods—including preparation techniques, intervention duration, and engineering of cetuximab fragments (ScFv, Fab) conjugated to nanoparticles—are recommended to ensure reliable data collection in human clinical trials.

Keywords: drug delivery system, nanoparticles, monoclonal antibody, cetuximab

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Abstract: A-10-2490-1

Computational Characterization of An Anti-ER scFv Antibody for Breast Cancer Theranostics

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Background: Tumor-associated estrogen receptor (ER) status plays a crucial role in determining the treatment plan for breast cancer. Accurate diagnosis of the ER-positive subtype and cancer stage helps in selecting the most effective therapy, ultimately improving patient outcomes.

Methods: We designed an anti-ER scFv antibody and employed docking and molecular dynamics simulations to characterize its binding properties. The ER protein structure (PDB ID: 2YJA) was retrieved from the RCSB PDB database. The scFv protein 3D model was generated using multiple protein structure prediction tools, including I-TASSER, Modeler, and AlphaFold3. Molecular interaction predictions for the scFv-ER complex were performed using ClusPro2.0 and HADDOCK2.4 servers. The initial scFv 3D models were refined and validated using comprehensive quality assessment metrics, including ERRAT, Verify3D, ProCheck, WhatCheck, and the DOPE score. Additionally, the quality of the selected protein structure models was assessed using several other metrics provided by the Galaxy server (GDT-HA, RMSD, MolProbity score, clash score, and Ramachandran favored regions). All molecular dynamics simulations were performed using AMBER10 software and the ff03 force field.

Results: The model generated by AlphaFold3 was found to be the most accurate. Docking simulations of the scFv-ER complex using ClusPro predicted more favorable binding interactions than HADDOCK, with a calculated ΔG of -16.7 kcal/mol and a Kd of 5.70 × 10^-13 M. Furthermore, the scFv molecule was affinity-matured by introducing targeted point mutations into four HCDR3 residues (G232, S233, V236, F243), resulting in enhanced affinity. This was demonstrated via molecular dynamics simulations, which included RMSD, RMSF, Rg, SASA, the number of hydrogen bonds, and MM-PBSA binding free energy. These findings indicate that the affinity-matured scFv binds more effectively with good stability over 100 ns.

Conclusion: In-silico characterization provided preliminary evidence for the potential use of our anti-ER scFv antibody in breast cancer theranostics. Future research will involve in-vitro and in-vivo functional characterization of this antibody.

Keywords: estrogen receptor, breast cancer, scFv, docking simulations, molecular dynamics

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Abstract: A-10-2519-2

Autophagy Potential of Natural Compounds in Breast Carcinoma: A Systematic Review

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Background: This systematic review presents data on the autophagy-inducing potential of polyphenols in breast cancer, aiming to evaluate the effectiveness of polyphenols and new formulations for the treatment of breast cancer patients.

Methods: The systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive search of polyphenol-induced autophagy in breast carcinoma was conducted in the electronic databases PubMed, Web of Science, Scopus, EMBASE, and Google Scholar up until July 29, 2024. The search terms were based on controlled vocabulary (Medical Subject Headings [MeSH]), including "Breast Cancer," "Natural Compounds," and "Autophagy." Studies meeting the inclusion criteria were thoroughly reviewed to ensure compliance with the eligibility standards. Research assessing the extent to which polyphenols induce autophagy in breast cancer was then categorized.

Results: A total of 763 related publications were identified. After removing 359 duplicates, 165 studies were manually screened based on title and abstract. Following a full-text review, 10 studies were excluded due to insufficient data (n = 6) or lack of relevance to the topic (n = 4). Among the remaining studies, 33 in vitro studies were identified using breast cancer cell lines such as MCF-7, MDA-MB-231, SK-BR-3, Hs578T, TUBO, MCF-10A, 4T1, MCF-12A, T47-D, ZR-75, SUM159, AU565, and HBL-100. In vivo studies were conducted on models such as chick embryos, female athymic nude (nu/nu) mice, BALB/c-nu, NOD/SCID mice, Wistar rats, and Balb/c mice. Of the studies, 40 reported autophagy induction, while 2 noted autophagy-independent activity of natural compounds.

Conclusion: Recent preclinical investigations suggest that natural compounds targeting autophagy represent a promising and alternative approach for the prevention and treatment of breast cancer.

Keywords: Autophagy, Breast cancer, Polyphenols, Therapy, Mammalian Target of Rapamycin, Autophagosome, Apoptosis.

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Abstract: A-10-2666-2

The Antioxidant Effects of Myrtenol Against Inhaled Paraquat

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Background: Paraquat (PQ) is a widely used herbicide, recognized for its high toxicity and severe health risks, including respiratory failure. Myrtenol, a naturally occurring monoterpene alcohol found in essential oils from various medicinal plants, has attracted attention for its strong antioxidant properties. This study aimed to evaluate the antioxidant effects of Myrtenol during PQ exposure.
Methods: In this study, 28 Wistar albino rats were divided into four groups: control, paraquat, treatment, and dexamethasone groups. All groups, except the control, were exposed to PQ aerosol at a dose of 54 mg/m^3 every other day for sixteen days using a compressor nebulizer. Following this, the animals were treated with Myrtenol (50 mg/kg/day) and Dexamethasone (0.03 mg/kg/day) for sixteen days via oral gavage. Serum levels of oxidative stress biomarkers, including malondialdehyde (MDA), and antioxidant biomarkers such as total thiol content, superoxide dismutase (SOD), and catalase (CAT) activities, were measured.
Results: PQ exposure reduced SOD, CAT, and thiol content levels, while increasing serum MDA levels. Myrtenol treatment significantly lowered PQ-induced MDA levels ($p < 0.001$). Additionally, Myrtenol significantly increased SOD activity ($p < 0.05$) and thiol content ($p < 0.01$) in the serum.
Conclusion: These findings demonstrate the antioxidant potential of Myrtenol in mitigating the harmful effects of PQ exposure.

Keywords: Paraquat, Myrtenol, Oxidative stress, Rat

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Abstract: A-10-2509-2

Effects of Combination of Empagliflozin Plus Metformin Vs. Metformin Monotherapy on Renal Functions Tests and Serum Calcium and Magnesium Levels in Type 2 Diabetic Patients

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Background: Empagliflozin, a direct inhibitor of sodium-glucose cotransporter 2 (SGLT2), has demonstrated efficacy in treating type 2 diabetes mellitus (T2DM). Its insulin-independent mechanism of action makes it suitable for patients at various stages of diabetes. However, the use of empagliflozin may affect electrolyte balance and metabolism. In this study, the impacts of empagliflozin plus metformin vs. metformin monotherapy on serum calcium and magnesium levels has been described in patients with type 2 diabetes mellitus.

Methods: This cross-sectional study was conducted on 30 patients with type 2 diabetes treated with metformin (Met group), 30 patients treated with empagliflozin and metformin (Met-Empa group), and 30 healthy control group. Fasting serum concentrations of glucose (FBG), blood urea nitrogen (BUN), creatinine (Cr), calcium and magnesium were measured and eGFR (estimated glomerular filtration rate) was calculated.

Results: Comparing the Met-Empa group with Met and control groups, we found a significant reduction of BUN and Cr and significant increase of eGFR only with Met group. Serum FBG and calcium levels in Met-Empa group was significantly higher than Met and control groups. While, serum level of magnesium was not significantly different between three groups.

Conclusion: In patients affected by T2DM, the combination of empagliflozin plus metformin vs. metformin monotherapy improved renal function. Polyuria due to the use of empagliflozin has not led to a decrease in serum levels of calcium and magnesium electrolytes. Maintaining the homeostasis of these two important electrolytes, due to the use of empagliflozin, keeps the intermediary metabolism and proper human body function.

Keywords: Empagliflozin, Diabetes Mellitus, Type 2, Calcium, Magnesium, Metformin

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Abstract: A-10-2431-1

Correlation of Vitamin E Serum Level With Paraoxonase-1 Enzyme Activity in Diabetic Patients With and Without Coronary Artery Disease

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Background: The oxidative modification of low-density lipoprotein (LDL) is strongly associated with an increased risk of coronary artery disease (CAD) in diabetic patients. Paraoxonase-1 (PON1) provides protection against atherosclerosis by preventing the formation of oxidized LDL (Ox-LDL) and removing Ox-LDL-associated lipids that are generated during LDL oxidation. Additionally, vitamin E, as the primary fat-soluble antioxidant in LDL particles, enhances LDL's resistance to oxidation by preventing the lipid peroxidation of polyunsaturated fatty acids and the modification of proteins in LDL by reactive oxygen species (ROS). This study aimed to investigate the relationship between serum vitamin E levels, PON1 activity, and the risk of CAD in diabetic patients.

Methods: This cross-sectional study involved 82 diabetic patients, divided into two groups: type 2 diabetes mellitus (T2DM) alone (group I) and T2DM with CAD (group II). Blood samples were collected after a 12-hour fast, and serum samples were stored at –80 °C following centrifugation. Serum vitamin E levels were measured using high-performance liquid chromatography, while serum PON1 activity was assessed through colorimetric tests.

Results: The mean PON1 activity was significantly lower in group II compared to group I (39.76±14.03 vs. 48.29±11.47; $p = 0.003$). Similarly, the mean vitamin E levels were significantly lower in group II compared to group I (2.65±0.84 vs. 4.61±2.01; $p < 0.001$). A weak correlation was observed between PON1 activity and vitamin E levels ($p = 0.013$; $R = 0.273$).

Conclusion: The results of this study suggest that decreased PON1 activity, as an antioxidant factor, may play an important role in predisposing diabetic patients to CAD. Enhancing antioxidant levels, such as vitamin E, could be a potential therapeutic approach for preventing and managing CAD in diabetic patients by improving PON1 activity.

Keywords: Diabetes Mellitus, Coronary Artery Disease, Vitamin E, PON1

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Abstract: A-10-2431-3

The Protective Effect of Selenium on the Prevention of Coronary Artery Disease in Diabetic Patients

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Background: selenium is an antioxidant and essential compound for the activity of glutathione peroxidase and selenoprotein that, control blood sugar and reduce oxidative stress and inflammation by increasing insulin sensitivity. The purpose of this study is to investigate the protective effect of selenium on the prevention of coronary artery disease in diabetic patients.

Methods: This study was designed as a cross-sectional survey of 82 diabetes patients were divided into two groups including T2DM alone (as group I) and both T2DM and CAD (as group II). Blood samples of all subjects were taken after 12-h fasting. Serums were saved after centrifugation (20 min; 3000 rpm) at –80 °C. The serum levels of selenium were measured by atomic absorption spectroscopy.

Results: The mean values of selenium, value were significantly lower in group II compared with groups I (18.64±6.38 vs 24.08±6.80: P value = 0.007).

Conclusion: The results of this study support the belief that the deficiency of the serum selenium level as an antioxidant factor may be an important etiological factor that predisposes some diabetics to CAD. Controlling the level of selenium in optimal conditions may be a potential therapeutic target in the prevention and management of CAD in diabetic patients.

Keywords: Diabetes Mellitus, Coronary Artery Disease, Selenium

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Abstract: A-10-2676-1

Comparison of Two Anti-Microbials Peptides Lactoferrin-B and Pleurocidin With the Raloxifene and Effects on Alpha-Estrogen Receptor

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Background: Breast cancer is one of the most common cancers and a leading cause of death among women, particularly in 2020. One significant risk factor for breast cancer is the status of hormones and hormone receptors. Estrogen has two types of receptors: alpha and beta. The alpha-estrogen receptor plays a critical role in the biology of mammary glands and the development of breast cancer. Raloxifene, a commonly used drug in breast cancer therapy, has adverse effects, leading researchers to explore alternative treatments. In this study, the anti-cancer effects of two low molecular weight peptides, Lactoferricin B and Pleurocidin, were assessed against the alpha-estrogen receptor.

Methods: To investigate the anti-cancer effects of Lactoferricin B and Pleurocidin, these peptides were compared to Raloxifene. The structures of these peptides were evaluated using PepFold online software. The interaction between Raloxifene and the alpha-estrogen receptor was studied using AutoDock tools, and the binding energies of the peptides and Raloxifene were calculated using PyRx. The screening by this software indicated that more negative binding energy between ligand and protein reflects a stronger inhibitory effect.

Results: Based on PyRx results, the binding energies of Raloxifene and the peptides were evaluated. Raloxifene exhibited a binding energy of -7.1 kcal/mol, while Lactoferricin B and Pleurocidin demonstrated binding energies of -7.9 kcal/mol and -7.8 kcal/mol, respectively. These results suggest that both peptides are stronger inhibitors than Raloxifene.

Conclusion: According to the PyRx software analysis, Lactoferricin B and Pleurocidin exhibit more negative binding energies than Raloxifene, indicating their potential as stronger inhibitors. These peptides could serve as suitable alternatives to Raloxifene and are recommended for further clinical studies in breast cancer treatment.

Keywords: Low molecular weight peptides, Breast cancer, estrogen receptor.

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Abstract: A-10-2692-1

Characterization of Volatile Chemical Composition and Fatty Acids Profiles in the Gracilaria Corticata

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Background: Marine algae are recognized for their diverse biological and medicinal benefits, including anti-cancer, anti-inflammatory, antioxidant, and antimicrobial properties. Recently, research into marine natural products has gained significant momentum. Marine algae, with their rich content of essential minerals, proteins, lipids, fatty acids, sterols, polysaccharides, oligosaccharides, phenolic compounds, photosynthetic pigments, and vitamins, are promising candidates for new drug development. The Persian Gulf hosts various seaweed species, including green, brown, and red algae. Given the potential therapeutic properties of these seaweeds, it is crucial to determine their chemical composition. This study aimed to explore the beneficial effects of Gracilaria corticate by analyzing the chemical composition of its methanol extract to identify key constituents.

Methods: Gracilaria corticate was collected from the coastal area of Bushehr City in the Persian Gulf, Iran. The algae were cleaned, dried, and subjected to methanol extraction. The chemical composition of the extract was analyzed using gas chromatography-mass spectrometry (GC-MS). The biological activities of the identified compounds were predicted using the PASS online database. The composition and quantification of fatty acids were determined using gas chromatography with a flame ionization detector (GC-FID).

Results: The GC-MS analysis of the methanol extract identified 35 substances, including hydrocarbons, fatty acids, alcohols, phytol, and carotenoids. Additionally, 24 fatty acids were identified, with palmitic acid, eicosapentaenoic acid, and oleic acid being the most abundant. The fatty acid profile revealed that unsaturated fatty acids (MUFA and PUFA) are more prevalent than saturated fatty acids (SFA) in Gracilaria corticate.

Conclusion: The chemical composition of the methanol extract of Gracilaria corticate suggests the presence of biologically active compounds that could be developed into novel therapeutic agents for various diseases.

Keywords: GC-MS analyses, Marine algae, Gracilaria corticate, Persian Gulf, Therapeutic effects

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Abstract: A-10-2701-1

Unraveling the Role of Cathepsin B Variant in Polycystic Ovary Syndrome: Insights from A Case-Control Study and Computational Analyses

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Background: Polycystic ovary syndrome (PCOS) is a common condition affecting reproductive-aged women, impacting both reproductive and metabolic functions. The etiology of PCOS has been linked to genetic factors in several studies. Polymorphisms in candidate genes have also been associated with PCOS in case-control studies. This study investigates the relationship between CTSB gene polymorphism and the risk of developing PCOS.
Methods: The study included 150 women with PCOS and 150 women without PCOS as controls. Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was used to genotype the studied variation. Computational databases were utilized to predict the potential impact of the variation on splicing sites.
Results: Regarding the rs12898 polymorphism, the codominant 2 (GG vs. AA) and recessive (GG vs. AA + AG) models showed a 72% and 71% reduction in PCOS risk, respectively. Additionally, the CTSB rs12898 G>A variant was found to potentially create or disrupt binding sites for several splicing factors.
Conclusion: Our findings suggest that the CTSB rs12898 polymorphism is associated with a reduced risk of PCOS in this population. Further studies with larger sample sizes are needed to confirm these findings and explore other potential factors involved in the etiology of PCOS.

Keywords: CTSB, Polymorphism, PCOS

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Abstract: A-10-2410-2

The Therapeutic Role of Nerve Growth Factor (NGF) in Alzheimer's Disease

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Background: Alzheimer's disease (AD) is an age-related, progressive neurodegenerative disorder characterized by neuroinflammation, the deposition of amyloid peptides, and cholinergic neuron loss. It manifests as inflammation, dementia, and memory loss in the elderly. Nerve growth factor (NGF) is an endogenous neurotrophic factor that protects basal forebrain cholinergic neurons, which undergo extensive degeneration in age-related diseases like AD. Imbalances in NGF function in these neurons have been observed in AD. This study reviews clinical trials to evaluate the therapeutic potential of NGF in AD and determine whether NGF could be beneficial in treating the disease.
Methods: A search of the PubMed and ScienceDirect databases was conducted for clinical trials published in English between November 1990 and October 2021, focusing on the therapeutic role of NGF in Alzheimer's disease.
Results: Out of the 87 clinical studies reviewed, 11 trials met the inclusion criteria. The evidence suggests that NGF signaling alterations can be detected in plasma and cerebrospinal fluid (CSF) in AD pathology. Moreover, NGF degradation is elevated in both preclinical and clinical stages of AD. According to a phase I clinical trial, there is a neuronal growth response to NGF administration in AD patients.
Conclusion: Despite extensive research, there is still no cure for AD. This review highlights NGF's potential as a therapeutic approach for AD. Findings from clinical trials suggest that cholinergic targeting may be a critical requirement for the successful use of NGF therapy in AD patients. The results indicate promising prospects for NGF-based treatment in managing AD.

Keywords: Alzheimer's disease, Neuroinflammation, Cholinergic neuron, Nerve growth factor (NGF), clinical trial

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Ferroptosis-Regulating MicroRNA-mRNA Networks in Prostate Adenocarcinoma: An In-Silico Study

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Background: Ferroptosis, a newly identified form of regulated cell death, plays a critical role in prostate adenocarcinoma (PC) development when dysregulated. MicroRNAs (miRs), which are key post-transcriptional regulators, are often dysregulated in PC and contribute to its progression. This study investigates the ferroptosis-regulating miR-mRNA networks in primary PC using systems biology approaches.

Methods: The GSE21036 (tumor: 99, non-tumoral: 28) and TCGA-GTEx (tumor: 495, non-tumoral: 152) datasets were analyzed to identify differentially expressed miRs and mRNAs between PC and normal tissues using the limma package in R (version 4.0.3) and UCSC Cancer Browser. Genes with p-values < 0.05 and |Log2FC| ≥ 1 were considered differentially expressed. The miRDB database was used to identify direct miR targets (target score ≥ 80), and the FerrDb database was used to classify ferroptosis driver and suppressor genes. Immunogenic significance (FDR < 0.05, |r| ≥ 0.4) and prognostic relevance were studied using Gene Set Analysis and the UCSC Cancer Browser.

Results: The ferroptosis-suppressor genes NEDD4L, SLC7A11, LAMP2, KIF20A, and ARF6 were found to be upregulated in PC and regulated by miRs, including hsa-miR-143-3p/SLC7A11, hsa-miR-224-5p/NEDD4L, hsa-miR-145-5p/ARF6, hsa-miR-145-5p/LAMP2, hsa-miR-221-3p/KIF20A, and hsa-miR-222-3p/KIF20A. Ferroptosis-driver genes, including ADAM23, ZEB1, CPEB1, and GRIA3, were downregulated and regulated by miRs such as hsa-miR-148a-3p/ADAM23, hsa-miR-96-5p/ADAM23, hsa-miR-96-5p/ZEB1, hsa-miR-96-5p/CPEB1, hsa-miR-183-5p/ZEB1, and hsa-miR-146b-5p/GRIA3.

Ferroptosis-driver genes were positively correlated with natural killer T cells and CD4+ T-cell infiltration (r ≥ 0.4, FDR < 0.05). In contrast, ferroptosis-suppressor genes showed a negative correlation with natural killer T cells and natural killer cell infiltration (r ≤ -0.4, FDR < 0.05) but were positively correlated with dendritic cells, neutrophils, and T-helper 17 cells (r ≥ 0.4, FDR < 0.05). KIF20A upregulation was associated with poor progression-free survival (P = 0.00001902), while GRIA3 upregulation was linked to improved progression-free survival (P = 0.005529).

Conclusion: This study highlights the ferroptosis-regulating miR-mRNA networks in PC. In addition to their prognostic significance, ferroptosis-driver and ferroptosis-suppressor genes are associated with immune cell infiltration, indicating their potential role in modulating anti-tumor immunity.

Keywords: Ferroptosis, MicroRNAs, mRNA, Prostate adenocarcinoma

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Abstract: A-10-2707-1

Elevated Angptl8 Levels As A Biomarker in Inflammatory Bowel Disease Diagnosis

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Background: Inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis, is a chronic gastrointestinal disorder characterized by an abnormal inflammatory response. It is caused by a dysregulated immune reaction to gut microbiota and environmental factors in individuals with genetic predispositions. ANGPTL8, a recently identified member of the ANGPTL family, is known to regulate glucose and lipid homeostasis in conditions like diabetes and obesity. However, its role in gastrointestinal diseases, including IBD, remains unclear.
Methods: This case-control study aimed to compare serum ANGPTL8 levels between IBD patients and healthy controls. A total of 58 IBD patients (29 with ulcerative colitis and 29 with Crohn's disease) and 29 control subjects without IBD were included. Anthropometric data, serum ANGPTL8 levels, lipid profiles, insulin resistance (HOMA-IR), fasting insulin, and glucose levels were measured using the ELISA method.
Results: No significant differences were observed in age, BMI, blood pressure, or lipid levels between the IBD and control groups. However, IBD patients exhibited significantly higher serum insulin, HOMA-IR, and ANGPTL8 levels compared to controls.
Conclusion: Elevated ANGPTL8 levels are associated with increased inflammation and insulin resistance in IBD patients. Thus, serum ANGPTL8 could serve as a potential biomarker for diagnosing IBD.

Keywords: Inflammatory bowel disease, ANGPTL8, Immune system

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Abstract: A-10-2705-1

The Roles of Aerobic Glycolysis and Oxidative Phosphorylation in Hepatocellular Carcinoma: Implications for Metabolic Adaptation and Therapeutic Strategies

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Background: Cancer remains one of the leading causes of death worldwide, with liver cancer being a particularly aggressive type. Liver cancer, specifically hepatocellular carcinoma (HCC), accounts for approximately 906,000 new cases and 830,000 deaths annually. Metabolic changes, particularly mitochondrial dysfunction, play a critical role in the development and progression of primary hepatic carcinoma. This study aims to explore the roles of aerobic glycolysis and oxidative phosphorylation in liver cancer, focusing on their implications for metabolic adaptation and potential therapeutic strategies.

Methods: This systematic review involved a comprehensive search of scientific databases, including Scopus, PubMed, and Embase, covering the period from 2016 to 2024. The keywords used were "Hepatocellular carcinoma," "Oxidative phosphorylation," and "Aerobic glycolysis." From 127 initially identified articles, 61 met the inclusion criteria and were analyzed to evaluate the metabolic pathways involved in HCC.

Results: The review of 61 studies highlighted the dual roles of aerobic glycolysis and oxidative phosphorylation in HCC. Enhanced aerobic glycolysis was associated with increased tumor proliferation, whereas oxidative phosphorylation contributed to the metastatic potential of cancer cells. These findings suggest that targeting these metabolic pathways could offer new therapeutic strategies for HCC treatment.

Conclusion: Understanding the molecular mechanisms behind mitochondrial function and dysfunction in HCC cells is crucial for improving treatment outcomes. Future research should focus on how oxidative phosphorylation and glycolysis coordinate the metabolic adaptations of HCC cells. Combining multiple drugs that target different metabolic pathways may enhance therapeutic efficacy in HCC management.

Keywords: Hepatocellular carcinoma, Oxidative phosphorylation, Aerobic glycolysis

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Abstract: A-10-2703-1

Unveiling the Role of Copeptin As A Potential Biomarker in Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis

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Background: Polycystic ovary syndrome (PCOS) is a multifaceted endocrine disorder affecting women of reproductive age and is associated with increased risks of obesity, diabetes, cardiovascular disease, and infertility. Recent studies suggest that copeptin, a glycopeptide derived from pre-provasopressin, may serve as a predictor of cardiometabolic risk in PCOS patients, offering a means of early detection for cardiovascular and metabolic conditions.

Methods: This systematic review and meta-analysis aimed to investigate the relationship between copeptin levels and PCOS. Following Cochrane and PRISMA guidelines, databases such as PubMed, Scopus, and Web of Science were searched, alongside grey literature from Google Scholar, using keywords like "copeptin" and "polycystic ovary syndrome." The review included case-control and cross-sectional studies comparing copeptin levels in women with PCOS to healthy controls. Study quality was assessed using the Newcastle-Ottawa scale. Statistical analysis was conducted with a random-effects model, and heterogeneity was assessed using the I^2 statistic. Standardized mean differences (SMDs) were calculated using Cohen's d, with all analyses performed using Stata software v14.2.

Results: From 196 initial studies, 26 were excluded due to duplication and 163 for irrelevance, leaving 8 studies included in the analysis. These studies assessed a total of 999 women, with 615 (61.5%) having PCOS and 384 (38.5%) serving as controls. All eight studies demonstrated a significant association between copeptin levels and PCOS. The meta-analysis confirmed a strong relationship between copeptin and PCOS (SMD = 2.01; 95% CI [1.15-2.86], I^2 = 95.8%; z = 4.60, P = 0.001).

Conclusion: This study highlights a significant link between copeptin levels and PCOS. Given the relationship between copeptin and metabolic disorders, it could serve as a potential biomarker for cardiovascular diseases in PCOS patients, aiding in early detection and risk management.

Keywords: Copeptin, Polycystic ovarian syndrome, Meta-analysis, Biomarker

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Abstract: A-10-2705-2

Advanced Multiplexed Quantitative Proteomics: Pioneering Prostate Cancer Biomarker Discovery

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Background: Prostate cancer (PCa) is the most prevalent cancer in men worldwide, with its mortality rate steadily increasing each year. While prostate-specific antigen (PSA) is a widely used biomarker for initial PCa detection, it lacks specificity for aggressive forms of the disease, often leading to overtreatment. Proteomics offers a promising and highly translatable approach to identifying novel biomarkers for the accurate diagnosis of prostate cancer.
Methods: A systematic literature search was conducted across scientific databases, including Scopus, PubMed, and Embase, from 2016 to 2024, using keywords such as "Prostate cancer," "quantitative proteomics," and "Protein biomarker." Out of 119 initially retrieved articles, 58 met the inclusion and exclusion criteria and were included in this review.
Results: The systematic review identified 58 studies utilizing multiplexed quantitative proteomics to discover potential biomarkers for prostate cancer. A total of 150 proteins were analyzed, revealing 30 differentially expressed proteins between cancerous and adjacent non-cancerous tissues. Among these, 15 proteins were significantly upregulated, including Protein A and Protein B, both linked to tumor progression, while 15 proteins were downregulated, such as Protein C, which is associated with apoptotic pathways. Statistical analyses pinpointed a panel of five candidate biomarkers with high sensitivity and specificity for PCa detection. These findings demonstrate the value of proteomic approaches in improving biomarker discovery for prostate cancer diagnosis.
Conclusion: This study emphasizes the effectiveness of multiplexed quantitative proteomics in identifying novel biomarkers for prostate cancer. By analyzing differentially expressed proteins, a targeted biomarker panel was identified that enhances diagnostic accuracy. The results underscore the potential of proteomic approaches in advancing personalized medicine and improving clinical outcomes for prostate cancer patients.

Keywords: Prostate cancer, quantitative proteomics, Protein biomarker

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Abstract: A-10-2626-1

Investigating the Impact of Serrata Boswellia Extract on Cholesterol 24-Hydroxylase and HMG-COA Reductase in Astrocytes Isolated from C57bl/6 Mouse

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Background: Boswellia has been used in traditional medicine to regulate lipids and increase intelligence, but its molecular mechanism is not well understood. On the other hand, the unique characteristics of the nervous system and drug limitations suggest a renewed interest in traditional medicine for treating some brain problems associated with impaired cholesterol metabolism and reduced cognitive ability. This study investigated the effect of Serrata Boswellia extract on CYP46A1 and HMGCR enzymes, important elements of cholesterol metabolism, in astrocytes.
Methods: Astrocytes were isolated and cultured from C57BL/6 mice. Boswellia hydroalcoholic extract was prepared and its safe concentration on astrocytes was determined by MTT method. The effect of Serrata Boswellia extracts on CYP46A1 and HMGCR enzyme levels was investigated using Western blotting.
Results: The results of the MTT assay showed a slight increase in astrocyte bioavailability at 20 µg/ml of BS or less and a significant decrease at 50 µg/ml or higher. Treatment with BS extract significantly increased CYP46A1 protein levels compared to the control group, while HMGCR protein levels did not show any significant changes.
Conclusion: Our research findings shed light on the molecular mechanism behind the intelligence and memory-boosting effects of SB, which has been emphasized in traditional medicine. Furthermore, as CYP46A1 is exclusively expressed in the brain, we hypothesize that because Serrata Boswellia increases CYP46A1, it could be used in combination with normal cholesterol-lowering drugs in some diseases related to brain cholesterol accumulation.

Keywords: Boswellia, HMGCR protein, Cholesterol 24-Hydroxylase, cholesterol.

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Abstract: A-10-2706-1

Evaluating the Therapeutic Potential of Resveratrol in Mitigating Insulin Resistance in Skeletal Muscle: A Systematic Review

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Background: The global rise in type 2 diabetes mellitus (T2DM) presents a significant health challenge, with insulin resistance playing a central role in its development, particularly in skeletal muscle. Insulin resistance in muscle disrupts glucose homeostasis, contributing to the progression of T2DM. While current treatments offer some benefits, there is a continuous need for novel therapeutic approaches. Resveratrol, known for its anti-diabetic properties, has been proposed as a potential candidate for improving insulin resistance in skeletal muscle. This study investigates resveratrol's effects on insulin resistance and explores the underlying molecular mechanisms.

Methods: A systematic literature search was conducted using databases such as PubMed, Scopus, and ISI Web of Science up to November 2022. Keywords included "resveratrol," "muscle," "T2DM," "diabetes mellitus," "insulin resistance," "insulin sensitivity," "impaired glucose tolerance," and "glucose intolerance." Relevant titles, abstracts, and full texts were reviewed. The study encompasses results from cell culture, animal, and human studies.

Results: A total of 94 articles were identified for review. After screening for duplicates and irrelevant studies, 83 original papers met the inclusion criteria and were included in this systematic review. Analysis of preclinical studies shows that resveratrol has beneficial effects on insulin resistance in skeletal muscle by modulating key pathways, such as insulin signaling, inflammation, oxidative stress, mitochondrial function, endoplasmic reticulum stress, and glucose and lipid metabolism. These findings suggest that resveratrol exerts multifaceted effects to improve insulin sensitivity in skeletal muscle. However, variability in clinical trial results warrants caution in applying these findings to humans.

Conclusion: Preclinical evidence indicates that resveratrol holds promise for enhancing insulin sensitivity in skeletal muscle through multiple biological pathways. However, further research through well-designed human trials is necessary to confirm its efficacy and potential as a therapeutic agent for T2DM.

Keywords: Resveratrol, Skeletal muscle, Insulin resistance.

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Abstract: A-10-2709-1

Nucleophosmin: A Phosphorylated Nucleolar Protein Regulating Cellular Stress Responses

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Background: Nucleophosmin (NPM1) is a nucleolar protein involved in multiple cellular functions, such as ribosome biogenesis, chromatin remodeling, and regulation of stress responses. Ubiquitously expressed in tissues, NPM1 is found in the nucleolus, nucleoplasm, cytoplasm, and extracellular spaces. It plays a crucial role in various biological processes, including cell cycle regulation, cell proliferation, DNA repair, and apoptosis. NPM1 is highly expressed in cancer cells and solid tumors, with its mutation being a primary cause of acute myeloid leukemia (AML). This study focuses on the role of phosphorylated NPM1 in cellular stress responses.

Methods: This review study was conducted by systematically searching scientific databases, including Scopus, PubMed, and Embase, from 2016 to 2024 using keywords such as "Nucleoplasmin," "Nucleophosmin," "Stress response," and "Nucleolar phosphoprotein." A total of 84 relevant articles that met the inclusion criteria were extracted and analyzed.

Results: The findings reveal that oxidative stress significantly increases NPM1 phosphorylation at specific serine residues. Phosphorylated NPM1 translocates from the nucleolus to the cytoplasm, where it interacts with key stress response proteins like p53. Cells with inhibited NPM1 phosphorylation showed increased sensitivity to oxidative stress and higher rates of apoptosis compared to control cells.

Conclusion: These results suggest that phosphorylated NPM1 plays an essential role in mediating cellular responses to oxidative stress by regulating protein interactions and localization. The translocation of NPM1 may aid in activating protective pathways, particularly those involving p53. Understanding the regulatory mechanisms of NPM1 phosphorylation offers potential therapeutic insights for treating stress-related diseases and cancer. Further research is needed to clarify the specific signaling pathways underlying NPM1-mediated stress responses.

Keywords: Keywords: Nucleoplasmin, nucleophosmin, stress response, nucleolar phosphoprotein

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Abstract: A-10-2711-1

The Formation of IMPDH Cytoophidia in Response To Insulin During 3T3L1 Pre-Adipocyte Differentiation

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Background: Investigating the molecular mechanisms behind the differentiation of pre-adipocytes into adipocytes, known as adipogenesis, is crucial for understanding and addressing obesity. Inosine 5'-monophosphate dehydrogenase (IMPDH) is a key enzyme in the purine nucleotide synthesis pathway, regulating the intracellular pool of guanine nucleotides. IMPDH can form structures called cytoophidia, which enhance GTP production and reduce allosteric inhibition by GTP. This study focuses on the role of IMPDH during the differentiation of 3T3-L1 pre-adipocytes in response to insulin treatment.

Methods: Immunofluorescence techniques were used to detect the presence and behavior of IMPDH during the differentiation of 3T3-L1 cells at various time points following insulin treatment.

Results: Upon insulin treatment, IMPDH rapidly formed cytoophidia within the first few minutes of exposure. Cytoophidia were observed as early as 1 minute post-insulin treatment, with their presence diminishing over time and completely disappearing between 30 to 60 minutes.

Conclusion: The formation of cytoophidia in response to insulin treatment appears to play an important role in insulin signaling. However, the specific implications of IMPDH cytoophidia formation in relation to insulin signaling require further investigation. These findings highlight the critical involvement of IMPDH in adipocyte differentiation and its potential association with obesity.

Keywords: IMPDH; cytoophidia; insulin; adipogenesis

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Abstract: A-10-2665-2

Enzymes Profile as Diagnostic Biomarkers of Colorectal Cancer

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Background: Colorectal cancer results from the uncontrolled proliferation of epithelial cells in the colon and rectum lining. This systematic review investigates two specific enzymes—Fucosyltransferase-4 (FUT4) and Galectin-3—which have potential utility as chemical biomarkers for colorectal cancer diagnosis.

Methods: A systematic review was conducted by searching for relevant articles using keywords such as "colorectal cancer," "biomarker," "fucosyltransferase-4," and "galectin-3" across databases including PubMed, ISI Web of Knowledge, Google Scholar, and Scopus. The search covered literature published between 2010 and 2023.

Results: Fucosyltransferases play an important role in cancer progression through the fucosylation of cellular components. Fucosyltransferase-4 is particularly significant, as it is responsible for the alpha-1,3 fucosylation of Lewis antigens on cancer cell surfaces—key markers associated with colorectal cancer. In colon cancer, the expression of Lewis antigen is regulated by fucosyltransferases 3 and 4. Inhibition of FUT4 reduces selectin-mediated adhesion and metastasis and decreases the expression of Lewis antigens in colon cancer cell lines.

Galectin-3, an intracellular protein, inhibits apoptosis and promotes cancer cell survival, playing a role in enhancing adhesion and metastasis. Recent clinical studies show a significant correlation between elevated levels of these enzymes and colorectal cancer.

From the literature search, 12 relevant articles were identified: 7 systematic reviews, 2 original research studies, and 3 clinical trials. Eight of these were selected for detailed analysis in this review.

Conclusion: Measuring the levels of Fucosyltransferase-4 and Galectin-3 could serve as a non-invasive method for detecting colorectal cancer, offering potential for improved diagnostic strategies.

Keywords: Colorectal cancer, biomarker, fucosyltransferase-4, galectin-3

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Abstract: A-10-2809-1

Differential Expression of Neurodegeneration-Related Genes in Neuroblastoma Sh-Sy5y Cells Under the Influence of Cyclophilin A: Could the Enzyme Be A Probable Inducer and Therapeutic Target for Alzheimer's Disease?

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Background: The role and mechanism of Cyclophilin A (CypA) in regulating gene expression related to Alzheimer's disease (AD) remain unclear. CypA, a multifunctional protein, has been observed at elevated levels in the cerebrospinal fluid (CSF) of individuals susceptible to AD. This study aims to explore the influence of CypA on gene expression, particularly focusing on inflammation and cell death pathways associated with AD.

Methods: The toxicity of recombinant human Cyclophilin A (rhCypA) and its mutant form (R55A) was assessed using the MTT assay. Prior to this, the purified recombinant protein was validated through enzymatic activity assays and western blot analysis. Following treatment with rhCypA and transient transfection with a CypA construct, real-time PCR and western blotting were employed to evaluate the expression of factors involved in key signaling pathways, with a focus on inflammation and apoptosis.

Results: The MTT assay revealed that CypA was non-toxic to SH-SY5Y cells at concentrations ranging from 100 to 1000 nM. Real-time PCR and western blot analyses demonstrated that CypA modulates the expression of genes involved in inflammation—such as IL1β, CD147, TREM2, S100A9, and NLRP3—as well as genes related to pyroptosis, including ASC and CASPASE1, regardless of its enzymatic activity. Conversely, the expression of proline-directed protein kinases (GSK3β, ERK1/2, CDK5, P38MAPK) and cell death markers (BAX, AIF, CASPASE 3) were influenced by CypA's enzymatic activity. Furthermore, enzymatic activity of CypA affected the production of different phosphorylated Tau species (P-Thr231, P-Ser202/Thr205, P-Thr181, and P-Ser262) and the gene expression of amyloid precursor protein (APP), key biomarkers of AD.

Conclusion: CypA can modulate gene expression in SH-SY5Y neuroblastoma-like cells through mechanisms that are either dependent or independent of its enzymatic activity. The impact of this multifunctional protein on gene expression varies based on the site of action, dosage, and exposure duration.

Keywords: Cyclophilin A, Inflammation, Gene Expression, Post Translational Modifications, Alzheimer's Disease

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Abstract: A-10-2795-1

Evaluation of the Diagnostic Value of Vaginal Fluid Urea and Creatinine As Biochemical Indicators for Prepartum Rupture of Membranes in Comparison With Placental Alpha Microglobulin-1 (PAMG-1)

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Background: Premature rupture of membranes (PROM) is a common complication in obstetrics and gynecology, posing significant risks for both mother and fetus. Timely and accurate diagnosis is essential for appropriate management. While biochemical markers such as placental alpha microglobulin-1 (PAMG-1), a major protein in amniotic fluid, are widely used for PROM diagnosis, other markers like creatinine and urea concentrations in vaginal fluid have also been proposed. This study aims to evaluate the feasibility of using urea and creatinine concentrations in vaginal fluid as diagnostic tools for PROM in comparison to PAMG-1, which serves as the standard test.

Methods: A total of 200 pregnant women with an average gestational age of 37 to 39 weeks were included in this study. Participants were divided into a study group (with PROM) and a control group (without PROM). Diagnostic tools used included sterile speculum examination, nitrazine test, and Ferning test to detect fluid leakage from the cervix. Vaginal fluid samples were collected and analyzed for concentrations of creatinine, urea, and PAMG-1. Receiver operating characteristic (ROC) curve analysis was used to assess the accuracy, sensitivity, and specificity of the tests, and Pearson's correlation coefficient was applied to measure correlations between these values.

Results: Vaginal fluid from the study group showed significantly higher concentrations of urea, creatinine, and PAMG-1 compared to the control group. The PAMG-1 test demonstrated 95% sensitivity, 97% specificity, and 95% accuracy for PROM diagnosis. In comparison, optimal cut-off values for creatinine (0.29 mg/dL) and urea (15 mg/dL) yielded 90% sensitivity, 91% specificity, and 90% accuracy in diagnosing PROM.

Conclusion: Although the diagnostic sensitivity and specificity of urea and creatinine tests are slightly lower than those of the PAMG-1 test, they can still serve as effective diagnostic markers for PROM due to their simplicity, ease of measurement, and low cost.

Keywords: PROM, PAMG-1, amniotic fluid, creatinine, urea

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Abstract: A-10-2713-1

Targeting Mannose Metabolism: A Promising Approach for Cancer Treatment

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Background: Cancer cells often rely on altered metabolic pathways to sustain their rapid growth and proliferation. One such crucial pathway is mannose metabolism, which supports glycoprotein synthesis and cellular signaling. This systematic review evaluates the efficacy of targeting mannose metabolism in various cancer types as a potential therapeutic strategy.

Methods: A comprehensive literature search was conducted across databases such as Scopus, PubMed, and Embase between 2016 and 2024, using keywords including "chemotherapy," "cancer," "mannose metabolism," and "tumor." The inclusion criteria focused on both in vitro and in vivo studies investigating the effects of mannose deprivation and mannose-1-phosphate isomerase inhibitors on cancer cells. The selected studies were analyzed for their impact on cell viability, metabolic profiling, and apoptosis induction in cancer cells.

Results: A total of 15 studies were identified that demonstrated significant reductions in cancer cell viability through the inhibition of mannose metabolism. These studies included a variety of cancer cell lines, such as breast, lung, and pancreatic cancers. Metabolic profiling consistently showed a reduction in glycoprotein synthesis and an increase in apoptotic markers in treated cells. In vivo studies further confirmed these findings, with targeted disruption of mannose metabolism leading to slowed tumor growth and improved survival rates in xenograft models.

Conclusion: This review highlights the critical role of mannose metabolism in cancer cell survival and proliferation. Disrupting this pathway induces metabolic stress and promotes apoptosis in tumor cells, presenting a promising therapeutic target. The potential for integrating mannose metabolism inhibitors with existing cancer treatments offers a novel approach for improving patient outcomes. Future research should aim to clarify the underlying mechanisms and assess the clinical applicability of targeting mannose metabolism in oncology.

Keywords: Chemotherapy, cancer, mannose metabolism, tumor

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Abstract: A-10-2713-2

Protacs: Innovative Strategies for Enhancing Cancer Immunotherapy

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Background: Proteolysis-targeting chimeras (PROTACs) represent a novel therapeutic strategy that harnesses the ubiquitin-proteasome system to selectively degrade target proteins. This systematic review evaluates the potential of PROTACs to enhance cancer immunotherapy by targeting immunosuppressive pathways within the tumor microenvironment.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords PROTACs, immunotherapy, cancer. The total of 68 articles meeting predefined inclusion criteria were extracted and analyzed for their findings related to PROTACs and their impact on immune modulation in cancer.

Results: Our findings demonstrate that PROTACs effectively degrade PD-L1 and CTLA-4, leading to enhanced T cell activation and proliferation in vitro. In vivo, administration of PROTACs resulted in significant tumor regression compared to controls, with increased infiltration of cytotoxic T cells and reduced immunosuppressive cells in the tumor microenvironment.

Conclusion: This study highlights the potential of PROTACs as a promising adjunct to existing cancer immunotherapies. By selectively targeting immunosuppressive proteins, PROTACs can restore T cell function and improve anti-tumor immunity. These results warrant further investigation into the clinical applicability of PROTACs in combination with established immunotherapeutic agents, offering a new avenue for enhancing therapeutic efficacy in cancer treatment.

Keywords: PROTACs, immunotherapy, cancer

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Abstract: A-10-2714-1

Hematopoietic Cell Kinase Increases Through the Lipid Treatment of Vascular Smooth Muscle Cells

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Background: It is well established that lipids play a significant role in the process of atherosclerosis through various signaling pathways. This study investigates the effects of palmitic acid (PA) on the gene and protein expression levels of hematopoietic cell kinase (HCK) in vascular smooth muscle cells (VSMCs).
Methods: Human VSMCs were treated with 0.5 mM palmitic acid based on cellular viability studies conducted over a 24-hour period. The expression levels of the HCK gene and protein were assessed using quantitative reverse transcription polymerase chain reaction (qRT-PCR) and Western blotting techniques, respectively.
Results: Gene network analysis predicted that the HCK gene serves as a hub in cell proliferation and migration. In ex vivo studies, HCK expression levels were significantly increased in VSMCs treated with palmitic acid ($p < 0.05$). Furthermore, total HCK protein expression levels also increased in VSMCs, with a significant rise in phosphorylated HCK (p-HCK) levels ($p < 0.01$).
Conclusion: This study suggests that palmitic acid may enhance proliferation in VSMCs through HCK-related signaling pathways.

Keywords: Atherosclerosis, Palmitic acid (PA), Hematopoietic cell kinase (HCK), Vascular smooth muscle cells (VSMCs)

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2716-1

A Quantum Mechanical Investigation on Tovorafenib

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Background: Tovorafenib, a potential cancer therapy, targets kinases critical to cancer progression. Understanding its electronic properties is essential for optimizing its therapeutic efficacy. Density Functional Theory (DFT) calculations provide valuable insights into Tovorafenib's molecular characteristics, aiding in this understanding.
Methods: DFT calculations were performed on Tovorafenib using the GAUSSIAN 09 software. The molecular structure was optimized using gradient procedures at the restricted Hartree-Fock (HF) and B3LYP levels of theory. The 6-311G basis set was chosen for its balance between computational efficiency and accuracy. The optimization aimed to achieve the molecule's lowest energy conformation, confirmed by the absence of imaginary frequencies in the vibrational analysis, indicating the stability of the optimized structure.
Results: The optimization of Tovorafenib's molecular structure revealed critical structural parameters, including bond lengths, bond angles, and dihedral angles. The electronic energy of the molecule was calculated to be -1,761,659.12 kcal/mol, providing insights into the molecule's inherent stability. Molecular orbital energies were also determined, identifying the highest occupied molecular orbital (HOMO) at -0.26196 eV and the lowest unoccupied molecular orbital (LUMO) at -0.09904 eV. The HOMO-LUMO gap, an important indicator of molecular reactivity, was computed to be 0.16292 eV. Additionally, thermodynamic parameters and Mulliken atomic charges were derived, offering a comprehensive understanding of the molecule's electronic structure. The dipole moment, measured in Debye, was found to be X=4.1191, Y=3.7595, Z=1.4771, with a total dipole moment of 5.7692 Debye.
Conclusion: DFT calculations using the B3LYP/6-311G method successfully optimized Tovorafenib's structure and provided detailed electronic properties. The HOMO-LUMO gap underscores the drug's reactivity and stability, which are vital for its function as a kinase inhibitor. This study demonstrates the effectiveness of computational methods in enhancing our understanding of Tovorafenib's molecular features, supporting its potential as a cancer treatment.

Keywords: Tovorafenib, Density Functional Theory, B3LYP, 6-311G, HOMO-LUMO gap, molecular optimization, cancer therapy.

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Abstract: A-10-2716-3

Calculation the Feathers of the Drug Iptacopan Using Density Functional Theory (DFT)

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Background: Iptacopan is an investigational oral drug targeting the alternative complement pathway, showing promise in treating rare kidney diseases and other complement-mediated disorders. Understanding its electronic structure is crucial for optimizing its pharmacological properties. Density Functional Theory (DFT) calculations, particularly with the B3LYP method, offer valuable insights into these molecular aspects, essential for the drug's development.

Methods: In this study, DFT calculations were performed on Iptacopan using the GAUSSIAN 09 software. The molecular structure was optimized at the B3LYP level of theory, combined with the 6-311G basis set, aiming to achieve the molecule's lowest energy conformation. The absence of imaginary frequencies in the vibrational analysis confirmed the stability of the optimized structure.

Results: The structural optimization of Iptacopan revealed precise details of its molecular geometry, including bond lengths, bond angles, and dihedral angles (Figure 1). The electronic energy of the molecule was calculated to be -866,880.50 kcal/mol, indicating its intrinsic stability. Further electronic property analysis determined the highest occupied molecular orbital (HOMO) at -0.19937 eV and the lowest unoccupied molecular orbital (LUMO) at -0.05367 eV. The HOMO-LUMO gap, a critical parameter for assessing molecular reactivity and chemical stability, was calculated to be 0.1457 eV. Additionally, Mulliken atomic charges and dipole moments were computed, with the dipole moment components being X=5.8430 D, Y=-0.1552 D, Z=-2.2631 D, resulting in a total dipole moment of 6.2679 Debye. These parameters offer a comprehensive understanding of Iptacopan's electronic structure and behavior.

Conclusion: The DFT calculations using the B3LYP/6-311G method successfully optimized Iptacopan's structure and revealed critical electronic properties. The HOMO-LUMO gap analysis provided insights into the drug's reactivity and stability, essential for its role in inhibiting the alternative complement pathway. These findings contribute to the ongoing development and optimization of Iptacopan as a therapeutic agent for complement-mediated disorders.

Keywords: Iptacopan, Density Functional Theory, B3LYP, 6-311G, HOMO-LUMO gap, molecular optimization, alternative complement pathway, pharmacological properties.

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Abstract: A-10-2187-1

Investigation of Rosmarinic Acid Derivatives As Potential Dna Gyrase Inhibitors Using Molecular Docking Studies

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Background: Bacterial resistance to antibiotics poses significant challenges for developing new drugs to treat infectious diseases. DNA gyrase, a member of the bacterial type II topoisomerase family, catalyzes DNA topology modifications and represents an attractive target for combating infections. This study investigates the antibacterial activity of rosmarinic acid derivatives against the DNA gyrase enzyme.

Methods: The molecular docking process was carried out using AutoDock software to predict the mode of interaction between the best conformations of the derivatives and the binding site of the DNA gyrase enzyme. The 3D structures of rosmarinic acid derivatives were obtained from PubChem and converted into PDB format using AutoDock. Subsequently, the derivatives were docked into the binding site of DNA gyrase (PDB ID: 5L3J) with AutoDock software. The pharmacokinetic properties and drug-likeness of the selected compounds were also evaluated using SwissADME analysis.

Results: The docking results demonstrated that the rosmarinic acid derivatives exhibited a strong binding affinity for the DNA gyrase enzyme. These derivatives interacted robustly with specific amino acid residues in the active site of DNA gyrase, forming hydrogen bonds with Asp73, Asn46, Thr165, and Arg136. Additionally, the drug-likeness and pharmacokinetic properties of these compounds displayed favorable characteristics.

Conclusion: These findings suggest that rosmarinic acid derivatives may serve as potential DNA gyrase inhibitors, warranting further studies to explore their therapeutic applications.

Keywords: DNA gyrase, rosmarinic acid derivatives, Molecular Docking

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Abstract: A-10-2198-1

A Systematic Review of the Mechanisms and Signaling Pathways of Flutetozumab in Treating Acute Myeloid Leukemia

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Background: Acute myeloblastic leukemia (AML) is the most prevalent hematological malignancy in adults and the second most common in children. It is characterized by significant heterogeneity due to chromosomal abnormalities, gene mutations, and alterations in the expression of multiple genes and microRNAs. The five-year survival rate for AML is approximately 62%, with relapse being a major concern following allogeneic hematopoietic cell transplantation (HCT). Consequently, there is an urgent need for new therapeutic strategies. Flotetuzumab is a dual-affinity retargeting antibody that targets CD123 and CD3, showing promise in the treatment of AML, particularly in pediatric patients. While the anti-cancer effects of immunotherapies have been recognized for years, research on the mechanisms of Flotetuzumab is more recent. This study aims to review the therapeutic mechanisms of Flotetuzumab in AML.

Methods: This systematic review analyzed articles from PubMed, Google Scholar, and Scopus without time limitations. In August 2024, two researchers conducted an independent search using the MeSH terms: ("Acute myeloblastic leukemia" OR "Acute myeloid leukemia") AND ("Flotetuzumab") AND ("signaling" OR "signaling pathway"). Inclusion criteria comprised English-language research articles focused on AML, while exclusion criteria included non-English articles, studies on other immunotherapies, clinical trials, review articles, and studies on acute lymphoblastic leukemia (ALL).

Results: A total of 13 studies were identified. After excluding duplicates and unrelated articles, the titles and abstracts of six articles were screened. Following a full-text assessment, three studies were included. Research on the THP-1 cell line and primary AML samples at diagnosis and post-HCT relapse indicated that Flotetuzumab can enhance MHC class II expression on AML cells and activate T cells through interferon (IFN)-γ-related signaling.

Conclusion: The available studies suggest that Flotetuzumab exerts its anti-cancer effects through IFN-γ-related signaling pathways. Further research is essential to fully elucidate the mechanisms underlying the action of Flotetuzumab in AML.

Keywords: Flutetuzumab, AML, signaling, IFN-γ

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Abstract: A-10-2170-2

The Investigation of Gene Expression Changes in Glutamate Receptor Subunits in Peripheral Blood Lymphocytes of Ischemic Stroke Patients

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researches has focused on the causes of this phenomenon. Glutamate, which is implicated in brain regions affected by injury, leads to an increase in intracellular calcium ion levels. This process, acting as a trigger for molecular apoptotic cascades, ultimately results in neuronal death. In this study, we investigated gene expression changes in the main subunits of glutamate receptors and pathways involved in their reduction.

Methods: We initially collected blood samples from 34 ischemic stroke patients, isolating lymphocytes and serum. From these samples, we separated NMDA receptor subunits NR2A, NR2B, NR3A, and NR3B. Real-time PCR was then employed to assess gene expression changes in these glutamate subunits.

Results: The expression of NR2A and NR3A subunits showed a significant reduction in ischemic stroke patients compared to the control group. NR2B subunit expression was absent in blood lymphocytes, while NR3B subunit expression was very weak. Therefore, studying gene expression of these two subunits in blood is not feasible.

Conclusion: These findings suggest a potential impact of glutamate on NR2A and NR3A subunits, contributing to the occurrence of ischemic strokes in the brain, with implications for blood lymphocytes.

Keywords: NMDA, cerebral strock, ischemic stroke

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Abstract: A-10-2292-2

Evaluating the Role of Vitamin D3 in Modulating Insulin Resistance and Glycemic Control Among Type 2 Diabetic Nephropathy Patients

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Background: Type 2 diabetes mellitus (T2DM) is a major public health concern characterized by chronic hyperglycemia, insulin resistance, and a relative deficiency of insulin. This condition often leads to severe complications, including diabetic nephropathy, which increases the risk of mortality and adverse outcomes such as cardiovascular diseases and kidney failure. Recent studies suggest that vitamin D, known for its anti-inflammatory and immunomodulatory properties, might influence glycemic control and insulin resistance in T2DM.
Methods: This case-control study included a total of 120 participants, consisting of 30 healthy individuals and 90 patients diagnosed with T2DM and nephropathy. The patient group was divided into three subgroups based on their albuminuria status (normoalbuminuria, microalbuminuria, and macroalbuminuria). Blood samples were collected to measure fasting blood glucose (FBS), HbA1c, lipid profile, blood urea, serum creatinine, albumin-to-creatinine ratio (ACR), glomerular filtration rate (GFR), calcium, and vitamin D3 levels.
Results: Significant differences were observed among the study groups and controls in lipid profile, FBS, HbA1c, blood urea, serum creatinine, ACR, GFR, calcium, and vitamin D3 levels ($p=0.0001$). However, fasting blood sugar, insulin, and HOMA-IR levels showed no significant differences across the groups ($p>0.05$). Notably, patients with macroalbuminuria had significantly lower GFR and higher insulin resistance compared to other groups.
Conclusion: Lower levels of vitamin D3 are associated with increased insulin resistance and poorer glycemic control in T2DM patients with nephropathy. Incorporating vitamin D3 as a supplementary biomarker may enhance early prediction and diagnosis of diabetic nephropathy, potentially preventing further renal decline in these patients.

Keywords: Diabetic nephropathy, Microalbuminuria, Vitamin D3, Insulin resistance, Glycemic control, Type 2 diabetes mellitus (T2DM).

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Abstract: A-10-2236-1

Investigation of the Relationship Between Apelin Levels and Atherosclerosis Severity in Patients With Coronary Heart Disease

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Background: Cardiovascular disease (CVD) is the leading cause of death globally, responsible for about one-third of all fatalities. Research indicates that apelin may serve as a biomarker for diagnosing cardiovascular diseases. This study aims to investigate the relationship between apelin levels and atherosclerosis severity in patients with coronary heart disease.

Methods: In this study, 70 participants were categorized into two groups: healthy individuals and those with coronary artery obstruction, as determined by an international expert following angiography. Patients with coronary artery occlusion were further subdivided into one-vessel, two-vessel, and three-vessel occlusion groups based on the number of affected vessels. Blood samples were collected from selected patients, and serum was separated to measure lipid profiles, including triglycerides, cholesterol, LDL, HDL, and apelin levels using the ELISA method.

Results: In this study, coronary artery occlusion prevalence was 54.3% in men and 45.7% in women. The highest frequency of coronary heart disease occurred in the 51-60 age group (30%), while the lowest was in those under 40 (5.7%). A comparison of Aplin values in patients with coronary artery occlusion versus the control group revealed a significant increase in CAD patients ($p<0.05$), particularly in those with three vessel disease. Additionally, triglyceride and LDL levels were significantly elevated in patient groups compared to the control group ($p<0.05$).

Conclusion: The study found a strong positive correlation between apelin, triglycerides, and other biochemical parameters, highlighting their significance as ideal indicators for disease diagnosis and monitoring, particularly in relation to the coronary arteries of the heart.

Keywords: Aplin, coronary heart disease, Biomarker

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Abstract: A-10-2719-1

Utilizing Targeted Protein Degradation in Immunotherapy: Exploring the Interactions Between Proteolysis Targeting Chimeras and the Ubiquitin-Proteasome System

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Background: Targeted protein degradation (TPD) has emerged as a novel therapeutic strategy in immunotherapy, particularly through the use of proteolysis-targeting chimeras (PROTACs). These compounds selectively induce the degradation of specific oncoproteins, potentially enhancing immune responses against tumors. This review aims to synthesize current findings on the efficacy of PROTACs in modulating immune responses in cancer therapy.
Methods: A systematic literature search was conducted across databases such as PubMed, Scopus, and Web of Science for studies published up to 2023. Inclusion criteria focused on preclinical and clinical studies evaluating PROTACs in the context of immunotherapy. Data were extracted regarding the types of targeted proteins, mechanisms of action, and observed immune response outcomes.
Results: A total of 25 studies met the inclusion criteria. Most studies reported that PROTACs effectively degraded oncoproteins, leading to enhanced apoptosis in cancer cells. Notably, the degradation of immunosuppressive factors resulted in increased T-cell activation and infiltration within the tumor microenvironment. Combination therapies involving PROTACs and immune checkpoint inhibitors showed synergistic effects, significantly improving anti-tumor responses.
Conclusion: The findings suggest that PROTACs represent a promising approach to enhance immunotherapy by reshaping the tumor microenvironment and overcoming resistance mechanisms. Future research should focus on optimizing PROTAC design for specific cancer types and further elucidating their mechanisms of action. Overall, TPD could play a crucial role in advancing cancer treatment paradigms by integrating targeted degradation strategies with existing immunotherapeutic approaches.

Keywords: Immunotherapy, Targeted Protein Degradation, PROTACs

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Abstract: A-10-2721-1

The Role of Extracellular Heat Shock Protein 90 Alpha (ehsp90α) in Cancer Progression and Therapeutic Strategy Development

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Background: Extracellular Heat Shock Protein 90 Alpha (eHsp90α) has emerged as a critical player in cancer biology, influencing tumor progression and immune evasion. This study investigates the role of eHsp90α in cancer progression and its potential as a therapeutic target.

Methods: This systematic review was conducted by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 using the keywords "Extracellular heat shock protein 90 alpha," "Cancer biomarker," and "Cancer target." A total of 78 articles meeting the inclusion criteria were extracted and analyzed.

Results: Our findings demonstrate that elevated levels of eHsp90α correlate with increased tumor aggressiveness and poor patient prognosis across multiple cancer types. Functional assays revealed that inhibition of eHsp90α significantly reduced cell migration and invasion while promoting apoptosis. Mechanistically, eHsp90α was found to modulate key oncogenic pathways, including PI3K/Akt and MAPK signaling, leading to enhanced tumor cell survival and proliferation.

Conclusion: This study highlights the pivotal role of eHsp90α in cancer progression, suggesting it as a promising biomarker for tumor aggressiveness and a potential therapeutic target. Targeting eHsp90α may offer a novel strategy for cancer treatment, particularly in cases resistant to conventional therapies. Further research is warranted to explore eHsp90α inhibitors in clinical settings and their potential synergistic effects with existing treatment modalities.

Keywords: Extracellular heat shock protein 90 alpha, Cancer biomarker, Cancer target

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Abstract: A-10-2685-2

Detection of A Fah Gene Variant Using Whole-Exome Sequencing and in Silico Analysis in A Lorestani Child

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Background: Mutation in the FAH gene causes the metabolic disorder tyrosinemia type I, an autosomal recessive disease located on chromosome 15q25.1. The fumaryl acetoacetate hydrolase (FAH) enzyme is essential for the final breakdown of tyrosine; its deficiency results in tyrosinemia. Without treatment, this condition manifests as a severe, progressive disease that can lead to early death. Clinical manifestations due to liver dysfunction typically present within the first months of life, and tyrosinemia type I is characterized by liver and kidney disorders. In its acute form, symptoms include hepatomegaly, poor growth, diarrhea, vomiting, and jaundice within weeks of birth. If untreated, affected individuals may not survive past infancy.
Methods: Genomic DNA was extracted from blood samples, followed by physical examination, ultrasound, and whole genome sequencing. Sanger sequencing was employed to confirm the findings. The FoldX plugin on the YASARA program was used to calculate the change in Gibbs free energy (ΔΔG).
Results: Exome sequencing identified a nonsense mutation, c.709C>T: p.R237X, in exon 9 of the FAH gene within Lorestani families. Sanger sequencing confirmed this nonsense variant in the FAH gene in our patient. According to FoldX analysis, the p.R237X mutation in FAH is classified as a destabilizing mutation, with its ΔΔG value indicating potential disruption of FAH function, which can lead to clinical disorders.
Conclusion: Identification of FAH gene variants provides reliable information for genetic counseling. Prenatal diagnosis of the FAH gene is crucial for improving treatment options and prognosis.

Keywords: FAH gene, Sanger sequencing, Whole Genome Sequencing

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Abstract: A-10-2718-1

Application of Mesenchymal Stem Cells (MSC) in Bone Regeneration: A Systematic Review

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Background: Stem cell-based treatments represent a primary strategy for improving bone diseases. Bone is one of the tissues capable of regeneration; however, in cases of extensive damage or when spontaneous repair is not feasible—even with pharmacological or surgical interventions—challenges arise. Currently, bone grafts are predominantly used for such injuries, but they face limitations due to issues like the availability of suitable graft tissue and immune reactions. Stem cells are undifferentiated and potent cells with two unique characteristics: the ability to replicate and the capacity to differentiate into various cell types. This review discusses the application of stem cells in the treatment of bone diseases.

Methods: To identify relevant articles for this research, we searched the keywords “Mesenchymal stem cells,” “Bone,” and “Regeneration” in Google Scholar, PubMed, and Web of Science databases. After linking the findings, the articles were reviewed, and relevant content was extracted.

Results: After examining 122 articles, those without a direct connection to the research title and purpose were excluded. Ultimately, 89 relevant articles were included in the study. The clinical application of mesenchymal stem cells (MSCs) for bone regeneration necessitates attention to two critical issues: the design of biocompatible scaffolds that minimize side effects and avoid immunological responses, and the use of stem cells that exhibit minimal clinical side effects despite their high regenerative potential.

Conclusion: Bone tissue defects can be influenced by environmental factors and congenital abnormalities, leading to functional impairments. Tissue engineering approaches utilizing stem cells and scaffolds have significantly advanced this field, providing functional therapeutic solutions for bone regeneration.

Keywords: Keywords: MSC, Bone, Regeneration, Tissue engineering

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Abstract: A-10-2461-1

Relationship Between Pon1 Promoter T (-107) C Variant and Paraoxonase and Arylesterase Activities in Coronary Artery Disease

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Background: Paraoxonase-1 (PON1), an enzyme associated with high-density lipoprotein (HDL) particles, is believed to play a role in the molecular pathogenesis of coronary artery disease (CAD). This study aimed to evaluate the association between the PON1 promoter T (-107) C polymorphism, enzyme activity, and the extent of coronary artery stenosis in Iranian patients.

Methods: A total of 99 patients underwent coronary angiography to determine the number of stenotic vessels and were classified into three groups: single vessel disease (SVD), two-vessel disease (2VD), and three-vessel disease (3VD). The RFLP analysis was utilized to determine the T (-107) C genotype distribution, while serum PON1 activities (paraoxonase and arylesterase) were measured using spectrophotometry. Data were analyzed using SPSS software.

Results: The T (-107) C polymorphism was significantly associated with serum arylesterase activity ($P<0.01$) but not with paraoxonase activity ($P>0.05$). The homozygous genotypes (CC and TT) were inversely distributed in the SVD group compared to the 3VD group. Furthermore, the frequency of the CC high activity genotype decreased as the number of stenotic vessels increased in patients.

Conclusion: Arylesterase activity, as a function of promoter activity, is related to the severity of stenosis, suggesting that it may be a contributing factor in the progression of the atherosclerotic process in stenotic vessels.

Keywords: Paraoxonase-1, Coronary artery, Arylesterase

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Abstract: A-10-2474-1

Current Diagnostic Methods for CS and Evaluate Their Efficacy

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Background: Cushing's syndrome (CS) is a complex endocrine disorder that can cause significant morbidity and mortality if not properly diagnosed and managed. Due to its similarities with other conditions, a thorough biochemical assessment is crucial for accurate diagnosis. Traditional cortisol measurement methods have been enhanced by newer techniques, such as late-night salivary cortisol (LNSC), urinary free cortisol (UFC), and the dexamethasone suppression test (DST), which are reliable diagnostic tools for CS. This study investigates current diagnostic methods for CS and evaluates their efficacy.

Methods: A literature search was performed using databases like PubMed, Scopus, and Google Scholar for articles published from January 2020 to December 2023. Keywords included cortisol, Cushing, saliva, and late-night. Sources were verified, duplicate titles were removed using EndNote software, and abstracts were reviewed for relevance. The quality of related articles was assessed with JBi tools before being included in the study.

Results: A total of 450 articles were reviewed, resulting in the selection of 53 relevant studies for this review, highlighting various diagnostic approaches and outcomes. Some studies indicate that late-night salivary cortisol (LNSC) is preferred due to its non-invasive nature and ease of collection. While LNSC enhances diagnostic accuracy, factors like age, sex, body mass index, and comorbidities can influence values. Older males with health issues may show elevated LNSC levels without Cushing's syndrome. Recent studies suggest cortisone administration may clarify cortisol's circadian rhythm and improve evaluation of adrenal function.

Conclusion: Immunoassay-based cortisol measurements can yield false positives due to cross-reactivity with other steroids. Despite high specificity and sensitivity, chromatography-mass spectrometry is underutilized in clinical practice. Current research highlights the need for ongoing assessment of LNSC and UFC levels in response to treatment in Cushing's disease. An integrative approach to cortisol measurement is essential for enhancing diagnostic outcomes and patient management.

Keywords: Cushing's disease, cortisol measurement, diagnostic methods

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2605-2

Is There Any Link Between Iglon5 Autoantibodies and Chronic Insomnia Disorder?

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Background: Anti-IgLON5 disease is a novel form of cell-surface autoimmunity primarily characterized by abnormal sleep structure, bulbar symptoms, and movement disorders. Unfortunately, many individuals with anti-IgLON5 disease are diagnosed only in advanced stages, which are marked by neuroinflammation and neurodegeneration. Given the role of sleep deprivation in predicting neurodegenerative disorders, this study aimed to investigate the presence of IgLON5 autoantibodies in the serum of individuals with isolated chronic insomnia disorder.
Methods: Blood samples were collected from 22 individuals (16 females, mean age 42.1 ± 9.3 years, range 21-65) diagnosed with chronic insomnia disorder (CID) based on the Pittsburgh Sleep Quality Index (PSQI) and full-night video-polysomnography (V-PSG). A control group of 22 healthy individuals (14 females, mean age 41.8 ± 11.7 years, range 21-65) was also assessed using the PSQI. An indirect immunofluorescence cell-based test was employed to detect serum IgLON5 autoantibodies. Statistical analyses were performed using SPSS® version 26.0.
Results: Anti-IgLON5 antibodies were identified in the serum of four individuals with chronic insomnia disorder, with a titer of 1/10.
Conclusion: The detection of IgLON5 autoantibodies in certain individuals with chronic insomnia disorder suggests a potential causal role in the condition, indicating a need for more targeted treatment strategies. Furthermore, recognizing anti-IgLON5 disease in its early stages may facilitate effective and timely interventions.

Keywords: Chronic insomnia, IgLON5 autoantibody, Anti IgLON5 disease

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Abstract: A-10-2767-1

Application of Fast Silver Staining Method To Detect VWD Mutations Using SSCP

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Background: Von Willebrand disease (VWD) is the most prevalent inherited bleeding disorder worldwide. Certain mutations in the VWD gene are commonly associated with the disease and represent an important first step in identifying its genetic causes. Various methods are available for mutation detection, including single-strand conformation polymorphism analysis (SSCP). Traditionally, Ethidium bromide dye has been used for staining SSCP gels; however, it is a known carcinogen. This study presents a rapid and safe alternative method using fast silver nitrate staining.

Methods: In the fast silver nitrate method, gel fixation and staining were performed using a solution containing 5% ethanol, 1% nitric acid, and 0.1% AgNO3 for 5 minutes. Following this, the gel was rinsed with double-distilled water. A developing buffer (1.3% NaOH, 0.65% Na2CO3, and 0.4% HCOH) was then applied to the gel for 2-3 minutes until the bands became visible. The reaction was subsequently stopped using a stopping buffer containing 5% ethanol and 1% nitric acid for 1 minute.

Results: The fast silver staining method effectively produced sharp SSCP bands on polyacrylamide gels (PAGE). The gels were easily photographed or scanned, revealing clear movement of the different bands.

Conclusion: The fast silver staining method is a cost-effective and safe alternative to Ethidium bromide, yielding reliable results for detecting mutations associated with Von Willebrand disease.

Keywords: Von Willebrand Disease, point mutation, SSCP, fast silver nitrate staining

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Abstract: A-10-2730-1

The Up-Regulation of miR-146a and miR-29b Via Exosomes Protects Against Liver Fibrosis By Inhibiting the TGF-B/smad3c Signaling Pathway

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Background: Hepatic fibrosis is characterized by the increased proliferation and activation of hepatic stellate cells. Transforming growth factor-beta (TGF-β) stimulates these stellate cells, leading to the development of liver fibrosis. MicroRNA-146a and microRNA-29b have been identified as significant regulatory factors in fibrogenesis. In this study, we investigated the ability of exosomes to alleviate liver fibrosis by enhancing the antifibrotic effects of miR-146a and miR-29b.

Methods: The LX-2 cells were exposed to TGF-β for 24 hours. Subsequently, the cells were treated with exosomes for an additional 24 hours. Following this treatment, the mRNA expression levels of alpha-smooth muscle actin (α-SMA), collagen1α, miR-146a, and miR-29b, as well as the protein levels of phosphorylated Smad3 (p-Smad3), were evaluated.

Results: The findings revealed a significant elevation in the expression of α-SMA (5.37-fold, $P < 0.0001$) and collagen1α (3.87-fold, $P < 0.001$) genes, as well as an increase in the levels of p-Smad3 protein (5.87-fold, $P < 0.0001$) in the presence of TGF-β. Moreover, the expression of miR-146a (0.54-fold, $P < 0.05$) and miR-29b (0.46-fold, $P < 0.01$) genes exhibited a notable decrease compared to the control group under the influence of TGF-β. In our investigation, the administration of exosomes effectively mitigated the TGF-β-induced up-regulation of α-SMA (3.26-fold, $P < 0.01$) and collagen1α (1.76-fold, $P < 0.01$) genes, as well as the p-Smad3 protein (2.86-fold, $P < 0.01$), in LX-2 cells.

Conclusion: Our results suggest that exosomes effectively impede the continuous activation of hepatic stellate cells (HSCs) by enhancing the antifibrotic effects mediated by miR-146a and miR-29b. Moreover, exosomes demonstrate inhibitory effects on the TGF-β/Smad3 signaling pathway, resulting in decreased extracellular matrix (ECM) accumulation in the context of in vitro liver fibrosis.

Keywords: Hepatic stellate cells, TGF-β/Smad3, Exosomes, miR-146a and miR-29b

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Abstract: A-10-2733-1

Protacs: Present and Future Promise As A Precision Medicine Approach in the Fight Against Cancer

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Background: Proteolysis targeting chimeras (PROTAC) are an emerging precision medicine strategy, which targets key proteins for proteolytic degradation to ultimately induce cancer cell killing. These hetero-bifunctional molecules hijack the ubiquitin proteasome system to selectively add polyubiquitin chains onto a specific protein target to induce proteolytic degradation. Importantly, PROTACs have the capacity to target virtually any intracellular and transmembrane protein for degradation, including oncoproteins previously considered undruggable, which strategically positions PROTACs at the crossroads of multiple cancer research areas

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords Proteolysis targeting chimera, targeted protein degradation, targeted therapy, cancer, 86 articles related to inclusion criteria were extracted and then analyzed.

Results: Our findings indicate that PROTACs have successfully degraded key oncogenic proteins, leading to reduced tumor growth in preclinical models. Notably, PROTACs targeting mutant forms of p53 and BRD4 demonstrated significant antitumor activity, with some compounds entering clinical trials. The ability to simultaneously degrade multiple targets was highlighted as a major advantage, potentially overcoming resistance mechanisms associated with traditional therapies.

Conclusion: PROTACs represent a transformative approach in cancer therapy, offering a new avenue for targeting proteins that have eluded conventional drug development. Their capacity for selective degradation opens up possibilities for personalized treatment strategies tailored to individual tumor profiles. However, challenges such as delivery mechanisms, off-target effects, and long-term safety remain. Future research should focus on optimizing PROTAC design and expanding their application in clinical settings, aiming to enhance therapeutic outcomes in cancer patients through precision medicine.

Keywords: Proteolysis targeting chimera, targeted protein degradation, targeted therapy, cancer.

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Abstract: A-10-2733-2

B-Glucan: A Powerful Adjuvant for Enhancing Immunotherapy in Gastrointestinal Tumors

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Background: Immunotherapy has revolutionized cancer treatment, yet its efficacy in gastrointestinal tumors remains suboptimal. β-Glucan, a natural polysaccharide derived from yeast and fungi, has emerged as a potential adjuvant to enhance immune responses. This study investigates the role of β-glucan in augmenting immunotherapy for gastrointestinal tumors.

Methods: This study is a review study by searching scientific databases such as Scopus, PubMed, and Embase from 2016 to 2024 by using the keywords Beta glucan, immunotherapy, gastrointestinal tumors, 78 articles related to inclusion criteria were extracted and then analyzed.

Results: Co-administration of β-glucan significantly enhanced the activation of T cells and natural killer (NK) cells compared to immunotherapy alone. Tumor growth inhibition was markedly greater in the β-glucan group, with a 40% reduction in tumor volume. Additionally, elevated levels of pro-inflammatory cytokines, including IL-6 and TNF-α, were observed in the β-glucan-treated.

Conclusion: These findings suggest that β-glucan acts as a potent immune modulator, enhancing the efficacy of immunotherapy in gastrointestinal tumors. By promoting immune cell activation and increasing pro-inflammatory cytokine production, β-glucan may overcome some of the limitations of current immunotherapeutic strategies. Future clinical trials are warranted to explore the synergistic potential of β-glucan in combination with existing immunotherapeutic regimens, aiming to improve patient outcomes in gastrointestinal cancers.

Keywords: Beta glucan, immunotherapy, gastrointestinal tumors.

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Abstract: A-10-2401-1

Antioxidant Effects of Betaine in Oxidative Stress

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Background: Betaine has been known as an antioxidant and methyl group donor in previous studies. This review article examines the effect of betaine on oxidative damage including gastric damage caused by indomethacin in rats, homocysteinemia and oxidative damage caused by levodopa in rat kidney, oxidative stress caused by ethanol in rat liver, Parkinson's induced by 6_Hydroxydopamine in rats, as well as the oxidative effects caused by ethanol in rat testes and the effect on ischemia reperfusion of the testis, its effect on the Alzheimer's disease model caused by beta amyloid and its effect on oxidative stress caused by ethanol and the reduction of total homocysteine in The cerebellum of rat pays.

Methods: In this review, Google Scholar, Web of Science, and Scopus databases were searched using the keywords betaine, homocysteine, and antioxidant enzymes; There was no time limit for the search, and original and complete articles about studies conducted on Wistar rats were selected and reviewed.

Results: 364 articles were initially found in the search of the investigated databases. 54 articles were included in the secondary evaluation according to the subject under review, and finally, by removing 44 articles, 10 articles were included in the final review and meta-analysis. In this article, the effect of betaine on oxidative damage was investigated. The obtained results showed that betaine as methyl group donor and antioxidant can be effective in reducing the complexity caused by oxidative stress.

Conclusion: Betaine has shown antioxidant and protective effects in induced diseases and seems to be a useful antioxidant in pretreatment groups.

Keywords: Betaine, Antioxidant enzymes, levodopa, Parkinson's disease, Alzheimer's disease, liver, Homocysteine

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Abstract: A-10-2735-1

Determination of the Effect of Melatonin and Doxorubicin on KYSE-30 Esophageal Cancer Cell Line

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Background: Esophageal cancer (EC) is the sixth most common cause of cancer-related deaths globally. One of the treatment strategies for this cancer involves the use of radiotherapy, either alone or in combination with chemotherapy. Various adjuvants, such as melatonin and doxorubicin, are often employed to mitigate the side effects of radiotherapy and enhance its therapeutic efficacy. This study aims to investigate the effects of melatonin and doxorubicin on esophageal cancer cells.

Methods: The viability of KYSE-30 esophageal cancer cells was assessed after treatment with varying concentrations of melatonin (0.07 to 10 mM) and doxorubicin (0.5 to 64 µg/ml) using the MTT-assay after 48 hours of incubation. Subsequently, one of the optimal concentrations of melatonin, as well as the IC50 concentration, along with concentrations higher and lower than the IC50, were further examined for qualitative apoptosis using DAPI nuclear staining and a fluorescent microscope.

Results: Doxorubicin at all tested concentrations showed a significant toxic effect on KYSE-30 cancer cells, reducing cell survival ($P < 0.0001$), with an IC50 value of 6.7 µg/ml. Melatonin also exhibited toxicity toward KYSE-30 cancer cells at higher concentrations during the 48-hour incubation period, except at 0.07 mM ($P < 0.0001$), with an IC50 value of 3.5 mM.

Conclusion: The study results demonstrate that melatonin can exert cytotoxic effects on esophageal cancer cells at high concentrations, while doxorubicin shows toxicity at all tested concentrations.

Keywords: Melatonin, Esophageal cancer, doxorubicin

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Abstract: A-10-2187-2

Molecular Docking and ADME Studies of Berberine Against Monkeypox Virus Methyltransferase Vp39

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Background: An outbreak of monkeypox, caused by the monkeypox virus (MPXV), poses a threat to both endemic and non-endemic regions. The VP39 methyltransferase enzyme in MPXV plays a pivotal role in viral RNA replication and transcription, making it a potential target for inhibiting virus replication. This study aimed to investigate the inhibitory effects of berberine on MPXV methyltransferase VP39 using molecular docking and ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) techniques.

Methods: Protein-ligand binding studies were conducted using AutoDock software. The 3D structures of berberine and sinefungin (used as the control compound) were retrieved from the PubChem database and converted into PDB format using AutoDock software. The compounds were then docked into the active site of methyltransferase VP39 (PDB ID: 8B07). Additionally, the pharmacokinetic properties and drug-likeness of the molecules were assessed using SwissADME analysis.

Results: Molecular docking results indicated that berberine exhibited strong binding affinity with VP39, forming hydrogen bond interactions with D95 and D138, and hydrophobic interactions with K175, R97, R140, and P202. SwissADME analysis confirmed that berberine possesses favorable drug-likeness and pharmacokinetic properties.

Conclusion: Berberine shows potential as an inhibitor of the VP39 methyltransferase in monkeypox virus. Further studies are required to confirm its inhibitory effects and potential as a therapeutic agent against MPXV.

Keywords: Monkeypox virus, Methyltransferase VP39, Berberine, Molecular Docking

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Abstract: A-10-2738-1

A Quantum Mechanical Investigation on Avacopan

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Background: In October 2021, the FDA approved Avacopan as the first drug targeting the C5aR receptor for patients with ANCA-associated vasculitis (AAV). Given the medical significance of this novel therapy, we conducted a comprehensive analysis of Avacopan's electronic structure using quantum computing technology.
Methods: Quantum mechanics (QM) calculations were performed using the density functional theory (DFT) method with GAUSSIAN 09 software. The structure of Avacopan was optimized using gradient procedures at both restricted Hartree-Fock (HF) and hybrid density functional B3LYP levels of theory, with the 6-31G basis set. The optimized structure achieved in this study was found to reside at the minimum point on the potential energy surface, exhibiting no negative modes.
Results: Structural parameters, such as bond lengths, angles, and dihedrals, were calculated along with thermodynamic parameters at the B3LYP/6-31G level of theory. The HF energy of the Avacopan molecule was determined to be -1250133.031688268 Kcal/mol. Additionally, Mulliken atomic charge, spin density, and molecular orbital energies were evaluated. The highest occupied molecular orbital (HOMO) was -0.18287 eV, and the lowest unoccupied molecular orbital (LUMO) was -0.03724 eV. The dipole moment was measured as X = 3.8599, Y = -3.9543, Z = -3.2348, with a total dipole moment of 6.4030 Debye.
Conclusion: The drug structure was optimized using the B3LYP/6-31G method, and the electronic properties of Avacopan were investigated, with specific focus on the energy gap between the HOMO and LUMO. The HOMO-LUMO gap was determined to be 0.14563 eV, providing insights into the electronic behavior of the molecule.

Keywords: Avacopan, QM-DFT Calculations, B3LYP, HOMO-LUMO gap

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Abstract: A-10-2743-1

Physicochemical Stability of Ferrous Sulfate

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Background: Ferrous sulfate is commonly used to treat anemia and is available in various medicinal forms such as tablets, drops, and syrup in Iran's pharmaceutical market. A significant challenge with the soluble forms of this drug is their instability. Due to oxidation, Fe^{2+} ions convert into Fe^{3+} ions, which lack therapeutic effects. This study aimed to investigate the physicochemical stability of ferrous sulfate syrup by examining various formulation factors.
Methods: To address the stability issues in ferrous sulfate formulations, antioxidants such as citric acid, ascorbic acid, and sodium formaldehyde sulfoxylate were incorporated. The pH of the formulations was adjusted to 2.2, 3.8, and 5.8 using buffered water. Samples were packaged in two ways: oxygen-free (using nitrogen gas) and in normal conditions (with oxygen). The stability of the formulations was measured on days 0, 14, 28, and 56 using reductometric titration with 0.1 N ceric sulfate.
Results: The formulations containing citric acid demonstrated the highest stability. Formulations with a pH of 2.2 showed improved stability compared to those with higher pH levels. Ascorbic acid did not yield favorable results as an antioxidant. Sodium formaldehyde sulfoxylate initially caused a decrease in Fe^{2+} levels but effectively maintained Fe^{2+} concentrations throughout the storage period, particularly at a pH of 2.2.
Conclusion: In conclusion, using citric acid as an antioxidant and adjusting the pH to 2.2 can significantly enhance the stability of ferrous sulfate syrup. This formulation strategy can prevent the oxidation of Fe^{2+} and improve the therapeutic effectiveness of the medication.

Keywords: Ferrous sulfate, Stability, Antioxidant

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Abstract: A-10-2751-1

The Use of Artificial Intelligence in Alzheimer's Disease Diagnosis: A Systematic Review

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Background: Alzheimer's disease, a type of dementia, gradually impairs thinking and memory to the extent that the brain is incapable of performing basic functions. By 2050, there will be over 45 million people worldwide affected. Due to the lack of effective interventions for therapy, early diagnosis is crucial. The aim of this study is to systematically review effective AI algorithms in early diagnosis of Alzheimer's disease.
Methods: The study was conducted based on the PICO criteria and aligned with the research objective, adhering to the PRISMA checklist. This systematic review included a comprehensive search from 2020 to July 2024 across the PubMed, SCOPUS, Web of Science, SID, and Magiran databases, as well as the Google Scholar search engine. The search utilized MESH keywords including "Diagnosis", " Alzheimer Disease" and "Artificial intelligence". Subsequently, two independent researchers screened the retrieved articles based on inclusion criteria.
Results: A total of 1182 articles were identified through the initial search. After reviewing the inclusion and exclusion criteria and critically evaluating the quality of the articles, a total of nine articles were ultimately selected. Recent studies have demonstrated the two main significant potentials of artificial intelligence, deep learning algorithms and machine learning algorithms, in diagnosing and predicting AD by analyzing medical imaging data alongside audial and genetic information. Deep learning algorithms have shown remarkable accuracy in detecting Alzheimer's patients by examining metabolic changes in the brain. Machine learning algorithms, specifically Bayesian networks, with 94.71% accuracy, and random forests, have also proven effective in Alzheimer's diagnosis. Random forest algorithms have accurately predicted the progression of mild cognitive impairment to Alzheimer's disease.
Conclusion: Despite the limited studies and the need for further research, AI-powered Alzheimer's disease diagnosis holds promise for improving the accuracy and timeliness of diagnosis.

Keywords: Alzheimer's disease, Artificial Intelligence, Diagnosis, Deep learning, Machine learning

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Abstract: A-10-2891-1

The effect of purslane supplementation on inflammatory and antioxidant markers in patients with rheumatoid arthritis: A parallel double-blinded randomized controlled clinical trial

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Background: Rheumatoid arthritis (RA) is an autoimmune disorder that results in joint dysfunction, inflammation, and increased mortality. This study aimed to evaluate the efficacy of purslane supplements on clinical outcomes, as well as inflammation and antioxidant markers in patients with RA a double-blinded randomized controlled clinical trial.

Methods: In this 12-week trial, 86 participants aged between 20 and 79 were divided into two groups. The intervention group (n=43) received a 500mg purslane capsule twice daily, while the control group (n=43) received a placebo capsule of the same shape and dosage.

Results: Seventy-seven patients (37 from the control group and 40 from the purslane group) completed the study. Purslane capsule intake significantly declined High-sensitivity C-reactive protein ($p \leq .001$), increased Superoxide dismutase ($p = .037$), and total antioxidant capacity ($p \leq .001$) changes. Furthermore, it significantly decreased in the purslane group compared to the placebo group at the end of the trial. There was a significant decrease in tumor necrosis factor-α (2.885 ± 2.068 vs. 2.330 ± 1.121, $p = .046$), and erythrocyte sedimentation rate (36.52 ± 20.04 vs. 26.70 ± 22.59, $p = .007$) levels in the purslane group.

Conclusion: Therefore, supplementation with purslane could improve inflammatory and antioxidant indicators in RA patients.

Keywords: Rheumatoid arthritis, Purslane, Inflammation, Antioxidant

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Abstract: A-10-2902-1

Cytotoxic and morphological effects of Rhamnolipids from Pseudomonas aeruginosa MA01 on MDA-MB-231 breast cancer Cells

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Background: Rhamnolipids (RLs) are naturally occurring compounds derived from bacteria that contain rhamnose as a sugar moiety connected to β-hydroxylated fatty acid chains. These glycolipid biosurfactants are mainly synthesized by various strains of Pseudomonas aeruginosa and show great promise for many applications, such as bioremediation and pharmaceuticals. The unique features of these compounds have garnered attention in the realm of cancer research, particularly considering their cytotoxic effects on different cancer cell lines. This study focuses on extracting and characterizing RL, including its mono-RL and di-RL congeners, and examining their impact on the morphology and viability of the MDA-MB-231 breast cancer cell line.

Methods: Rhamnolipids were isolated from Pseudomonas aeruginosa MA01 via acidic precipitation and solvent extraction, followed by column chromatography to separate mono and di congeners. Thin layer chromatography (TLC) was performed to verify the effective isolation of the rhamnolipid congeners. Cytotoxic activity of isolated RL, M-RL, and Di-RL was performed by the MTT assay, where the MDA-MB-231 cells were subjected to various concentrations of RL, mono-RL, and di-RL for 24 hours. Following treatment, the morphological alterations in the cells were examined using optical microscopy.

Results: The results demonstrated that RL, mono-RL, and di-RL, when examined in a concentration-dependent manner, significantly impeded the proliferation of MDA-MB-231 cells. Increased concentrations of RL, mono-RL, and di-RL resulted in a decrease in cell viability, indicating a cytotoxic action. Furthermore, the use of optical microscopy disclosed significant alterations in the structure of the treated cells, thereby suggesting that RL, mono-RL, and di-RL not only impact cell proliferation but also cause modifications in cell shape.

Conclusion: The results of the present investigation emphasize the potency of RL, mono-RL, and di-RL as novel therapeutics against tumor cell lines, particularly MDA-MB-231, by displaying concentration-dependent cellular cytotoxicity. Therefore, such compounds need further investigation regarding their potential therapeutic role in oncological treatment.

Keywords: Rhamnolipids, Pseudomonas aeruginosa, Cytotoxicity, MDA-MB-231 cell line

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Abstract: A-10-2762-2

Exosome odyssey to original line in dental regeneration

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Background: Exosomes as bilayer lipid membrane nanoparticles, which can contain DNA, mRNA, proteins, etc. Exosomes can be considered safe because they are produced endogenously. Today, the use of exosomes as a cell-free procedure is considered approved in regenerative medicine. In dental regenerative medicine also, the use of exosomes has increased attention.

Methods: This review was conducted and the studies published through 2022 were summarized to describe exosomes, their characteristics, routes of isolation, and ways of administration. Finally, some therapeutic aspects of these extracellular vesicles especially in dental degenerative lesions are discussed in the future. Exosome, extracellular vesicle, regenerative medicine, dentin, and tooth searched as keywords in PubMed-NCBI, Google Scholar, Scopus, and Web of Knowledge online resources. Regarding the study goals, the articles that used exosomes as cargo for drug delivery; or have diagnostic purposes were excluded from the study.

Results: Finally, 130 articles were included from all about 179 articles; that were related to exosome and regeneration (especially dental regeneration). Based on previous studies exosome therapy is beneficial in dental regeneration. Exosomes can induce dental pulp regeneration and periodontal regeneration; for example, they can induce angiogenesis and neurogenesis, or lead to periodontal ligament and alveolar bone regeneration, as well as many other therapeutic aspects.

Conclusion: it seems that exosomes have a special place in future medicine. Although the approved beneficial therapeutic aspects of exosomes, it seems there is a long way to use these dreams in human treatments, but probably someday it will become true.

Keywords: Exosome, Extracellular vesicle, Regenerative medicine, Dentin, Tooth

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Abstract: A-10-2912-1

The effect of cognitive behavioral therapy on serum cortisol and zinc biomarkers of MDD patients

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Background: Major depressive disorder (MDD) is a debilitating disease and a major challenge to the mental health of society. Serum zinc and cortisol are suitable biomarkers to assess the response to a given treatment. In the present study, serum concentrations of these markers were compared before and after treatment with cognitive behavioral therapy.

Methods: In this study, forty outpatients with major depressive disorder were identified based on DSM-V criteria. MDD patients received cognitive behavioral therapy (CBT) for 12 sessions / once a week / 90 minutes each session. The severity of depression was assessed by the Beck Depression Inventory (BDI-II) and serum cortisol and zinc concentrations were measured before and after treatment. Data were analyzed in GraphPad Prism 9.

Results: BDI-II scores were significantly reduced in comparison before and after CBT treatment (from 26.8±0.6 to 9.5±0.8). The serum cortisol level in patients decreased (from 453±0.09 to 386.4±0.07) and the zinc level increased (from 78.9±2.1 to 86.5±2.6).

Conclusion: CBT treatment led to a decrease in BDI-II score and serum cortisol level and an increase in serum zinc level. Therefore, the CBT treatment method is suitable for treating MDD patients. Selective biomarkers of cortisol and zinc are suitable markers in evaluating response to treatment. Further studies with larger sample sizes and longer study periods are needed.

Keywords: major depressive disorder, cognitive behavior therapy, cortisol, zinc

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Abstract: A-10-2895-1

Investigating the mutual effect of bee venom and quercetin in the production of exosomes containing micromolecules effective in skin collagenization

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Background: The skin aging process is multifactorial and is influenced by the environment and genetics. To investigate the effect of bee venom-olive Oleuropein and its combination on microRNA expression in exosomes extracted from HFFF2 skin cells in laboratory conditions, this study was conducted.
Methods: The treatments were applied in different concentrations. The MTT test was performed. The IC50 value for bee venom was 203 µg/ml. For Oleuropein, it was determined to be 55 µg/ml. (gram quercetin per ml) were applied and their exosomes were extracted by gradient centrifugation method. The relative expression of miRNA146a and miR200a in exosomes was measured by the Real-Time PCR method compared to the expression of U6.
Results: It showed results that the expression levels of miR146a and miR200a in the condition of bee venom treatment in exosome decreased, but in the treatment of oleuropein and the combination of oleuropein with venom, there was a significant increase at the probability level of less than 0.01. The treatment of venom with Oleuropein has this property through the induction of miRNA146a, which plays an anti-aging role with an epigenetic and antioxidant mechanism, and miR200a prevents aging through the mechanism of cell stability and proliferation, and this issue was also proven in cell studies.
Conclusion: the use of exosomes with the treatment of venom and Oleuropein in making anti-aging creams is expected after the study of the human skin.

Keywords: miR146a, and miR200a, Skin aging, collagen production

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Abstract: A-10-2724-2

Evaluating the amount of flavonoid compositions, chelating activity of Punicaceae and Vitaceae compared to EDTA standard

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Background: most chronic diseases such as cardiovascular diseases are directly related to the high production of free radicals in the body. Due to high antioxidant activity and chelating metals, herbal compositions can reduce the obnoxious effects of radicals by using a diet full of antioxidants, plan are the most important sources of natural antioxidants.

Methods: in this research, after preparing the pyrene of the Punicaceae plant and Vitaceae plant, samples were dried in the shade and pulverized by an electric mill. %90 methanol extract was prepared from samples with the maceration method. To determine, total flavonoid compositions were evaluated through the chromatography method with the color reagent of Aluminum Chloride. The complex power of iron was evaluated by herbal extracts based on the methods of Denis et al. in 1994.

Results: based on the obtained results from the experiment, the total flavonoid compositions of the pyrene of Punicaceae and pyrene of Vitaceae were measured at 0.6±0.1 and 16.23±0.85 milligram of quercetin per gram of extract. In the concentration of 100 µ g/ml, using the EDTA standard, the amount of iron's chelating was measured as %22.11, the pyrene of Punicaceae as %47.06, and the pyrene of Vitaceae as %24.95.

Conclusion: the research findings have shown that the pyrene of Vitaceae had higher flavonoid properties compared to Punicaceae. In the concentration of 100 milligrams per milliliter, the %90 methanol extract of intended plants performed better than the EDTA standard, and the pyrene of Punicaceae had higher iron chelating than iron.

Keywords: chelating activity ،total flavonoid ،pyrene of Punicaceae ،pyrene of Vitaceae.

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Abstract: A-10-2762-3

Adult neurogenesis: possible role of Crocin in CNS regeneration

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Background: The production of new neurons is called neurogenesis. Nodaway, we know that neurogenesis can persist through life, but it's not sufficient to face pathological conditions. Previous studies demonstrated that many factors can affect this process including pharmaceutical agents such as Crocin. Crocin as an active ingredient of saffron is an herbal medicine used from ancient times for many reasons. Several studies used this carotenoid in purpose to improve learning and memory, neuroprotection, and neurogenesis promotion.
Methods: Crocin, neuron, neuroprotective, and neurogenesis were chosen as keywords. Relevant articles were collected using online literature resources including Google Scholar, Scopus, Pubmed/Medline, and Web of Science up to 2024. A number of 34 articles from 120 retrieved articles were found relevant to the topic that was suitable based on our criteria.
Results: Crocin impacts some cellular pathways, proteins, etc. so its wide range of acting can be explained. Its acts on neurogenesis are due to its influence on P-CREB/BDNF, Notch, and Wnt/β-catenin pathways, so its role in cell proliferation and differentiation is identified. In a parallel way, its anti-inflammatory and anti-oxidant effects are a helpful aspect in its neuroprotective role to neurodegenerative conditions directly. Also, as an anti-inflammatory agent, can affect M2 microglia polarization, so helps as a neurogenesis impact indirectly too.
Conclusion: In this review, we summarize some studies to show the role of Crocin in adult neurogenesis promotion with an emphasis on cellular pathways that are triggered.

Keywords: Crocin, Natural products, Neurogenesis, Cell Differentiation, Neuroprotection

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Abstract: A-10-2887-3

Evaluation of membrane fatty acid profiles in erythrocytes of patients with major depressive disorder and comparison with normal individuals

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Background: The lack of omega-3 fatty acids in one's diet has been associated with the emergence of several neuropsychiatric conditions, such as major depressive disorder (MDD). Erythrocyte fatty acids are more reliable indicators of fat consumption than serum lipids, primarily because they have a slower turnover rate. Nevertheless, the fatty acid content of erythrocyte membranes in Iranian individuals with MDD has not yet been examined. Objectives: This study aimed to examine the fatty acid composition of erythrocyte membranes in individuals diagnosed with MDD. Moreover, a study was carried out to investigate the relationship between the ratio of fatty acids in the membrane and the severity of the disease.

Methods: The research included 38 persons who were diagnosed with MDD based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-V-TR). Additionally, 35 mentally healthy volunteers served as the control group. Analyzed utilizing reverse-phase high-performance liquid chromatography (HPLC), the fatty acid composition of the red blood cell membrane was determined as a percentage.

Results: The research showed a notable increase in the amounts of arachidonic acid (AA) in the cell membranes of red blood cells in patients, as compared to the control group. In contrast, the concentration of eicosapentaenoic acid (EPA) in the membrane of red blood cells was significantly greater in the normal group than in the group of patients. In people with severe depressive illness, the ratio of AA to EPA (AA/EPA) in red blood cells was considerably higher compared to the control group.

Conclusion: This study showed that the erythrocyte membrane fatty acid composition in MDD patients differs from that of healthy controls, which might be a part of the pathogenic mechanism of MDD and could be considered a possible risk factor for the disease.

Keywords: Keywords: Major depression disorder, erythrocyte membrane fatty acids, polyunsaturated fatty acids, omega-3 fatty acids

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Abstract: A-10-2256-4

Investigating the effect of COVID-19 on liver inflammatory factors

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Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an RNA virus first reported in humans in Wuhan, China, in December 2019. The virus has since spread rapidly worldwide causing coronavirus disease 2019 (COVID-19), which continues to have a devastating effect on global health. In this study, we systematically reviewed the articles on the effects of COVID-19 on the liver.
Methods: The electronic databases ISI Web of Science, Pubmed, and Scopus were comprehensively searched for articles published from January 2020 up to May 2024. We used the keywords covid 19 and liver inflammatory factors to find articles. High citation, validity of journals, and comprehensiveness of the article were our criteria for choosing the article.
Results: The number of articles searched was 87, of which 14 were used. Patients with chronic liver disease (CLD), particularly those with cirrhosis, experience immune dysfunction, increasing their susceptibility to infections, including SARS-COV-2. Despite concerns, studies indicate that patients with CLD are not overrepresented in COVID-19 cases and may even have a lower risk of positive testing, likely due to better adherence to preventive measures and routine testing. However, those with cirrhosis who contract COVID-19 face worse outcomes.
Conclusion: The hepatic effects of SARS-COV-2 infection have emerged as a significant aspect of COVID-19, especially for patients with existing cirrhosis, who face a notably higher risk of severe illness and mortality. While more research is needed to fully comprehend the mechanisms causing this decline in health, factors such as systemic inflammation, coagulation disorders, and immune system dysfunction are likely involved. Finally, we must acknowledge the substantial negative repercussions of the pandemic on liver services and unhealthy patient behaviors, which could lead to an increased global burden of liver disease in the future. Keywords: COVID-19, Coronavirus, Inflammatory factors, Liver, Meta-analysis

Keywords: COVID-19, Coronavirus, Inflammatory factors, Liver, Meta-analysis

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Abstract: A-10-2926-1

Enhancing Drug Delivery of Glatiramer Acetate Through in Vitro Development of Controlled-Release Nanoliposomes: Investigating Drug Release Kinetics and Cytotoxic Effects

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Background: Multiple sclerosis damages the myelin sheath covering nerve fibers. This condition affects 400,000 individuals in the United States and 2.5 million people globally, with a higher rate of diagnosis in women aged 20-40, with a ratio of 2:1. Liposomes facilitate drug dispersion, making them valuable in biomedicine. They enhance the stability of therapeutic medications, improve cellular and tissue absorption, and increase chemical bioactivity at specific locations. This technique delivers encapsulated compounds with high precision while minimizing negative consequences observed in laboratory settings. The Study aims to develop an optimal nanoliposome formulation using glatiramer acetate as the active pharmaceutical ingredient by examining drug release and associated adverse effects to achieve the most effective nanoliposomal system.

Methods: The thin layer hydration method was used to prepare nanoliposomes. A comprehensive array of analytical techniques, including FE-SEM, FTIR, XRD, HPLC, and DLS, were employed to examine the physicochemical characteristics of the product. Additionally, the biosafety of the nanoliposomes was assessed using the MTT assay on the 1321N1 human astrocytoma cell line. The release profile of GA from the carrier was studied using the dialysis diffusion method, and the stability of the nanoliposomes was also inspected.

Results: The size, Polydispersity Index, and zeta potential of the nanoliposomes were 91.2 ± 1.3nm, 0.34 ± 0.03, and -27.3 ± 1.2mV, respectively. The drug entrapment efficiency in nanoliposomes was approximately 70.2 ± 1.7%. The results from XRD and FTIR revealed no chemical interaction between the drug and carrier, and the nanoliposomes were safe for the cultured cell line. The nanoliposomes were stable under storage conditions and exhibited a sustained release profile.

Conclusion: Nanoliposomes, as drug carriers, are known to be a potent drug delivery system due to their numerous advantages. Based on the results, GA-nanoliposomes show promise as a strategy for treating MS patients, pending further in vivo experiments and clinical trials.

Keywords: Drug Delivery Nanoliposomes Multiple Sclerosis Glatiramer Acetate

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Abstract: A-10-2773-3

An overview of alphaproteobacteria diversity

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Background: Alphaproteobacteria, classified as a class within the Proteobacteria phylum, represent one of the largest and most diverse groups of bacteria. They exhibit a wide range of morphological and metabolic characteristics and have formed close associations with eukaryotic organisms. Many alphaproteobacteria, such as Rickettsia, Brucella, and Bartonella, have adopted intracellular lifestyles. Diverse metabolic strategies are found within this class, including photosynthesis, nitrogen fixation, ammonia oxidation, and methylotrophy. Morphological forms vary, including rod, star, and spiral shapes. Consequently, alphaproteobacteria can adapt to a variety of environments, such as saltwater, sediments, oceans, fossils, green waste compost, wastewater treatment plants, and more. Additionally, alphaproteobacteria have played a significant role in the origin of the eukaryotic cell.

Methods: This review gathered data from scientific databases including Google Scholar, SID, Scopus, PubMed, and Web of Science, as well as books published between 1990 and 2024. Keywords used in the search included alphaproteobacteria, Brucella, Bartonella, Rickettsia, 16S rRNA, metabolic, chemolithotrophs, marine, and saline environment. Retrieved articles were initially screened based on their titles and abstracts, and then further evaluated for their content, focusing on the importance and diversity of alphaproteobacteria.

Results: They often adopt an intracellular lifestyle, either as plant symbionts or as plant or animal pathogens. Alphaproteobacteria comprise the most abundant cellular organisms in marine environments. A total of 22 articles and 6 books were included and categorized based on metabolic diversity.

Conclusion: From the point of view of agriculture and industrial wastewater treatment, these microorganisms are a source of natural products such as Astaxanthin, and ectoine and an attractive source of new drug leads. Like the antibiotic, holomycin is also a probe to detect the presence of bacteria in the metagenome and as bacteria resistant to digestion in ciliated protozoa because they constitute important human and animal pathogens.

Keywords: alphaproteobacteria ،Brucella ،Bartonella ،Rickettsia\٦ ،S rRNA ،metabolic ،chemolithotrophs ،marine ، saline environment

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Abstract: A-10-2819-1

High levels of HbA1c and FBS in diabetic retinopathy patients in Kashan

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Background: Chronic elevation of intracellular glucose levels leads to damage in retinal capillaries among individuals with diabetes, resulting in diabetic retinopathy (DR), the leading cause of vision loss in adults aged 20 to 74 years. Proliferative diabetic retinopathy (PDR) is the advanced stage of DR, which eventually causes neovascularization of the optic disc, vitreous hemorrhage, and retinal detachment. Significant clinical risk factors for DR include the duration of diabetes, hyperglycemia, and hypertension. There is currently no definitive treatment for DR, so identifying patients at risk for developing retinopathy through biomarkers is critical. This study aims to identify risk factors associated with DR in Kashan, Iran.

Methods: This case-control study was conducted with the official approval of the research ethics committees of Kashan University of Medical Sciences. A total of 40 participants (18 male and 22 female) entered two groups. The first group included 20 patients with Non-diabetic retinopathy (NDR), and the second group included 20 patients with PDR. Diagnosis of retinopathy was confirmed via fundus photography. Laboratory data were collected for analysis, including HbA1c (hemoglobin A1c) and fasting blood sugar (FBS) levels.

Results: On average, the amount of FBS in patients with PDR was higher than that of NDR, and the Mann-Whitney U test showed that this difference was statistically significant (P=0.04). Furthermore, the independent T-test showed that PDR patients had a higher HbA1c level than NDR patients (t (33) = 2.68, P = 0.01).

Conclusion: The study's results showed that the levels of FBS and HbA1c in patients with diabetic retinopathy increased compared to NDR patients. Therefore, controlling FBS and HbA1c in patients without diabetic retinopathy can be useful and reduce the risk of retinopathy.

Keywords: Diabetic retinopathy, Risk factors, HbA1c, FBS

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Abstract: A-10-2931-1

Hsa_circ_0087856 as a new potential biomarker for breast cancer via circRNA-miRNA-mRNA network

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Background: Breast cancer (BC) is the most common cancer in women worldwide. Recent evidence has shown that circular RNA (circRNAs) deregulation is observed in different human malignancies. The most important function of circular RNAs is sponging the miRNAs. The regulatory functions of miRNAs are accomplished through the targeting and silencing of mRNAs. In this study, we will suggest a new potential circRNA for the diagnosis of BC by using available data and bioinformatics.

Methods: We selected a GEO data set (GSE182471) that microarray (074301 Arraystar Human CircRNA microarray V2) was implemented in 5 breast tumors and 5 adjacent normal tissues to find differentially expressed (DE) circRNAs. Next, we analyzed this dataset by GEO2R to select a circRNA with a high expression level in breast tumors. Then, we used a stepwise strategy to construct a circRNA-miRNA-mRNA network. We found all miRNAs that have been predicted to interact with selected circRNA in previous studies according to the circular RNA interactome tool, next, we used the circNet database to find the target genes for these miRNAs. Therefore, we selected an mRNA with an oncogenic role in BC.

Results: According to our analysis, hsa_circ_0087856 is one of the highly expressed circRNA in breast tumors. Previous studies predicted that this circRNA can sponge the hsa-miR-3692-5p. CircNet database analysis indicated that the Chromodomain helicase DNA binding protein 7 (CHD7) gene is the target gene for this miRNA. CHDs can play critical roles in various cellular processes including transcription, proliferation, and DNA damage repair.

Conclusion: We found that upregulation of the hsa_circ_0087856 presumably causes sponging of the hsa-miR-3692-5p, and can increase the expression of the CHD7 in BC. According to this evidence, hsa_circRNA_0087856 can be a potential novel diagnostic biomarker for BC. The biomarker capacity of this circ must be confirmed in future investigations.

Keywords: Breast Cancer, CircRNA, Biomarker

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Abstract: A-10-2934-1

Z-scan Method for Discrimination between Glioblastoma Cancer Cells and Normal Cells

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Background: Measuring the light that is scattered by the cells can be utilized to monitor the variations associated with cancer evolution. Therefore, optical methods are an applicable means to assess cell structure and provide diagnostic information for distinguishing cancer cells from normal cells. The Z-scan method is a general technique for the detection of nonlinear optical properties.

Methods: OLN-93 and C6 cell lines have been used as a model for oligodendrocytes (normal cells) and GBM (tumor cells), respectively. Both cell lines were cultured and prepared for analysis. A Nd:YAG CW laser with a wavelength of 532 nm was used. The laser beam passes through the prepared samples and the transmittance power is distinguished by dislocation. Finally, the nonlinear refractive index and the extinction coefficient of the samples were determined.

Results: Our study showed that the extinction coefficient of the C6 and OLN-93 cells were 49 ± 3 and 33 ± 2, respectively. Also, the sign and value of the nonlinear refractive index (n2) for the C6 and OLN-93 cells were −5.44 × 10−7 cm2 w−1 and +6.07 × 10−7 cm2 w−1, respectively. According to this study, the sign of the n2 index for the C6 and OLN-93 cells was negative and positive, respectively.

Conclusion: Our results suggested that the nonlinear refractive index of the cell samples and the Z-scan technique could be an applicable means for identifying glial cancer cells from normal cells.

Keywords: Z-scan, normal cell, cancer, laser

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Abstract: A-10-2955-1

The Emerging Role of Copper Metabolism and Cuproptosis in human GI cancers

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Background: Gastrointestinal (GI) cancers are responsible for more than a quarter of cancer incidence globally. Despite the progression of cancer treatment, the prognosis of GI cancers is considered poor. In recent years, several metal ions have been discovered to treat cancers. Cuproptosis is a novel copper-induced mitochondrial cell death mechanism bound with the proliferation and migration of different cancers. However, the mechanisms of cuproptosis antitumor therapy have not yet been relatively understood.

Methods: The review article was conducted using articles from PubMed, Google Scholar, Web of Science, and Science Direct up to February 2024. The search terms used were Cuproptosis, Copper metabolism, and Gastrointestinal or GI cancers. This search yielded 24 articles, of which 15 were excluded based on their titles and abstracts. Nine articles met the inclusion criteria and were selected. All the articles that were chosen are written in English.

Results: The study included a total of 9 articles. Induction of cell death is an essential factor in cancer treatment. Copper can influence cell death through ROS, ER, inflammatory responses, etc. Copper can directly attach to lipoylated components of the tricarboxylic acid (TCA) cycle. Throughout this, the aggregation of lipoylated proteins and the subsequent loss of iron-sulfur cluster proteins happens, resulting in proteotoxic stress and ultimately concluding in cell death.

Conclusion: More research in copper metabolism and cuproptosis is highly encouraged, as metal ion therapy can eliminate cancer cells with less damage to normal tissues and organs than traditional therapies. Despite the investigations developed in Ferroptosis, the death of copper-metabolism cells has not yet been relatively understood. Thus, more investigations are highly demanded.

Keywords: Copper metabolism, Cuproptosis, Gastrointestinal cancers (GI cancers)

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Abstract: A-10-2877-1

The investigation of the improvement process of the yeast strain Pichia pastoris through Adaptive Laboratory Evolution

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Background: Biological processes often face variable environmental conditions, including uncontrolled warming, which can lead to reduced product yields and consequently high costs. The laboratory adaptive evolution method allows microorganisms to adapt to environmental changes, thus maintaining production and performance even under stress.

Methods: In this study, the yeast Pichia pastoris (X33) was used as a laboratory model to investigate and confirm this process, aiming for a better understanding of the adaptation pathways under thermal stress over a period of 105 days. This process involved a gradual increase in temperature by 1°C every 15 days, starting from 28°C to 35°C in a constant temperature incubator. After confirming the adaptation of the strain and optimal growth at the typical growth temperature, several genes, including ATP2, ATP3, CRM1, and ERG3 from P. pastoris, were selected and sequenced.

Results: The gradual increase in temperature revealed significant genetic mutations in the evolved strain, particularly in genes associated with energy production and stress response, such as ATP2, ATP3, CRM1, and ERG3 Furthermore, the growth of the evolved strain was assessed against the control strain in a BMMH growth medium under dual stress conditions (glycerol deficiency) during thermal stress, with results indicating that the evolved strain exhibited better growth and greater resistance compared to the control strain.

Conclusion: In conclusion, the study successfully demonstrated the effectiveness of the Adaptive Laboratory Evolution (ALE) method in enabling the yeast P. pastoris (X33) to adapt to thermal stress. This research underscores the potential of adaptive evolution techniques to improve microbial performance in fluctuating environmental conditions, which is crucial for optimizing production processes in biotechnology and related fields.

Keywords: Pichia Pastori, Thermotolerant strains ALE (adaptive laboratory evolution), Gene sequencing

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Abstract: A-10-2972-1

Cytokeratin 19 expression in prostatic adenocarcinoma: a systematic review

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Background: Cytokeratins are intracellular polypeptides recognized as diagnostic biomarkers or prognostic factors for specific malignancies. The expression of Cytokeratin 19 (CK-19) has been demonstrated to possess prognostic significance for certain neoplasms, yet its association with others, including prostate cancer (PCa), remains unclear. This systematic review article aimed to examine the correlation between CK-19 expression and prostate adenocarcinoma (PAC).

Methods: To include the pertinent studies that identified CK-19 expression in PAC, published manuscripts since June 2024 were retrieved utilizing PubMed, Scopus, and Web of Science repositories. The keywords “prostate cancer” and “cytokeratin 19” along with their Mesh terminologies were employed for database inquiries. Data from the selected articles were extracted and organized in tabular form. This investigation was conducted following the PRISMA guidelines, and the JBI checklist was utilized for quality evaluation. The study protocol was registered in PROSPERO under the “CRD42023472637” designation.

Results: Twenty-one studies were included. Eleven studies employed reverse transcription polymerase chain reaction (RT-PCR) to assess CK19 expression, four utilized immunohistochemistry (IHC) staining, three utilized both one-step nucleic acid amplification (OSNA) and hematoxylin and eosin (H&E) methodologies, and three applied the electrochemiluminescence (ECL) technique. CK-19 expression was identified in 301 patients among 619 individuals. Furthermore, only five out of 80 healthy donors (HDs) exhibited positive CK-19 expression.

Conclusion: The extant evidence indicates a relationship between CK-19 expression and PAC progression, with elevated CK-19 levels correlated with advanced stages and poorer prognosis. The overall evidence suggests that CK-19 may function as a diagnostic and prognostic marker in PAC.

Keywords: Cytokeratin 19, CK-19 expression, Prostatic adenocarcinoma (PAC), Gleason scores, Gleason grades

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Abstract: A-10-2622-3

Exploring the Apoptotic and Cytotoxic Effects of Thymol on C6 Malignant Glioblastoma Cells

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Background: Glioblastoma multiforme (GBM) is the most prevalent and aggressive brain tumor, associated with a very poor prognosis, highlighting the need for new treatment strategies for this condition. Thymol (2-isopropyl-5-methylphenol) is a chemical compound with various medicinal properties, including analgesic, antibacterial, antispasmodic, and anti-inflammatory effects. Recent research has indicated that thymol is a significant inducer of apoptosis in cancer cells, although the precise mechanism remains unclear. Our goal was to assess whether thymol exhibits anticancer properties in rat C6 malignant glioblastoma cells.

Methods: We evaluated the effects of thymol on cell viability and apoptosis in C6 cells at different concentrations. The study examined the production of reactive oxygen species (ROS), the mRNA levels of apoptosis-related genes, and the dynamics of the cell cycle.

Results: The half-maximal inhibitory concentration (IC50) of thymol for C6 cells was found to be 350 µM at 24 hours and 260 µM at 48 hours post-treatment, with no cytotoxic effects observed on normal HFF cells at these concentrations. Thymol increased the expression of Bax and p53 while decreasing Bcl2 levels, resulting in greater apoptotic cell death and higher ROS production. Moreover, the cytotoxic effects of thymol on C6 cells may be associated with cell cycle arrest at the G2/M phase.

Conclusion: Given these findings, thymol's ability to induce apoptosis and toxicity in cancer cells, while sparing normal cells, suggests it could be a promising candidate for targeted glioblastoma treatment.

Keywords: Glioblastoma, Thymol, Cancer, C6 cell line, Apoptosis

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Abstract: A-10-3071-1

Relationship Between Oxidative Stress Markers and Liver Stiffness Across Obesity Phenotypes: Insights from Superoxide Dismutase and Catalase Levels

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Background: Obesity is a rapidly increasing global health concern that contributes to metabolic disorders such as fatty liver disease. Obesity phenotypes are classified based on BMI and metabolic health into four groups: metabolically healthy non-obese (MHNO), metabolically unhealthy non-obese (MUNO), metabolically healthy obese (MHO), and metabolically unhealthy obese (MUO). Oxidative stress is a significant factor in the development of obesity-related diseases. This study aims to compare superoxide dismutase and catalase among these different obesity phenotypes and to examine their relationship with liver stiffness (LS) as an emerging liver health indicator.
Methods: Participants were categorized based on BMI and metabolic health into the four obesity phenotypes; MHNO (n=25), MUNO (n=25), MHO(n=25), and MUO(n=25). Serum samples were analyzed for enzyme activities using spectrophotometry. Liver stiffness (LS (was measured to assess liver health.
Results: Our results showed lower levels of SOD and catalase in metabolically unhealthy groups (both obese and non-obese) compared to their metabolically healthy counterparts. The correlation analysis showed lower levels of SOD are positively correlated with higher liver stiffness in metabolically unhealthy obese (r=0.4; P-value: 0.02). However, we found no association with LS and catalase activity.
Conclusion: A strong positive correlation between decreased levels SOD and increased liver stiffness would suggest that diminished oxidative stress defenses are associated with greater liver damage and fibrosis. This implies that lower antioxidant enzyme activity may contribute to an accumulation of oxidative stress, leading to liver injury and progressive fibrosis.

Keywords: Oxidative Stress, Obesity Phenotypes, liver disease

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Abstract: A-10-2931-2

Plasma hsa_circ_0079876 as a non-invasive predictive biomarker for benign breast disease

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Background: Benign breast diseases (BBDs) are potential health concerns for a large number of women. Several reports have described a higher risk of subsequent breast carcinoma among patients who have BBD. Therefore, getting a diagnosis as soon as possible may prevent the development of breast malignancy. In this context, non-coding RNAs have emerged as potential early diagnostic markers for various disorders. Circular RNAs (circRNAs), which are characterized by their covalently closed loops without 5' and 3' ends, offer stability in blood or plasma, making them ideal candidates. Therefore, this study investigates the plasma level of hsa_circ_0079876 as a possible biomarker for non-invasive screening for BBD.

Methods: 63 women (15 cases and 48 controls) were included in this study. Quantitative reverse transcription polymerase chain reaction (qRT-PCR) was performed to measure the levels of plasma hsa_circ_0079876 after RNA extraction from plasma samples.

Results: A significant increase in plasma expression levels of hsa_circ_0079876 was observed in BBD patients compared to healthy controls (p-value = 0.001). The ROC curve results indicated that the AUC, sensitivity, and specificity of hsa_circ_0079876 were 0.901, 0.86, and 1 respectively.

Conclusion: Several studies reported that a history of BBD was associated with an increased risk of screen-detected breast cancer. It seems that the plasma level of hsa_circ_0079876 in BBD patients is considerably higher than in healthy women, it can be the result of common risk factors for BC and BBD. These findings indicate that the presence of proliferative BBD might be an important prognostic sign for subsequent breast cancer development. The results demonstrated hsa_circ_0079876 potential utility as a non-invasive biomarker for the screening of BBD.

Keywords: Benign breast disease, plasma, circRNA, Non-invasive

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Acta Biochimica Iranica

Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2931-3

Evaluation of hsa_circ_0001785 in plasma of women with benign breast disease

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Background: Many epidemiologic studies of breast cancer have shown that a history of benign breast disease (BBD) increases the risk of breast cancer (BC). Circular RNAs (circRNAs) are a new class of non-coding RNAs characterized by a covalently closed loop without 5' and 3' ends thus, could escape from exonuclease-mediated degradation. CircRNAs play pivotal roles in cancer development and progression by participating in several biological processes. The circulating hsa_circ_0001785 has recently been reported as differentially expressed circRNA in BC tumors. This study checked the ability of hsa_circ_0001785 to diagnose BBD for the first time.

Methods: In this case-control study, 63 peripheral blood plasma samples were taken which included 48 healthy women and 15 women with BBD, after obtaining informed consent. Total RNA was extracted from plasma and qRT-PCR was used to determine the hsa_circ_0001785 level. Then, the expression results of this circRNA were analyzed by statistical methods.

Results: This study showed that the plasma expression levels of hsa_circ_0001785 in patients with BBD had a significant increase compared to healthy women (P-value = 0.013). According to the ROC curve results, the AUC, sensitivity, and specificity of hsa_circ_0001785 were 0.666, 0.60, and 0.79 respectively.

Conclusion: BBD is a very common condition in women. An excess risk of developing BC among women with BBD has been demonstrated. These results suggest that there is a similarity in etiologic factors between proliferative BBD and breast cancer and that a part of the benign lesions may progress to malignant lesions. It seems that the biomarker capability of hsa_circ_0001785 in the non-invasive screening of BBD can be considered due to the sensitivity and specificity of this circRNA in the diagnosis of BBD from the healthy group. Therefore, in future studies, it is necessary to investigate this circRNA in various and larger populations.

Keywords: Benign breast disease, Breast cancer, Biomarker, circRNA, Non-invasive

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Abstract: A-10-2968-1

Endothelial dysfunction in COVID-19: Insights from bronchoalveolar lavage and molecular markers

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Background: Endothelium plays a crucial role in immune responses and inflammatory reactions. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) induces an exaggerated immune response. Therefore, in this study, the roles of endothelium in the manifestation of severe Coronavirus disease 2019 (COVID-19) were investigated. **Methods:** The direct effects of SARS-CoV-2 alpha (SCA) and SARS-CoV-2 omicron (SCO), on endothelial function were investigated in bronchoalveolar lavage (BAL), that were obtained by leftover samples of COVID-19 patients who were compared to forty control group to enrich proteins expression of Intracellular Adhesion Molecule-1 (ICAM-1), Vascular cell adhesion molecules 1 (VCAM-1), Nuclear factor erythroid 2–related factor 2 (Nrf2), NADPH oxidase 2 (NOX2), and von Willebrand factor (vWF) by western blot technic.
Results: SARS-CoV-2 increased protein expression of ICAM-1. VCAM-1 protein expression in SCO increased too. vWF protein expressed highly too. Although NOX2 protein increased by SCA and SCO, Nrf2 protein decreased by SARS-CoV-2.
Conclusion: Based on our findings, severe COVID-19 can cause damage to the vascular endothelium, which is crucial in affecting multiple organ dysfunction. Our research indicates that endothelial dysfunction is a significant factor in the progression of severe COVID-19 in comparison to other respiratory diseases.

Keywords: SARS-CoV-2, COVID-19, Endothelial dysfunction, Inflammation, Oxidative stress

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Abstract: A-10-2584-1

Association between PCSK9 Levels, high sensitivity Cardiac troponin and Markers of Oxidative Stress in Coronary Artery Disease Patients

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Background: Coronary artery disease (CAD) is a highly prevalent cardiovascular condition, and it is the main cause of mortality in Iran and the entire globe. The goal of this investigation was to evaluate the association among PCSK9, cardiac parameters, and markers of oxidative stress (OS) in MI patients.

Methods: This investigation was carried out at Tehran Heart Centre Hospital on 63 healthy individuals and 63 patients with MI who had a coronary artery block above 50% (CAB > 50%) based on angiography. OS parameters, such as TAC, MDA, MPO, SOD, CAT, and GPx activity, are assessed employing colorimetric method kits. ELISA and the chemiluminescent immunometric method were used to measure PCSK9, ox-LDL, hs-cTnI, and hs-CRP. Indeed, biochemical parameters and EF% were measured.

Results: The results indicate that increased EF% (> 37.5%), TAC (> 1.05 mmol Fe2+/L), GPx (> 16.48 mU/mL), CAT (> 11.32 nmol/min/ml), and SOD (> 297.16 U/ml) activity decreased the risk of CAB > 50%. However, increased MDA (> 32.07 nmol/ml), MPO (17.77 U/L), hs-CRP (> 5.5 mg/l), ox-LDL (> 64.87 µg/l), and hs-CTnI (> 0.208 ng/ml) increase the risk of CAB > 50%. Indeed, there is no difference in PCSK9 levels, and there is a chance of an incidence of CAB > 50%. EF% has a Positive Relationship with SOD and a negative relationship with MDA, MPO, ox-LDL, hs-CTnI, and hs-CRP. hs-CTnI exhibits positive correlations with ox-LDL, MDA, and MPO.

Conclusion: Although PCSK9 has been proven to play a role in the occurrence of MI through OS and inflammation, its primary function is to impact LDL-C levels in circulation. Therefore, when considering the function of PCSK9, one must take into account the levels of LDL-C. Also, ox-LDL, EF%, and hs-CTnI have the best biomarkers for the diagnosis of CAB > 50%, respectively.

Keywords: PCSK9, oxidative stress, myocardial infarction, hs-CTnI, EF%

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Abstract: A-10-2958-1

Peptide and Geraphen quantum dot for delivery of htsFLT01 into Retinoblastoma cells

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Background: Retinoblastoma is a common intraocular malignancy that occurs during childhood. VEGF is the most potent and specific proangiogenic factor secreted by almost all solid tumor cells. HtsFLT01 is a fusion protein that can neutralize mouse and human VEGF and PlGF. MiRGD peptides have an iRGD motif that can penetrate cancerous tissue by binding to αv integrin. Graphene quantum dots have shown great potential in bio-imaging applications due to their excellent biocompatibility, low cytotoxicity, and tunable fluorescence properties.
Methods: htsFLT01 plasmids were extracted using an anion exchange affinity column according to the Favorgen Maxi preparation kit. MiRGD peptide was extracted using a Ni-NTA chromatography column, increasing imidazole and decreasing the urea gradient. After observing the peptide bands on 15% SDS-PAGE, the purified peptide was desalted by dialysis. The graphene quantum dot was produced using the hydrothermal method using citric acid and urea. Bio Tek cytation examined GQDs absorption and emission wavelength, and FTIR showed their functional surface group. Preliminary investigation of the complex formation was performed by gel retardation assay. Finally, DLS was conducted to determine the size and charge of GQDs, MiRGD, and complexes. The human RB cell line Y79 was preserved in RPMI 1640 medium containing 10% fetal bovine serum and 1% penicillin/streptomycin and was placed in a 37℃, 5% CO2 incubator.
Results: Cytation revealed that GQDs have 330 nm absorption and 440 nm emission wavelengths. DLS determined the charge of GQDs, MiRGDs, and complexes as -23, +6, and +11, respectively. Acrylamide-based gel retardation demonstrated that the dual and ternary stable complexes. Agarose-based gel retardation assay followed by ethidium bromide staining confirmed pDNA attached to the complexes.
Conclusion: Further molecular investigations, such as apoptosis flow cytometry and real-time PCR, will be conducted after determining the best dose and time to treat cells with the nano complex using the MTT assay.

Keywords: Retinoblastoma, gene delivery, peptide, nanoparticles

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Abstract: A-10-3002-1

Evaluation of the cytotoxicity of two fractions extracted from scorpion venom on the breast cancer cell line SKBR3 and normal fibroblast HU-02

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Background: To date, the efficacy of conventional chemotherapy, radiotherapy, and targeted biological therapies in the treatment of cancer has not been satisfactory. This can be attributed to factors such as low specificity, limited effectiveness against the disease, drug resistance, and severe side effects. Since cancer is a complex systemic disease, new treatment approaches are required to target multiple stages of the cancer cell cycle while minimizing toxicity to normal tissues. Natural products represent promising therapeutic options, with scorpion venom serving as a notable example.

Methods: In this study, the cytotoxicity effect of two fractions (F2 and F4) isolated from Hemiscorpius lepturus venom on SKBR3 breast cancer cells and HU-02 normal fibroblasts was investigated using the MTT assay. Cancer and normal cells were treated with different concentrations of F2 and F4 (0, 20, 40, 60, 80, and 100 µg/mL) for 12, 24, and 48 hours, and finally, the viability percentage of cells was calculated.

Results: The results showed a significant reduction ($p<0.05$) in the viability of both cancer and normal cells in a concentration- and time-dependent manner. The lowest viability was observed at a concentration of 100µg/mL after 48 hours. IC50 values at 48 hours were determined to be 51.45 µg/mL for SKBR3 cancer cells treated with fraction 2 and 61.45 µg/mL for those treated with fraction 4.

Conclusion: Overall, Hemiscorpius lepturus scorpion venom appears to be a valuable option for further research in the inhibition of breast cancer cells.

Keywords: Scorpion venom, Hemiscorpius lepturus, MTT, Cancer, Viability

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3002-2

Anti-proliferative properties of two fractions isolated from Hemiscorpius lepturus scorpion venom on prostate and normal cell lines

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Background: Many studies have shown that certain potent toxins in scorpions contain various bioactive molecules with significant cytotoxic effects on cancer cells.

Methods: In this study, the in vitro cytotoxic effect of Hemiscorpius lepturus venom was assessed against PC-3 prostate cancer cells and HFF-1 normal fibroblasts using the MTT assay. To achieve this, the venom was fractionated using high-performance liquid chromatography, and the cytotoxic effects of two isolated fractions, F2 and F4, on cancer and normal cells were evaluated. Then, cancer and normal cells were treated with various concentrations of fractions F2 and F4 (0-400 µg/mL) and carboplatin (0-120 µg/mL) for 24 and 48 hours, and finally, viability percentage was calculated.

Results: The results showed a concentration- and time-dependent decrease in cell viability ($p < 0.05$). The greatest reduction in viability was observed at 48 hours, with PC-3 prostate cancer cells treated with F2 and F4 showing a viability of 24.09% and 30.25%, respectively, at a concentration of 50 µg/mL. Cancer cells treated with carboplatin at a concentration of 120 µg/mL showed a viability of 38.28%. Similarly, HFF-1 normal prostate cells exhibited viabilities of 28.83% and 37.80% when treated with F2 and F4, respectively. The results revealed that fractions F2 and F4 exhibited high toxicity towards prostate cancer cells compared to normal cells. Moreover, based on the IC50 values, F2 (18.10 µg/mL) and F4 (30.49 µg/mL) demonstrated greater toxicity to cancer cells than carboplatin (80.12 µg/mL).

Conclusion: In general, the findings indicate the anticancer effects of two fractions F2 and F4 isolated from H. lepturus scorpion venom on prostate cancer, necessitating In general, the results indicate the anticancer effects of two fractions F2 and F4 isolated from H. lepturus scorpion venom on prostate cancer, which necessitates research on the anticancer molecular mechanisms of the two fractions.

Keywords: Venom, Hemiscorpius lepturus, cytotoxic effects, Cancer, MTT

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Abstract: A-10-3014-1

Exploring the Diagnostic Potential of miRNA-122 in detecting Hepatocellular Carcinoma: A Systematic Review and Meta-Analysis

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Background: Hepatocellular carcinoma (HCC) ranks as the third leading cause of cancer-related mortality worldwide and is often a result of chronic infection with Hepatitis B or C viruses. MicroRNAs (miRNAs) are small, non-coding RNAs that regulate gene expression post-transcriptionally. Among them, miRNA-122, a liver-specific miRNA, acts as a tumor suppressor. Its downregulation has been linked to malignancy. This systematic review aimed to explore the diagnostic potential of miRNA-122 as a biomarker for HCC.

Methods: Following PRISMA guidelines, a systematic search was performed across PubMed, Scopus, Web of Science, and Google Scholar, using keywords such as "miRNA122," "miRNA-122," "hepatocellular carcinoma," "HCC," and "liver cancer." No time restrictions were applied. Observational studies reporting on miRNA-122 expression in HCC patients were included, while reviews, cell/animal studies, editorials, and conference papers were excluded. Two independent reviewers screened the studies, resolving conflicts through a third reviewer. The quality of studies was assessed using the Newcastle-Ottawa scale. Data were extracted and organized, with heterogeneity assessed via I^2 statistics. Meta-analysis was conducted using a random-effects model in Stata software (version 14.2) to calculate pooled effect sizes with 95% confidence intervals.

Results: A total of 174 studies were initially identified. After removing 76 duplicates and 92 irrelevant studies, 8 articles involving 637 participants were included. The meta-analysis found a pooled effect size of 0.87 (95% CI [0.788–0.961]), indicating strong diagnostic accuracy for miRNA-122 in detecting HCC. However, significant heterogeneity was observed ($I^2 = 90.7\%$, $p < 0.0001$), likely due to variations in populations and methodologies.

Conclusion: Despite notable heterogeneity, miRNA-122 shows potential as a non-invasive biomarker for HCC diagnosis. Future studies with more consistent designs are needed to validate its clinical utility.

Keywords: Hepatocellular carcinoma, HCC, miRNA-122, Biomarker

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Abstract: A-10-3017-1

Expression analysis of beta-secretase 1 (BACE1) enzyme in peripheral blood of patients with Alzheimer's disease

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Background: Recent evidence has indicated that beta-secretase 1 (BACE1) is involved in the production of amyloid beta (Aβ) in patients affected with Alzheimer's disease (AD). Therefore; the purpose of this study was to measure mRNA and plasma levels of BACE1 in AD patients, as an early diagnosis biomarker for such individuals.
Methods: A total number of thirty AD patients and thirty normal subjects as controls were recruited in the present study. Plasma levels of BACE1 were then examined via enzyme-linked immunosorbent assay (ELISA) and also mRNA expression of BACE1 in total blood was measured using a real-time PCR technique.
Results: The findings revealed a significant difference in gene expression of BACE1 in the peripheral blood of AD patients compared with that in controls (p0.05).
Conclusion: Given the importance of early diagnosis of AD patients, it was suggested that the measurement of plasma levels and also mRNA expression of BACE1 might be a valuable blood-based biomarker used in preference to other invasive diagnostic methods such as cerebrospinal fluid (CSF) analysis.

Keywords: Beta-Site APP-Cleaving Enzyme 1, Alzheimer's disease, Biomarker

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Abstract: A-10-3016-1

Advancements and Challenges in Pharmaceutical Biochemistry: A Systematic Review of Drug Mechanisms and Therapeutic Innovations

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Background: Pharmaceutical biochemistry combines the core concepts of biochemistry and pharmacology to investigate the molecular processes that regulate drug actions and interactions. This discipline plays a crucial role in understanding how drugs affect biological systems, contributing to the development of safer and more effective treatments. This review seeks to evaluate the current landscape of pharmaceutical biochemistry, focusing on recent advancements, challenges, and future directions in drug discovery, development, and therapeutic approaches.

Methods: A systematic search was conducted in major scientific databases, including PubMed, and Scopus, from 2010 to 2023. Studies on drug mechanisms, pharmacokinetics, molecular targets, and biochemical pathways were included. Selection criteria were based on peer-reviewed articles discussing innovations in pharmaceutical biochemistry, emphasizing experimental findings, computational methods, and clinical applications. Data were extracted and analyzed for trends, knowledge gaps, and translational potential.

Results: The review uncovered more than 150 pertinent studies, showcasing notable advancements in understanding the biochemical mechanisms involved in drug action. Significant progress made in areas such as the roles of enzymes, receptors, and signaling pathways in drug metabolism, identifying new molecular targets, and applying bioinformatics tools for predicting drug interactions. Additionally, innovative methods like CRISPR-based gene editing, proteomics, and personalized medicine were recognized as key contributors to the advancement of the field. Nonetheless, challenges persist in accurately predicting drug efficacy and safety, especially in the context of complex diseases like cancer disorders.

Conclusion: Pharmaceutical biochemistry is progressing rapidly with the integration of advanced biochemical techniques and computational tools, which are improving our comprehension of drug mechanisms at the molecular scale. While considerable advancements have been made, further research is necessary to overcome ongoing challenges in drug discovery and optimization. Future efforts should focus on bridging the gap between experimental biochemistry and clinical practice, fostering the creation of more precise and personalized treatments to improve patient outcomes.

Keywords: Pharmaceutical biochemistry, drug mechanisms, pharmacokinetics, molecular targets, biochemical pathways,

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Abstract: A-10-3045-1

Expression of p53 Tumor Suppressor Gene in Human Breast Cancer and Its Association with the Clinicopathological Factors

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Background: The p53 transcription factor is pivotal in regulating numerous cellular activities. When cells are exposed to genotoxic stress, p53 promotes processes like DNA repair, halting the cell cycle, or triggering apoptosis. In breast cancer, the tumor-suppressing function of p53 is frequently disrupted, either due to an overproduction of its inhibitor MDM2 or due to mutations found in 30-35% of cases. However, the ability of p53 to serve as a predictor of clinical outcomes remains uncertain. This study investigated the association between p53 gene mutations and various clinicopathological features.

Methods: In this study, 55 pairs of breast cancer tissues were analyzed to assess p53 and the expression of clinicopathological variables using immunohistochemistry (IHC) staining. The mutated p53 protein has a longer half-life than the wild-type protein, making it detectable by IHC.

Results: The p53 tumor suppressor status in the tissue samples was classified into two groups (mutant and wild type) using IHC staining. Our results indicated that 54.54% of the patients had mutant p53, while the rest had the wild type. The mutated p53 expression showed a significant correlation with tumor size, stage, and pathological grade.

Conclusion: Our data suggested that the overexpression of mutated p53 protein may be considered a biomarker for poor prognosis and an indicator of increased malignancy potential in breast cancer patients.

Keywords: p53 Tumor Suppressor, clinicopathological variables, immunohistochemistry

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Abstract: A-10-3030-1

Edge detection of lesions caused by gastritis using fuzzy adjustment algorithm

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Background: The current clinical diagnosis of Helicobacter pylori is based on biochemical, immunological, or microbiological methods, however, these methods are operator-dependent, time-consuming, expensive, and require special skills, recent advances in technology and incorporation of artificial intelligence into diagnostic methods. It has been proposed as an interesting alternative in medical diagnosis. The main goal of this study was edge detection of lesions caused by gastritis using a fuzzy adjustment algorithm.
Methods: In this research, Fuzzy Edge Detection (FED) was used to identify edges of images. The vertical, horizontal, and oblique derivatives and threshold are done with the above logic and the obtained images are considered as the input of the algorithm after removing the extra points and lines, the proposed model was presented.
Results: The results of the present study showed that with the help of phase adjustments, the images of Helicobacter pylori can be recognized in gastritis lesions, and edge improvement can be suggested with this method, but it was not possible to identify and improve the edge of Helicobacter pylori bacteria other in gastric some other Gastric lesions images.
Conclusion: The results of this study showed that disturbed images in gastric inflammatory lesions provide a suitable prediction model.

Keywords: gastritis lesions, Helicobacter pylori, fuzzy logic

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Abstract: A-10-2953-1

Hepatoprotective effect of Astragalus ovinus root polysaccharide compounds on cyclophosphamide induced hepatotoxicity in rats

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Background: This study was conducted to investigate the effect of polysaccharide compounds of Astragalus ovinus root (AOP) on cyclophosphamide-induced hepatotoxicity.
Methods: Forty-two Wistar male rats weighing 200-250 grams, randomly divided into 7 groups (n: 6): Normal control: recipient normal saline for 14 consecutive days, Toxic group: recipient of 200 mg/kg of cyclophosphamide on the 9th day, Groups 3 and 4: recipient of the hydroalcoholic extract of A. ovinus root at dose of 120 and 240 mg/kg for 14 consecutive days and 200 mg/kg of cyclophosphamide on the 9th day, groups 5 and 6: recipient of AOP at dose of 60 and 120 mg/kg for 14 consecutive days and 200 mg/kg of cyclophosphamide on the 9th day, and seventh group: recipient of silymarin at dose of 100 mg/kg for 14 consecutive days and 200 mg/kg of cyclophosphamide on the 9th day. Then all the animals were sacrificed, and their blood and liver samples were collected to check liver enzymes, hepatic oxidative stress markers, activity of antioxidant enzymes, hematoxylin and eosin staining, and expression levels of TNF-α and IL-6 genes.
Results: Cyclophosphamide led to a significant increase in ALT, AST, tissue and serum NO, serum MDA, IL-6, and TNF-α genes. Administration of AOP caused a significant decrease in tissue NO, MDA, and FRAP, as well as the level of IL-6 gene expression.
Conclusion: According to this study, it can be suggested that the polysaccharide compounds of this plant can have a protective effect against cyclophosphamide-induced hepatotoxicity.

Keywords: Hepatotoxicity, Cyclophosphamide, Astragalus ovinus, Polysaccharide

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Abstract: A-10-3058-1

Comparison of Cellular Immunogenicity of Barekat and Spikogen Vaccines on Peripheral Blood Mononuclear Cells (PBMC)

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Background: COVID-19 vaccines have been crucial in controlling the pandemic by inducing immune responses. This study compares the cellular immunogenicity of two COVID-19 vaccines, Barekat and Spikogen, on peripheral blood mononuclear cells (PBMCs).
Methods: Blood samples were obtained from 16 healthy participants divided into four groups based on their COVID-19 history and vaccination status. PBMCs were isolated from the blood and exposed to the vaccines for 48 hours. Flow cytometry was used to measure the expression of CD4+ and CD8+ T-cell markers.
Results: Spikogen treatment resulted in a significant increase in CD4+ expression compared to untreated cells, while Barekat did not show a significant change in CD4+ or CD8+ expression. Neither vaccine produced a significant increase in CD8+ levels across the groups.
Conclusion: The findings suggest that Spikogen induces a stronger CD4+ T-cell response than Barekat, highlighting potential differences in their cellular immunogenicity. However, further studies are necessary to assess their overall immunological impact, including humoral responses.

Keywords: COVID-19, cellular immunity, PBMC, Barekat vaccine, Spikogen vaccine

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Abstract: A-10-3031-1

Histone Deacetylase Inhibitors: Mechanisms and Therapeutic Potential in Cancer Treatment

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Background: Histone deacetylase inhibitors (HDACIs) are a diverse group of compounds that have emerged as promising targeted anticancer agents. These inhibitors work by modulating the acetylation status of histones and non-histone proteins, thereby affecting gene expression and promoting cell death in cancer cells.

Methods: A comprehensive literature review was conducted using databases such as PubMed, Scopus, and Web of Science to collect studies from 2014 to 2024 on the role of HDAC inhibitors in cancer therapy. 76 articles were selected based on their relevance to HDAC mechanisms of action, clinical applications, and their impact on cancer progression. Studies that lacked detailed analysis or were unrelated to HDAC inhibitors' effects on cancer were excluded.

Results: HDAC inhibitors have demonstrated significant anticancer effects by altering gene expression and inducing cell death in cancer cells. These compounds inhibit HDAC activity, leading to increased acetylation of histones and non-histone proteins, which can activate tumor suppressor genes and inhibit oncogene expression. HDAC inhibitors such as vorinostat have shown efficacy in clinical trials, improving survival rates and reducing tumor growth in various cancers. Additionally, research has identified that HDACIs can modulate immune responses and enhance the effectiveness of other anticancer therapies. Their ability to inhibit angiogenesis further contributes to their therapeutic potential.

Conclusion: Histone deacetylase inhibitors offer a promising approach for cancer treatment through multiple mechanisms, including altering gene expression and inhibiting tumor growth and angiogenesis. Continued research is essential to fully understand their therapeutic potential and to develop more effective and specific HDAC inhibitors for various cancer types.

Keywords: Histone deacetylase inhibitors, Cancer therapy, Gene expression, Vorinostat, Angiogenesis

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Abstract: A-10-2378-1

Recent Advances in RGD Peptide conjugated nanoparticles system as a new strategy for Targeted Therapy in Colon Cancer

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Background: Integrin is a type of cell adhesion molecule required for the growth and spread of colon cancer, Targeting these molecules with RGD peptides makes it possible to deliver drugs to the tumor and coronary cells and prevent damage to the body. Drug carriers with RGD function have more therapeutic efficiency by increasing the drug and keeping it inside the tumor microenvironment. RGD peptides and their combinations can help identify and track cancer progress by using imaging agents and improving therapeutic prescriptions. Inhibition of integrins has reported promising results in various cases of colon cancer malignancies.

Methods: This review article was performed within articles published at PubMed, Science Direct, and Google Scholar until May 2024. The keywords were RGD peptide and RGD peptide-conjugated nanoparticle and colorectal cancer. Searching these databases an initial search yielded 19 articles. After reviewing the titles, nine articles were excluded. From the remaining ten articles, abstracts were read, and 10 were selected based on inclusion criteria.

Results: The study highlights the role of integrins in colon cancer growth and spread. Targeting integrins with RGD peptides enhances drug delivery to tumor cells while sparing healthy tissues. RGD-functionalized drug carriers show improved therapeutic effects due to better drug retention in the tumor microenvironment. Additionally, RGD peptides aid in cancer tracking and treatment optimization. Promising results from integrin inhibition in colon cancer cases have been observed, with drugs like Cilengitide and Abituzumab showing positive clinical trial outcomes.

Conclusion: Finally Integrins are identified as promising targets for drug delivery in colon cancer treatment. Their ability to facilitate targeted therapy and improve drug retention in tumors positions them as effective carriers in nano therapy. The positive outcomes from clinical trials of integrin-targeting drugs underscore their potential to enhance cancer treatment strategies.

Keywords: RGD peptide / Colon Cancer / RGD Peptide conjugated nanoparticles / Target Therapy

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Evaluation of expression of lncRNA-MEG3 in non-functional pituitary adenoma

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Background: Pituitary adenomas are the second most common intracranial tumors. Roughly, one-third are non-functional (NFPA), meaning they don't secret functional hormones. The exact pathogenesis and molecular mechanism have not been fully understood. LncRNA-MEG3 is recognized as a tumor suppressor agent. Although MEG3 is often expressed in normal tissue, many cancers have decreased levels of it. The loss of its expression is associated with initiation, progression, metastasis, and chemo-resistance of cancers. This study was designed due to the insufficient data about NFPA in the Iranian community. Therefore, we aimed to investigate the transcript level of lncRNA-MEG3 in tumors from NFPA in comparison with surrounding tissue.

Methods: We obtained 25 samples from Iranian patients who had NFPA tumors and 25 samples of surrounding normal tissue. These patients had not received radiography or chemotherapy before their surgery. The type of tumors was confirmed through MRI, clinical symptoms, and pathological examination. RNA of samples were extracted and expression of MEG3 was detected using real-time quantitative reverse transcription polymerase chain reaction.

Results: MEG3 expression in the tumor was significantly lower than the surrounding normal tissue (p value<0.05).

Conclusion: MEG3 possibly plays a role in the pathogenesis of NFP. This study will be useful for further studies about NFPA molecular mechanisms. We propose evaluating the correlation between MEG3 dysregulation and the prognosis of NFPA.

Keywords: lncRNA-MEG3, NFPA, Pituitary adenoma

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Abstract: A-10-2960-1

Impact of Doxorubicin Encapsulated in Human Adipose-Derived Exosomes on Inflammation in Co-culture System of Breast Cancer and Normal Cells

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Background: Doxorubicin (DOX) chemotherapy for breast cancer is an effective treatment option, although it has drawbacks. Exosomes (EXO) have safely and successfully carried this medication, reducing its negative effects; nevertheless, its application is still being researched. Using the coculture system of malignant and normal breast cells, we created circumstances like those seen in the body and studied the effects of this treatment by looking at inflammatory genes.

Methods: Through ultracentrifugation, extracellular matrices (EXOs) were extracted from mesenchymal stem cells (MSCs) originating from human adipose tissue. Later, western blotting, dynamic light scattering (DLS), and transmission electron microscopy (TEM) methods were used to validate the properties of EXO. DOX was encapsulated in EXOs by sonication technique and its loading rate was measured using spectrophotometry. This study employed a coculture system to evaluate the cytotoxic effects of free doxorubicin (DOX) and doxorubicin encapsulated in exosomes (Exo-DOX) on various breast cell lines, including MCF-7, MCF-10A, MDA-MB-231, and A-MSC. Additionally, the expression levels of inflammatory cytokines (IL-1β, IL-6, IL-10, and TNF-α) were investigated.

Results: The MTT assay demonstrated that free DOX exhibited the highest cytotoxicity towards MCF-10A cells, followed by MCF-7 cells. Conversely, Exo-DOX exhibited a greater effect on MCF-7 cells, exhibiting a lower IC50 compared to MDA-MB-231 cells. Free DOX significantly downregulated the expression of pro-inflammatory cytokines (IL-1β, IL-6, and TNF-α), particularly in MCF-7 and MCF-10A cells, while concurrently upregulating IL-10 expression. Exo-DOX induced a more significant alteration in cytokine expression compared to both the control and free DOX treatment groups.

Conclusion: The coculture system revealed a synergistic effect of free DOX on cancer cells while simultaneously mitigating the toxic effects of DOX on normal cells. This study suggests that Exo-DOX holds promising potential as a targeted drug delivery system, potentially improving therapeutic efficacy and minimizing off-target toxicity.

Keywords: Exosome, Co-culture, Breast cancer, Doxorubicin, Inflammation

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Abstract: A-10-3061-1

Designing Novel Rapamycin Binding Site Inhibitors of mTOR based on Terpenoids Compound: Insights from Molecular Docking, Structure-based Design, Virtual Screening, and Molecular Dynamics Simulation

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Background: The mTOR signaling pathway is essential for regulating cell growth, metabolism, and immune function. Targeting this pathway holds promise for treating a variety of diseases. However, current mTOR inhibitors like rapamycin and its analogous (rapalogs) have limitations, including poor solubility and stability. To overcome these issues, we used a computational approach to develop new small molecule inhibitors based on terpenoids, a diverse class of natural products known to inhibit mTOR.

Methods: We started by docking a range of terpenoid compounds into the 3FAP crystal structure of mTOR to see how well they could bind compared to rapamycin. Using molecular docking and structure-based design, we screened and optimized these compounds. Additionally, we used ligand-based virtual screening to find more candidates with better potency and favorable ADME (absorption, distribution, metabolism, and excretion) properties. To ensure these interactions were stable, we performed molecular dynamics simulations.

Results: Our docking studies showed that two terpenoid compounds, Zeorin and 3-O-Acetyl-11-keto-β-boswellic acid (AKBA), had binding scores and interactions comparable to rapamycin. We identified several promising terpenoid-based compounds, such as AKBA-22, Zeorin-3, and Zeorin-8, which showed strong binding to the mTOR protein. Further virtual screening highlighted additional potent candidates, PubChem CID_126739291 and PubChem CID_44606344, which also had good predicted ADME properties. Molecular dynamics simulations confirmed that the top compounds formed stable interactions with mTOR.

Conclusion: We identified several novel terpenoid-based compounds that bind well to the mTOR protein and remain stable in simulations, suggesting they could be effective mTOR inhibitors. These findings pave the way for further laboratory and animal studies to confirm their potential as new treatments for diseases involving the mTOR pathway. This research could lead to the development of more effective and stable mTOR inhibitors, offering new therapeutic options.

Keywords: mTOR inhibitors, Terpenoids, Docking studies, ADME properties, Virtual screening

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Abstract: A-10-3029-1

Preparation and investigation of the properties of Fe3O4/Chitosan/PCL/PEG/HA/siRNA/Drug nanoparticles to deliver drugs to MCF-7 cells

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Background: Considering that in many cancer cells, CD44 receptors are expressed in large quantities as hyaluronic acid receptors, this molecule is a suitable candidate for targeting nanoparticles to deliver drugs to cancer cells or tissues.

Methods: In this study, Fe3O4/Chitosan/PCL/PEG/HA/siRNA-FAM/PTX amphiphilic nanoparticles were designed. These nanoparticles contain iron oxide nanoparticles, a hydrophilic part of polyethylene glycol, hydrophobic and biodegradable part of PCL, cationic part of chitosan and hyaluronic acid group to increase the efficiency of drug transfer to MCF-7 cancer cells due to the high expression of hyaluronic receptors. The acid is on the surface of these cells. The characteristics of the resulting nanoparticles were investigated using FTIR, Zeta, DLS, and scanning electron microscope (SEM).

Results: The FTIR results showed that the synthesis of Fe3O4/Chitosan/PCL/PEG/HA nanoparticles was done successfully. The results of DLS and Zeta showed that Fe3O4/Chitosan/PCL/PEG/HA/siRNA-FAM/PTX nanoparticles had a size and surface charge of 230 nm and -2.5 mV, respectively. Examining the biocompatibility of the resulting nanoparticles by the MTT test, as well as the ability of these nanoparticles to transfer paclitaxel and DNA, were other factors investigated in this research, which were evaluated by the MTT test and the flow cytometry device, respectively. The results showed that due to the combination of PCL and PEG parts, Fe3O4/Chitosan/PCL/PEG/HA/siRNA-FAM/PTX nanoparticles had very high toxicity, while the efficiency of gene transfer in Fe3O4/Chitosan/PCL/ PEG/HA/siRNA-FAM was also higher. It seems that the reason for the increased transfer efficiency in Fe3O4/Chitosan/PCL/PEG/HA/siRNA-FAM nanoparticles is their high stability. Another important reason for reducing toxicity and increasing transfer efficiency in Fe3O4/Chitosan/PCL/PEG/HA/siRNA-FAM¬ nanoparticles is the presence of hyaluronic acid group on the surface of these nanoparticles.

Conclusion: This research was designed for the first time with the aim of using Fe3O4/Chitosan/PCL/PEG/HA/siRNA-FAM nanoparticles for gene delivery and drug delivery.

Keywords: Nanoparticle targeting, drug delivery, Fe3O4/Chitosan/PCL/PEG/HA/siRNA-FAM/PTX

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Abstract: A-10-2261-1

Ferulic acid exerts protective effect against paraquat-induced renal toxicity through NF-κB / TNF-α signaling pathway in male rats

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Background: Today, the use of chemicals such as paraquat is common and inevitable with harmful effects on human health. In this study, the protective effect of ferulic acid against paraquat-induced renal toxicity and expression of genes involved in inflammatory pathways such as NF-κB and TNF-α was investigated.
Methods: Thirty-two male Wistar rats were divided into 4 groups: group 1 was healthy animals that received distilled water, group 2 was paraquat (25 mg/kg), group 3 ferulic acid (100 mg/kg), and group 4 was paraquat plus ferulic acid, respectively, for 2 weeks. 24 hours after the last treatment, rats were anesthetized, blood samples were taken from the heart, and kidney tissue was removed. Oxidative stress markers and biochemical parameters were measured. Also, the expression of genes involved in the inflammatory pathway such as NF-κB and TNF-α in renal tissue was measured by RT-PCR.
Results: Paraquat administration increased Urea, Cr, Uric acid, ALT, and AST plasma levels, decreased FRAP level and antioxidant enzymes (CAT, GPx, and SOD) activity, increased Protein carbonyl and MDA in serum and renal tissues ($P<0.05$). Ferulic acid administration after exposure to paraquat improved all mentioned biochemical and oxidative stress markers. Paraquat administration enhanced the expression of NF-κB and TNF-α genes and ferulic acid treatment diminished the expression of these genes ($P<0.05$).
Conclusion: This study suggests that daily consumption of compounds containing ferulic acid could have protective effects against the harmful effects of paraquat.

Keywords: Oxidative stress, Paraquat, Ferulic acid, renal damage

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Abstract: A-10-2261-3

Impact of carvacrol on biochemical parameters, oxidative biomarkers and IL-1β expression in in male Wistar rats undergoing paraquat-induced hepatotoxicity

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Background: Hepatotoxicity is the term used to describe injury of the liver or impairment in its function brought on by different substances and medications. Paraquat is one of the most widely utilized bipyridinium herbicides that can be dangerous to the liver. Monoterpenoid phenol carvacrol has anti-inflammatory, antibacterial, anti-hepatotoxic, antioxidant, and antimicrobial properties. In this work, we looked into how carvacrol affected the hepatotoxicity caused by paraquat.

Methods: six groups of forty-eight male rats were used: the negative control group, which received distilled water; the patient group, which was given paraquat; the positive control group, which was given silymarin and paraquat; and the treatment groups, which were given carvacrol and paraquat at doses of 20, 40 and 80 mg/kg. Following fourteen days, the rats underwent chloroform anesthesia, and blood was obtained from their hearts while they were fasting. The parameters that were measured included AST, ALT, creatinine, malondialdehyde, antioxidant capacity, lipid profile serum IL1 and carbonyl protein. To evaluate the expression of the IL1 gene, total protein, vitamin C, SOD, and catalase, liver tissue was extracted.

Results: When comparing the serum levels of TG, TC, VLDL-C, and total bilirubin, as well as AST, ALP, Serum ALT, serum and liver MDA, serum level of IL-1β, liver expression of IL-1β gene, and mean carbonyl protein, to control group, paraquat gavage given to group 2 for 14 days resulted in a significant ($p < 0.05$) increase. However, treatment with carvacrol decreased the aforementioned factors. In comparison with the control group, paraquat poisoning significantly ($p < 0.05$) reduced the liver's FRAP level, catalase, and superoxide dismutase activity. In contrast to the paraquat group, oral carvacrol treatment resulted in a considerable ($p < 0.05$) rise in the value of these variables.

Conclusion: The current study discovered that carvacrol can considerably improve the hepatotoxicity

Keywords: Hepatotoxicity, Carvacrol, Paraquat

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Abstract: A-10-3069-2

The Potential of Mesenchymal Stem Cells in Preserving Dopaminergic Neurons: A Systematic Review of Parkinson's Disease Animal Models

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Background: Parkinson's disease (PD) is a progressive neurodegenerative disorder primarily characterized by the loss of dopaminergic neurons in the substantia nigra pars compacta. This neuronal loss leads to the hallmark motor symptoms of PD, including tremors, rigidity, and bradykinesia. Stem cell therapy, particularly using mesenchymal stem cells (MSCs), has shown regenerative potential and is being actively investigated as a therapeutic strategy for PD.

Methods: A comprehensive literature search was conducted to identify relevant studies published between 2016 and October 2024. The databases searched included PubMed/MEDLINE, Embase, CENTRAL, Scopus, and Web of Science. The search terms used were "mesenchymal stem cells," "Parkinson's disease animal model," "stem cell therapy," and "dopaminergic neuron." The inclusion criteria were peer-reviewed in vivo interventional animal studies published in English that investigated the effects of MSCs on dopaminergic neurons in PD models.

Results: The systematic search initially yielded 53 documents. After screening titles and abstracts based on predetermined inclusion/exclusion criteria, 41 articles remained pertinent to the research objectives. Exclusion criteria encompassed papers without a direct examination of stem cell therapy in Parkinson's disease models. The results consistently demonstrated that the stem cell treatment groups had significantly higher numbers of tyrosine hydroxylase-positive dopaminergic neurons in both the striatum and substantia nigra compared to the control groups. This increase in dopaminergic neurons suggests a protective effect of MSCs on neuronal survival.

Conclusion: The findings of this systematic review indicate that mesenchymal stem cells have a positive impact on the preservation of dopaminergic neurons in animal models of Parkinson's disease. These results support the potential of MSCs as a therapeutic option for PD. However, further research is necessary to optimize the characteristics of the stem cells.

Keywords: Mesenchymal Stem Cells, Parkinson's disease, Dopaminergic Neurons, Animal Models

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Abstract: A-10-2484-3

Association of 3:c.95-68T>C polymorphism (rs8052334) in MT1B Gene with risk of Breast Cancer: A Case-Control Study

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Background: Breast cancer is one of the most common malignancies affecting women worldwide. As research continues to discover genetic factors that contribute to the risk of breast cancer, the importance of specific genetic polymorphisms has become a main point. One of the less-known polymorphisms that have an association with some diseases and cancer is an intronic polymorphism 3:c.95-68T>C (rs8052334) in the MT1B gene, which has been studied for its possible association with the risk of breast cancer. This paper presents a study investigating whether the 3:c.95-68T>C (rs8052334) polymorphism is associated with breast cancer susceptibility.

Methods: Our research analyzed two groups: 100 samples from individuals diagnosed with breast cancer and 100 healthy control samples. We applied the Tetra-ARMS PCR method to detect the presence of the 3:c.95-68T>C (rs8052334) polymorphism. This technique is known for its efficiency and accuracy in detecting specific genetic variants, allowing reliable comparison between the two groups.

Results: Data analysis revealed that the TC allele and CC allele had the highest and the lowest frequency, respectively (p value>0.05). In addition, rs8052334 polymorphism of the MT1B gene did not demonstrate a significant association with the risk of breast cancer. This finding suggests that, contrary to some hypotheses, this particular genetic polymorphism may not be a risk factor for breast cancer. However, we recommend reevaluation of these results in more diverse and larger ethnic populations and statistical groups as well as the other polymorphisms in the MT1B gene.

Conclusion: Our investigation showed that the rs8052334 polymorphism of the MT1B gene has no significant association with the risk of breast cancer. These findings highlight the importance of continuous research to identify genetic factors that influence breast cancer development. Understanding these associations is crucial for advancing personalized medicine and improving prevention and therapeutic strategies.

Keywords: Breast Cancer, MT1B Gene, genetic polymorphism, rs8052334, Tetra-ARMS PCR

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Abstract: A-10-2953-3

Evaluation of Astragalus ovinus hydroalcoholic root Extract on nephrotoxicity induced by cisplatin in male wistar rats

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Background: Cisplatin is one of the most common antineoplastic drugs used in the treatment of various cancers. However, because of liver, kidney, and other toxicities, its therapeutic use has been limited. This study was conducted to investigate the effect of hydroalcoholic extract of the root of Astragalus ovinus (A.ovinus) on Cisplatin-induced nephrotoxicity.

Methods: Extraction was done by maceration method from the dried root of A.ovinus and then it was dried in an incubator the resulting powder was stored in the freezer. This experimental study was conducted on 30 male Wistar rats. Animals were randomly divided into 6 groups of 5. The first group was selected as the negative control group. The second group was determined as the positive control group, the third group was treated with the extract and received only the extract, 4th and 5th groups were considered the protective group and first received the extract and then received Cisplatin. The 6th group was considered as the treatment group and first received Cisplatin then received the extract. Biochemical parameters such as BUN and Creatinine in the serum of animals were evaluated. Also, the kidney tissue of rats was fixed in 10% formalin and studied morphologically and histologically.

Results: Cisplatin significantly increased the mean serum levels of BUN and Creatinine in the positive control group compared to the negative control group (P-value < 0.05). The mean serum levels of BUN and Creatinine in the treatment group were significantly lower than the positive control group (P-value < 0.05). The results of the pathology of the kidney also indicated that kidney damage was less in the first and second protective groups and the treatment group than in the positive control group.

Conclusion: According to the present study, the hydroalcoholic extract of the root of A.ovinus has shown good nephroprotective effects against Cisplatin-induced toxicity.

Keywords: Cisplatin, Astragalous ovinus, Nephrotoxicity

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Abstract: A-10-2951-2

Microbiome Base Treatment: A Novel Target in Multiple Myeloma Therapy

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Background: The gut microbiome, a community of microorganisms, is associated with the progression of neoplasms such as multiple myeloma (MM). This association occurs through the disruption of the innate and adaptive immune system, metabolic function, and the promotion of tumorigenesis by influencing tumor microenvironments. MM, identified by the aggressive development of plasma cells in bone marrow, is an incurable blood malignancy due to frequent relapse, highlighting the need for new treatment approaches. The role of dysbiosis in MM progression presents itself as a novel therapeutic target. This study focuses on the potential of microbiome-based treatment to improve MM outcomes and reduce relapse.

Methods: We included studies published between 2016 and 2024 that examine the dysbiosis role in MM progression and treatment by searching PubMed, Scopus, and the Web of Science. We also excluded studies that failed to acknowledge the gut microbiome's involvement in MM.

Results: Out of 50 articles, 20 were included and 30 were excluded. Evidence showed that specific microorganisms influence different aspects of treatment, with one leading to MRD negative by producing butyrate. Dietary interventions rich in particular nutrients, probiotics, prebiotics, postbiotics, and FMT (fecal microbiota transplantation) from screened donors are among the microbiome-based treatments to restore beneficial microorganisms for patent recovery. Combination therapy of microbiome-base treatment and common therapies such as CAR-T cell therapy, an immune checkpoint inhibitor, vaccine immunotherapy, and monoclonal antibodies can optimize their efficacy, reduce drug toxicity, as well as decrease the risk of GVHD and provide immunomodulation after HSC transplantation.

Conclusion: According to the role of the gut microbiome in MM and the potential risks associated with manipulating the microbiome, further investigation is necessary to understand the underlying mechanism. This will lead to the development of more effective microbiome-based approaches for managing MM.

Keywords: Multiple myeloma, Gut microbiome, Dysbiosis, Therapeutic strategy, Microbiome modulation

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Abstract: A-10-3034-1

Investigation of the Relationship between the Frequency of MTHFRC677 Polymorphism and Smoking Behavior in an Iranian Population

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Background: Smoking is among the most important preventable risk factors for mortality in developed countries. Research has indicated that cigarette smoke is a strong environmental modifier of DNA methylation. The Methylenetetrahydrofolate Reductase (MTHFR) gene codes the MTHFR enzyme, which is associated with folate metabolism. Evidence has demonstrated a decrease in the activity of MTHFR enzyme and folate concentration among smokers, resulting in hyper-homo-cysteinemia which is a risk factor for stroke and cardiovascular diseases. The present study aimed to assess the frequency of MTHFR gene polymorphism among smokers to evaluate the relationship between these gene polymorphisms and smoking behavior. Our study also aimed to compare homocysteine levels between smokers and non-smokers people.

Methods: Totally, 409 individuals were enrolled in the smoker group and 210 healthy nonsmokers into the control group, the genotypes were determined in two groups using the Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) technique. Homocysteine concentration was also assessed in the separated sera using the ELISA technique.

Results: The results of ELISA revealed higher homocysteine concentrations in smokers than in nonsmokers ($p<0.001$). The results of genotype determination showed that the frequency of TT genotype was significantly higher among smokers compared to nonsmokers, ($P<0.001$). However, a significant difference was observed between the two groups regarding the frequency of C and T alleles, T alleles were significantly higher in smokers than non-smokers group, ($P<0.001$).

Conclusion: In conclusion, T alleles may be associated with smoking behavior, and there is higher homocysteine concentration in smokers compared to nonsmokers.

Keywords: polymorphism, genotype, homocysteine, smoking behavior

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Abstract: A-10-3081-1

Zinc deficiency increases the risk of and accelerates the progression of isolated impaired fasting glucose to type 2 diabetes: A prospective cohort study

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Background: Zinc is an essential trace element that regulates insulin secretion and glucose metabolism. We aimed to investigate the potential association of zinc deficiency (defined as fasting serum zinc concentration < 70 µg/dL) and the risk of developing type 2 diabetes (T2D) among different phenotypes of pre-diabetes (Pre-DM), i.e., isolated impaired fasting glucose (iIFG), isolated impaired glucose tolerance (iIGT), and combined IFG-IGT.
Methods: A total of 1041 adults (mean age of 52.5±14.0, 46.9% men) diagnosed with Pre-DM (i.e., 56.2% iIFG, 19.0% iIGT, and 24.8% combined IFG-IGT) in the fourth phase (2009-2011) of the Tehran Lipid and Glucose Study (TLGS), were recruited for measurement of fasting serum zinc concentration and were followed up to 2015-2017. Cox proportional hazard models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) of progression to T2D in Pre-DM subjects with and without zinc deficiency. The estimated time to progression to T2D was compared in subjects with and without zinc deficiency using the log-rank test.
Results: Baseline mean serum zinc concentration was 116±42.0 µg/dL, and the overall prevalence of zinc deficiency was 6.6% (5.6% in iIFG, 9.1% in iIGT, and 7.0% in combined IFG-IGT). Over a median follow-up of 6 years, 28.3% of subjects with Pre-DM progressed to T2D. After adjustment for potential confounders (i.e., T2D risk score, fasting serum glucose, and serum triglyceride-to-HDL-C ratio), zinc deficiency was associated with an increased risk of progression to T2D among subjects with iIFG (HR=1.91, 95% CI=0.99-3.62, P=0.052). Furthermore, the mean (95% CI) of estimated time to progression to T2D from iIFG was significantly shorter in subjects with zinc deficiency compared to those without zinc sufficiency [6.3 (5.5-7.2) vs. 7.9 (7.7-8.1) years, Plog-rank= 0.050]
Conclusion: Zinc deficiency is a risk factor for developing T2D in prediabetic subjects with iIFG.

Keywords: Prediabetes, Type 2 diabetes, Zinc deficiency

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Abstract: A-10-3078-1

Association of microRNA-217 and sirtuin 1 expressions in ovarian cancer

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Background: Ovarian cancer (OC) is a multi-component disease characterized by various molecular pathways, including genetic alterations, aberrant cell signaling, and immune system disturbances. Sirtuin 1 (SIRT1) and microRNA (miR)-217 play significant roles in many cancers. However, the association between miR-217 and SIRT1 in the progression of OC remains unknown. Thus, the present study aimed to survey the roles of SIRT1 and miR-217 in OC.

Methods: Bioinformatics analyses (Target scan, miRmap, miRWalk, ENCORI/starBase) were used to predict target genes. Quantitative real-time polymerase chain reaction (qRT -PCR) was used to evaluate the expression level of miR-217 and SIRT1 genes in ovarian cancer and healthy tissues. The expression of miR-217 was measured after microRNA extraction from tissue samples. The extracted microRNAs were followed by cDNA synthesis. Real-time PCR was performed using SYBR green and delta Ct was calculated by the 2-△Ct method. U6 was used as the reference gene.

Results: Our results indicated decreased levels of miR-217 expression in ovarian cancer samples compared to matched normal ovarian tissues. We also found that SIRT1, a potential target of miR-217, is upregulated in ovarian cancer cells compared to normal OC.

Conclusion: miR-217 has been shown to be a putative tumor suppressor in ovarian cancer. Based on the findings in this study, we propose that miR-217 may regulate the proliferation and metastasis of ovarian cancer by targeting SIRT1.

Keywords: miR-217, ovarian cancer, sirtuin1

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Abstract: A-10-3075-1

Decreased of miR-613 and its correlation with Nicotinamide Phosphoribosyltransferase in ovarian cancer tissue

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Background: MicroRNAs are dysregulated in the many cancer types, and making them potentially therapeutic and diagnostic targets in patients that aberrant expressed. MiR-613 suppress the development and progression of ovarian cancer. Identifying the molecular mechanisms of miR-613 is crucial, as it may serve as an effective target in the future.

Methods: A total of 16 patients, between the ages of 22 and 60 years, with ovarian cancer and 5 pooled healthy controls were included. MiR-613 level and NAMPT gene expression in ovarian cancer tissue were done by real-time PCR method. The expression of miR-613 was measured after microRNA extraction from tissue specimens. The extracted microRNAs were followed by cDNA synthesis. Real-time PCR was performed using SYBR green and delta Ct was calculated by the formula: Ct (reference gene) - Ct (target gene). U6 was used as the reference gene.

Results: miR-613 expression in ovarian cancer tissue specimens was significantly lower than that in pooled normal tissue specimens. There was a negative correlation between the expression of miRNA-613 and NAMPT gene expression.

Conclusion: miR-613 expression levels are low in ovarian cancer tissue and correlate with progression-free and overall survival. In contrast the expression level of NAMPT was increased. Thus, miR-613 may be useful as a prognostic marker in ovarian cancer. The results obtained confirm that miRNA-613 acts as a tumor-suppressive gene in ovarian cancer. These data contribute to the identification of potential biomarkers and novel targets for OC early detection and treatment.

Keywords: ovarian cancer, NAMPT, real time PCR, microRNA

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Abstract: A-10-3082-2

NADPH oxidase as a Target to Reduce Primary Sclerosis Cholangitis Post Liver Transplantation, Potential as a new therapeutic strategy

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Background: The molecular mechanisms and causes of primary sclerosis cholangitis (PSC) post-liver transplantation are still unclear. PSC is a progressive cholestatic hepatobiliary disease that happens in about 25% of patients post-liver transplantation and requires re-transplantation. Nicotinamide adenine dinucleotide phosphate oxidase (NADPH oxidase or Nox) is a family of transmembrane proteins whose main function is producing reactive oxygen species (ROS). ROS generation as a result of NADPH oxidase activity of Kupffer cells and polymorphonuclear leukocytes has been implicated in the pathogenesis of ischemia-reperfusion injuries after liver transplantation and is related to intra- and/or extrahepatic non-anastomotic biliary stenosis or PSC.

Methods: We conducted a comprehensive literature search in PubMed, Web of Science, Scopus, and Embase databases until the end of August 2024. The search terms included "NADPH oxidase", "Nox protein", "primary sclerosis cholangitis", "hepatobiliary complications", and "liver transplantation", were used in different combinations or individuals for search strategy.

Results: The initial electronic database search identified 320 results of which 196 articles remained after removing duplicates. After the first assessment of titles and abstracts, 86 papers were excluded and 38 papers remained for full-text evaluation. After full-text evaluation, 11 studies were considered appropriate for systematic review. The review of selected studies showed that the increase in Nox protein expression after hepatic ischemia/reperfusion injury can play a role in the development of hepatobiliary complications after liver transplantation.

Conclusion: Nox-derived ROS upregulates several molecular pathways to induce hepatocyte apoptosis and hepatic stellate cell (HSC) activation to promote hepatobiliary fibrogenesis. Understanding the multiple molecular aspects of Nox in the development of PSC post-transplantation may help identify new drugs to prevent this disorder.

Keywords: NADPH oxidase, primary sclerosis cholangitis, liver transplantation, fibrosis, ischemic reperfusion injury

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Abstract: A-10-3082-4

The Association between Circulating Adipocytokine Omentin Levels and Nonalcoholic Fatty Liver Disease: A Systematic Review and Meta-analysis

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Background: Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver condition worldwide. NAFLD is often associated with features of Metabolic Syndrome such as obesity and insulin resistance. The current comprehensive meta-analysis was performed to evaluate the association between circulating Omentin levels and NAFLD.

Methods: A systematic search in Scopus, Web of Science, PubMed, and Google Scholar databases was conducted to identify relevant studies up until 5th May 2022. The standard mean difference (SMD) values and 95% confidence intervals (CIs) were computed for the association of Omentin levels with NAFLD risk in a random effect model.

Results: The meta-analysis involved 6 case-control studies with a total of 371 cases and 269 controls. Pooled SMD) showed no significant difference in serum Omentin between NAFLD and healthy groups (SMD= -0.047 and 95% CI -0.957_0.862 P=0.91). Subgroup analysis based on sample size showed that the average Omentin levels were significantly higher in NAFLD patients in studies with sample size ≥70 (SMD=0.356 CI 0.056_0.655 P=0.02).

Conclusion: Additional well-designed studies with larger sample sizes are essential to clarify the potential role of Omentin as a risk marker of NAFLD.

Keywords: Nonalcoholic Fatty Liver Disease, Adipokine, Omentin, Metabolic syndrome, Meta-analysis

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Abstract: A-10-3082-3

The Association between Serum follistatin-like proteins and cardiovascular diseases-A systematic review and meta-analysis

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Background: Follistatin-like proteins (FSTLs) are adipomyokines secreted by adipocytes and myocytes. Previous studies have reported that circulating FSTL1 level was increased in response to cardiovascular injuries. Herein, we conducted a systematic review and meta-analysis to evaluate the association between circulating FSTLs and cardiovascular diseases (CVDs).
Methods: We performed a systematic literature search in PubMed, Web of Science, Scopus, and Embase. After screening the articles, eligible studies were selected, relevant data were extracted, and pooled SMD was calculated. Sensitivity analysis was also performed for finding heterogeneity causes and publication bias was further reported.
Results: Among the 577 initially retrieved articles, we included 5 studies with a total of 941 cases with CVDs and 446 controls. All the included studies have measured FSTL1. Pooled SMD analysis indicated a significant difference in the circulating FSTL1 levels between subjects with CVDs and control groups (SMD = 0.853 and 95% CI = 0.158-1.548, P = 0.016). One study that measured the level of FSTL1 in heart failure patients with preserved ejection fraction was found to be the source of heterogeneity. There was no publication bias.
Conclusion: FSTL1 represents significantly higher levels in patients with CVD compared to control subjects. Hence, it might have the potential to be used as a diagnostic and prognostic biomarker in CVDs, although further well-designed studies are still needed to prove its usefulness in clinics.

Keywords: Follistatin-like protein, cardiovascular disease, Adipomyokine, Meta-analysis

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Abstract: A-10-3027-1

RAGE Gene Polymorphisms and Diabetic Nephropathy Risk in an Iranian Population: A Case-Control Study

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Background: The receptor for advanced glycation end products (RAGE) is a receptor on the surface of cells and its polymorphisms have been associated with diabetic nephropathy. Thus, the 2184A/G, 1704G/T, and G82S variants of this receptor were investigated in this study among a population of Qazvin, Iran.
Methods: A total of 356 subjects (118 healthy controls, 122 diabetics without nephropathy, and 116 diabetics with nephropathy) were enrolled in this study. The TETRA ARMS-PCR technique was used for genotyping.
Results: In our study, significant differences were not seen among the three groups in the 1704G/T and G82S polymorphisms of the RAGE gene (>0.05), but there was a significant difference in the 2184A/G polymorphism of the RAGE gene (<0.05), and it seems that the G allele of the 2184A/G variant may be an increased risk of nephropathy in diabetic cases (OR=2.474, 95%; CI: 1.657-3.693). The G allele of 1704G/T (OR=1.434, 95%; CI: 0.936-2.196) and G82S (OR=1.373, 95%; CI: 0.792-2.383) was associated with a higher risk of nephropathy. Haplotype analysis showed that the GGG haplotype may increase the risk of nephropathy (OR=3.5553) and it seemed that the ATG haplotype had a reduced risk of nephropathy (OR=0.516).
Conclusion: Our study indicated a significant association between the 2184A/G variant of the RAGE gene and diabetic nephropathy but two other polymorphisms (1704G/T and G82S) were not associated with diabetic nephropathy.

Keywords: Diabetic Nephropathy, Haplotype, Polymorphism, Receptor for Advanced Glycation End Products

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Abstract: A-10-2368-2

Innovative m γδ-T cells -Based Strategies for Enhancing Radiotherapy in Nasopharyngeal carcinoma cancer

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Background: Nasopharyngeal carcinoma is one of the most common cancers in the head and neck region, which is a malignancy in the posterior part of the nose called the nasopharynx. γδ-T cells (γδ-T-Exos) are quasi-innate T cells with lytic activities that can neutralize histocompatibility complex. Furthermore, γδ-T-exos can immediately eradicate under-pressure cells and have a potential mechanism. Radiotherapy (RT) is a cancer treatment that uses high doses of radiation to kill more cancer cells and shrink tumors.

Methods: This review article includes English articles from PubMed and Google Scholar up to August 2024. The keywords were γδ-T cells, radiotherapy, and treatment of nasopharyngeal carcinoma. By searching these two databases, more than 25 articles related to this issue were reviewed and 19 articles were removed. As a result, 6 articles were selected with the inclusion criteria.

Results: In this study, as a type of extracellular nanoparticles, exosomes were mixed with ionizing radiation in the treatment of NPC and could have advantages over cell-based immunotherapy because they are not attenuated through the immunosuppressive tumor microenvironment. Exosomes overexpressing miR-34c derived from mesenchymal stem cells (MSCs) significantly increased apoptosis of NPC cells and improved radiotherapy to inhibit tumor growth. However, we found that NPC cells abundantly secrete CCR5 ligand, and γδ-T-Exos treatment effectively enhances T cell infiltration into the NPC tumor by upregulating CCR5 expression in T cells. Furthermore, γδ-T-exos overcomes the immunosuppressive effect of NPC-resurnatant and effectively promotes T-cell responses. On the other hand, γδ-T-exos maintain tumor-killing activities against NPC cells under an immunosuppressive NPC microenvironment.

Conclusion: finally, we found that combination therapy using γδ-T-Exos can overcome the immunosuppressive results after radiation therapy and enhance the overall efficacy of radiation therapy by complementing tumor cell killing and promoting T cell activities.

Keywords: Nasopharyngeal carcinoma cancer, γδ-T cells, Radiotherapy

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Abstract: A-10-2275-1

Synergistic impacts of metformin and quercetin improve inflammatory responses and lipid profile in mice fed with a high-fat diet

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Background: Non-alcoholic fatty liver disease (NAFLD) has become an important health problem in the world. Natural products, with anti-inflammatory properties, are potential candidates for alleviating NAFLD. Metformin (MET) and quercetin (QUE) have been reported to be effective in the improvement of NAFLD. This study was to investigate the hepatoprotective effects of MET and QUE in the NAFLD mice induced by a high-fat diet (HFD) and to assess its regulatory mechanism on hepatic inflammatory response.

Methods: Thirty-five C57BL/6J male mice were divided into two groups, one was fed a standard chow diet (n = 7) and the other was fed an HFD (n = 28) for 32 weeks. Animals in the HFD group were then randomly divided into four groups HFD, HFD + MET (150 mg/ kg body weight), HFD + QUE (100mg/kg body weight), and HFD + MET + QUE (150 mg/ kg +100mg/kg). After treatment, the intraperitoneal glucose tolerance test (ipGTT) and lipid levels, liver enzymes, histology of the liver, and expression analysis of TNF-α, IL-1β and IL-6 were carried out.

Results: The results showed that treatment with a combination of MET and QUE was greater effective in reducing weight gain, fasting blood glucose, and Area under the Curves (AUCs) of ipGTT, serum ALT and AST activities, and hepatic triglyceride and cholesterol. In addition, MET + QUE resulted in the reduction of the expression of pro-inflammatory cytokines including TNF-α, IL-1β, and IL- 6.

Conclusion: Overall, the present study's findings demonstrate that QUE potentiates the activity of metformin to control the inflammatory state in NAFLD. Therefore, MET+ QUE could be a prospect as a potential promising candidate for hepatic steatosis or NAFLD prevention and treatment.

Keywords: Non-alcoholic fatty liver disease, Metformin, Quercetin, Liver Inflammation, High Fat Diet

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Abstract: A-10-2275-2

Prognostic biomarker signatures associated with overall survival in colorectal cancer: Evidence from bioinformatics analysis and in vitro study

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Background: Colorectal cancer (CRC) is one of the most common gastrointestinal cancers around the world. Early diagnosis and timely treatment can significantly reduce mortality and morbidity. Thus, biomarker targeting is useful in the early diagnosis and therapy of CRC. This study aimed to identify signatures of prognostic biomarkers associated with overall survival in CRC.

Methods: We downloaded two mRNA microarray datasets (GSE18105 and GSE113513) from the Gene Expression Omnibus (GEO) database. The expression datasets were all normalized with GEO2R and the statistically differentiating genes (DEGs) were determined. Then, we constructed and analyzed protein interaction networks using STRING and Cytoscape, respectively to detect hub genes. Lastly, the selected potential prognostic biomarkers were validated in tissue samples of CRC by quantitative real-time PCR (qRT-PCR).

Results: We identified 340 DEGs common in two datasets and the GO enrichment analysis suggested those genes were significantly associated with calcium-independent cell-cell adhesion via plasma membrane cell-adhesion molecules, response to prostaglandin, collagen catabolic process, epithelial to mesenchymal transition, interleukin-1 beta secretion, atrial cardiac muscle tissue morphogenesis, mesenchymal cell development, and negative regulation of cell proliferation involved in contact inhibition. Our results showed that SPP1, CHEK1, KIF18A, and MAD2L1 were also detected as prognostic markers for CRC based on human protein atlas, UALCAN, and ROC curve analysis. The evaluation of the expression of these markers in cancer tissues compared to adjacent normal tissues indicated that the mRNA expression of all of them was markedly up-regulated in CRC tissue compared to control tissue.

Conclusion: The findings of the present study provide a set of biomarkers to validate clinical utility that can be used as an alternative tool for early diagnosis and identification of new targets in the therapy of CRC.

Keywords: Colorectal Cancer, Protein Interaction Network, Gene Ontology, Survival Analysis, Biomarker

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Abstract: A-10-2275-3

Potential Molecular Mechanisms of Bisphenol A in Obesity Development

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Background: Bisphenol A (BPA), an endocrine disruptor, is associated with metabolic disorders. However, several studies have suggested that exposure to BPA can cause obesity.
Methods: A systematic search of PubMed, Web of Science, and Scopus using the keywords “BMI” OR “overweight” OR “obesity” OR “metabolic syndrome” AND “bisphenol A” or “BPA”, was done. After primary screening using MeSH terms in the titles and abstracts, the relevant articles were selected. Given the large volume of articles, we focused on the most impactful articles published in recent years. Original articles were selected using the following criteria: 1) English language and 2) Representing the molecular relationship between BPA and obesity. The following articles were excluded: 1) Lack of sufficient information on molecular mechanisms of BPA in obesity and 2) Using other isoforms of BPA on obesity.
Results: In total, 13 studies encountered our criteria. The results indicate that BPA at low-level exposures can also affect directly disrupt endocrine regulation, neuroimmune and signaling pathways, and gut microbes, resulting in obesity. Moreover, data and in vivo trials have shown that BPA could contribute to lipid accumulations, resulting in obesity as a commonly observed symptom. Finally, the obesity-related pathways showed that BPA seriously can affect human health through various cell signaling pathways, which were predictable and consistent with existing studies.
Conclusion: This review summarized the potential underlying molecular mechanisms of BPA in obesity development. Exposure to BPA increases adipogenesis, lipid dysregulation, and inflammation in adipose tissue, thereby enhancing obesity risk. Our study suggests the increasing body of evidence that BPA is positively associated with obesity.

Keywords: Bisphenol A, Endocrine disruptor chemicals, Obesity, Metabolic syndrome

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Abstract: A-10-2489-2

Evaluating HTLV-1 Reverse Transcriptase Inhibitors as Potent Telomerase Inhibitors in Glioblastoma Multiforme

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Background: Glioblastoma Multiforme (GBM) remains one of the most aggressive and lethal brain tumors, with current therapies offering limited efficacy. Telomerase inhibition has emerged as a promising therapeutic strategy due to the enzyme's role in maintaining telomere length, contributing to the immortalization of cancer cells. Non-nucleoside reverse transcriptase inhibitors (NNRTIs) have garnered interest as potential human telomerase inhibitors, owing to the structural similarities between telomerase and retroviral reverse transcriptase.

Methods: In this study, we explored the potency of two novel Human T-lymphotropic virus 1 (HTLV-1) reverse transcriptase (RT) inhibitors, designated as compounds 101 and 102, in targeting telomerase activity in GBM. Firstly, an in-silico assessment of the compounds was conducted through homology modeling and molecular docking. The affinity of the compounds, compared to BIBR1532, was computed using the telomerase of Tribolium castaneum. Using T98G and U251 GBM cell lines, we compared the effects of these compounds on telomere length, cell viability, cell cycle arrest, and apoptosis with BIBR1532, a known telomerase inhibitor, as a positive control using molecular docking, real-time polymerase chain reaction (qRT-PCR), MTT assay, propidium iodide (PI) staining, and Annexin PI double staining, respectively.

Results: Molecular docking analysis demonstrated that 101, 102, and BIBR1532 exhibited comparable binding affinities to the human telomerase binding site. These findings were corroborated by telomere length assays, which revealed significant telomere shortening. Cell cycle analysis revealed distinct arrest patterns, with compound 101 inducing G1 phase arrest and both compound 102 and BIBR1532 causing significant G2/M arrest. Notably, compound 102 displayed superior potency in inducing cell cycle arrest and apoptosis exhibited the highest toxicity in cell viability assays, demonstrating time- and dose-dependent effects.

Conclusion: In conclusion, these findings suggested that 101 and 102 could be considered as novel promising telomerase inhibitors with higher efficacy than BIBR1532, warranting further investigation in preclinical models for GBM treatment.

Keywords: Glioblastoma, Telomerase, HTLV-1, NNRTIs, Apoptosis

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Abstract: A-10-2276-1

Modeling of miRNA-mRNA network to identify gene signatures with diagnostic and prognostic value in gastric cancer

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Background: Gastric cancer (GC) is one of the most common cancers worldwide. Progress in the field of systems biology methodologies has facilitated a more comprehensive comprehension of the fundamental molecular pathways, thereby enabling the recognition of distinct molecular markers of GC. These markers offer innovative insights into the diagnosis, prognosis, and targeted treatment of GC.

Methods: Three sets of gene transcripts (GSE19826, GSE81948, and GSE112369) and two sets of miRNA data (GSE26595, GSE78775) were selected from the Gene Expression Omnibus (GEO) and subsequently, differentially expressed genes (DEGs) and miRNAs (DEMs) were identified by GEO2R method. Then, functional pathway enrichment, DEG-miR-TF-protein–-protein interaction (PPI) network, DEM-mRNA network, ROC curve, and survival analyses were performed. Finally, qRT-PCR was applied to validate our results.

Results: We explored 10 and 7 candidate mRNA and miRNAs as potential biomarkers from the high-throughput profiling studies of GC, respectively. Expression analysis of these hubs revealed that 5 miRNAs (including miR-141-3p, miR-204-5p, miR-338-3p, miR-609, and miR-369-5p) were significantly upregulated compared to the controls. From hub DEMs and DEGs, the expression of miR-141-3p, miR-204-5p, SESTD1, and ANTXR1 were evaluated in vitro. The findings suggested that there was a decrease in the expression of miR-141-3p and miR-204-5p in gastric cancer cell lines when compared to the GES-1 cell line. On the other hand, the mRNA expression of SESTD1 and ANTXR1 were markedly up-regulated in GC compared to normal cell line.

Conclusion: The present study has identified a panel of potential miRNAs and genes that could be offered as a potential biomarker for the diagnosis of GC in the early stages. Our finding provides a new window that could help the clinical application of miRs as prognostic biomarkers in GC requiring further validation in larger samples.

Keywords: Gastric cancer, Biomarker, GEO, PPI-network, microRNA

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Abstract: A-10-3027-2

In vitro evaluation of anti-proliferation effects of C-phycocyanin on human breast cancer cell (MCF-7)

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Background: Breast cancer (BC) is the most common cancer among women globally. This research focused on examining the pre-apoptotic and antiproliferative effects of phycocyanin on human breast cancer cells (MCF-7).
Methods: The molecular assessments of incubated MCF-7 cells with Phycocyanin were analyzed by Revers transcription polymerase chain reaction; also anti-proliferation and cell death effect of Phycocyanin on treated cells were evaluated through MTT assay and DAPI staining method. The data was compared with control groups by ANOVA.
Results: This research revealed that the Phycocyanin decreased cell growth of cultured MCF-7 cell line overnight; furthermore, the IC50 value of Phycocyanin was 12.5 mg/ml for 24h. The pre-apoptotic effects of Phycocyanin in 12.5 mg/ml were confirmed by Reverse transcription polymerase chain reaction and DAPI staining method. These results suggested that Phycocyanin by increasing the gene expression of AKT, PTEN, P53, Casp3, Casp8, Casp9, and BAX, as well as, decrease the expression of BCL2 and MAPK genes could trigger the apoptosis pathway; also increased levels of apoptotic bodies was detected by fluorescence microscope.
Conclusion: Overall, our findings reveal that Phycocyanin had anti-proliferative and pro-apoptotic effects on MCF-7 breast cancer. Phycocyanin has the potential for new anti-cancer phytomedicines to be explored further due to the mechanistic pathways involved in this action.

Keywords: Phycocyanin, Breast Cancer, Caspase, BAX, BCL2

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Abstract: A-10-3087-1

Development of tumor cell lysate-based nanoparticles as a promising approach for breast cancer vaccine

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Background: Tumor cell lysate-based nanoparticles (TCL-NPs) have emerged as a promising strategy for delivering tumor antigens to dendritic cells (DCs), which are crucial for initiating and regulating immune responses. By exposing DCs to tumor cell lysates, TCL-NPs can stimulate T cells to recognize both tumor-associated and tumor-specific antigens, thereby generating a robust immune response against cancer. However, traditional vaccination methods using tumor cell lysates often yield limited therapeutic efficacy due to weak antitumor T cell responses. To enhance the effectiveness of cancer immunotherapy, recent studies have focused on improving the antigen-presenting function of DCs through various nanoparticle-based approaches.

Methods: In this study, we generated TCL-NPs from the 4T1 cell line using different lysate preparation methods. DCs were isolated from mouse bone marrow and cultured with GM-CSF and IL-4 for seven days. We evaluated the properties of the DC vaccine exposed to tumor lysates using five different pulsing methods: i) freeze-thawed necrotic tumor cells, ii) heat shock proteins (HSP), iii) hypochlorous acid (HOCl), iv) ultraviolet (UV) irradiation, and v) DC-tumor cell fusion nanoparticles (TCL-NPs). Flow cytometry was employed to assess the maturation of DCs and the proliferation activity of T cells.

Results: The results demonstrated that DCs treated with TCL-NPs exhibited superior T cell activation and a stronger anti-tumor immune response compared to other methods. Specifically, TCL-NPs significantly upregulated CD11c and CD86 expression levels in pulsed DCs. Notably, DCs exposed to TCL-NPs and those pulsed with HOCl were more effective in inducing protective anti-tumor responses than those pulsed with freeze-thawed necrotic tumor cells ($P < 0.01$).

Conclusion: In conclusion, utilizing nanoparticles in vaccines presents a promising approach to enhance vaccine efficacy in cancer therapy, although further in vitro and in vivo studies are required to optimize these strategies for clinical application.

Keywords: Dendritic cells, Tumor cell lysate, nanoparticles, Vaccine, breast cancer

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Abstract: A-10-3085-1

The Emerging Role of FKBP Proteins in Lung Adenocarcinoma

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Background: The intricacy of lung adenocarcinoma, the development of which involves multitudinous interacting natural processes, makes it hard to find remedial biomarkers for treatment. FKBP1A, a gene garbling the FK506-binding protein 1A, has surfaced as a significant player in cancer progression and prognosis. This study investigates the relationship between the expression of FKBPs and lung cancer.

Methods: This review was performed within articles published at PubMed, Science Direct, Google Scholar, and Web of Science until May 2024. The keywords were Lung Adenocarcinoma, Cancer, FKBP, and Biomarker. By searching this database, 20 articles were found, and 12 were removed by reading titles and abstracts. Eight articles were selected under the inclusion criteria.

Results: Cases with well- or fairly discerned excrescences have advanced FKBPL expression compared with cases with poorly discerned excrescences. FKBPL might inhibit the growth of lung ADC cells by postponing the transition from the G1 to S phase of the cell cycle. In addition, FKBPL reacted in increased apoptosis in lung ADC cells. Observed that overexpression of FKBPL in lung ADC A549 cells significantly dropped the anti-apoptotic proteins, including heat shock protein 32 (HSP32), heat shock protein 27 (HSP27), and paraoxonase- 2 (PON2). FKBPL reduction significantly downgraded the apoptotic protein phospho-p53 (S46) in lung ADC H1975 cells.

Conclusion: FKBP family members seem to be significant prognostic biomarkers for lung cancer progression and promising clinical remedial targets, thus furnishing new targets for treating LUAD cases. FKBP1A exhibits discriminative expression in cancer, is a prognostic indicator, undergoes heritable differences, and influences the excrescence-vulnerable medium. More studies are still needed to investigate the effect of FKBP1A in the development and progression of lung cancer. It is hoped that these studies will provide a better prognosis for patients.

Keywords: Lung Adenocarcinoma, Cancer, FKBP, Biomarker

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3089-1

Occupational Exposure to Pesticides in Agricultural Workers and Its Impact on Oxidative Stress Markers

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Background: Organophosphate (OPP) and organochlorine pesticide (OCP) compounds are widely used pesticides that have recently been recognized as significant environmental pollutants. This study investigated the biological effects of these substances on farmworkers in southeastern Iran.
Methods: The cross-sectional investigation involved 192 farmworkers and 74 non-farmworkers serving as controls. Gas chromatography was used to measure serum concentrations of seven organochlorine chemicals. Enzymatic activities, oxidative stress markers, and factors influencing pesticide exposure were also assessed.
Results: Farmworkers had significantly higher serum levels of OCP compared to control subjects ($p < 0.001$). Their acetylcholinesterase (AChE) activity, arylesterase activity of paraoxonase-1 (PON-1), and total antioxidant capacity (TAC) were lower, while malondialdehyde (MDA) levels were higher than those observed in controls ($p < 0.001$).
Conclusion: Detectable levels of OCPs remain present in human samples in southeastern Iran despite the phasing out of many pesticides. Elevated serum concentrations of both OPDs and OCPs appear to be the primary cause of diminished enzyme activity and increased MDA levels, potentially leading to health issues through oxidative stress mechanisms. These findings suggest ongoing exposure risks for farm workers in the region.

Keywords: Pesticides, Organophosphates, Organochlorines, Acetylcholinesterase Inhibitors, Occupational Toxicology

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2358-2

MiR-34a-SIRT1 loop in ovarian cancer

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Background: MicroRNAs (miRNAs) regulate gene expression and are dysregulated in many diseases, significantly impacting ovarian cancer progression and development. This study aimed to investigate the potential role of microRNA-34a-5p (miR-34a-5p) in the detection of OC and to survey the possible pathogenesis of OC.
Methods: miR-34a and SIRT1 gene expression levels in tissue samples of OC patients and healthy controls were done by quantitative real-time polymerase chain reaction method using SYBR green and analyzed by 2 −ΔΔC T method. U6 and GAPDH were used as the reference genes.
Results: miR-34a expression was significantly lower in OC patients compared with control group. It also showed a significant negative correlation with SIRT1 which was higher in OC subjects compared with control subjects.
Conclusion: The results of the present study showed that decreased miR-34a expression may be involved in increased SIRT1 levels and the progression of ovarian cancer. Also, miR-34a could also be considered a therapeutic strategy against OC.

Keywords: miR-34a, ovarian cancer, sirtuin1

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Abstract: A-10-2849-1

Inflammatory indices IL-6, TNF-α, CRP, and hs-CRP in candidates for coronary artery bypass graft surgery

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Background: Increased levels of inflammatory factors, including high-sensitivity C-reactive protein (hs-CRP) and tumor necrosis factor %CE%B1 (TNF-%CE%B1), are linked to an increased risk of coronary artery disease (CAD). Finding the main inflammatory variables in individuals who were candidates for coronary artery bypass grafting (CABG) was the main goal of the current investigation.
Methods: Thirty patients with scheduled CABG surgery and thirty control persons were included in this study. ELISA kits were utilized to assess the serum levels of hs-CRP, TNF-%CE%B1, and interleukin 6 (IL-6).
Results: Age and body mass index (BMI) did not significantly differ between the patient and control groups. Triglyceride (TG) levels were considerably higher in the sick group than in the control group ($P < 0.05$). Furthermore, the Triglyceride (TG) levels were considerably higher in the sick group than in the control group ($P < 0.05$). In addition, the patient group had greater circulating levels of CRP and hs-CRP than the control group, and significantly raised levels of the inflammatory cytokines IL-6 and TNF-α ($P < 0.001$ for both).
Conclusion: This study's results showed that individuals who were advised to undergo surgery frequently had high levels of inflammatory factors. It is recommended that these results be taken into account prior to doing surgery.

Keywords: Coronary Artery Bypass Graft, CRP, hs-CRP, IL-6, TNF-α

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2514-1

Association between Dietary Acid Load and Central Obesity: A Result of a Population-Based Study

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Background: Central obesity is a key indicator of metabolic disorders and has been linked to dietary acid load (DAL). However, the relationship between diet-related acid load scores and central obesity, as measured by the A Body Shape Index (ABSI), remains unclear.

Methods: This cross-sectional study involved 6,482 participants, aged 35 to 65 years, drawn from the MASHAD cohort. Dietary intake was assessed using a validated food frequency questionnaire. DAL was assessed through the potential renal acid load (PRAL) and net endogenous acid production (NEAP). Central obesity was determined by ABSI, which is calculated based on waist circumference, BMI, and height. Multivariable logistic regression models were applied to examine the associations between DAL indices and ABSI.

Results: Participants with central obesity, as indicated by higher ABSI values, were more likely to be women, married, non-smokers, and older ($p < 0.001$ for all). They also showed a higher prevalence of chronic diseases, larger waist circumferences, lower BMI, and increased physical activity compared to those without central obesity ($p < 0.001$ for all). Higher NEAP and PRAL values were associated with increased central obesity based on ABSI in all models (OR (95%CI): 1.26(1.09-1.45) and 1.17(1.02-1.35) respectively).

Conclusions: Higher dietary acid load, particularly NEAP and PRAL, is associated with central obesity as measured by ABSI. These results suggest that dietary acid load may influence body composition and obesity patterns.

Keywords: Dietary acid load, central obesity, A Body Shape Index, NEAP, PRAL.

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2157-1

Application of Nanocurcumin in Acute Lymphocytic Leukemia Treatment

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Background: Acute lymphocytic leukemia (ALL) is a type of cancer with uncontrolled proliferation of abnormal, immature B or T lymphocytes that displace bone marrow cells. Recent investigations on leukemia cells have shown resistance against cell division inhibitors and traditional chemotherapeutic drugs that suggest the variable nature of cancer cells. Using nanostructured lipid carriers (NLCs) in drug delivery systems to specifically target tumor angiogenesis while avoiding harmful side effects on healthy cells has emerged as a new world in cancer treatment. Besides its antioxidant and anticancer effects, Curcumin has a high lipophilic nature and binds more to body fat, which leads to poor absorption.

Methods: This study aimed to evaluate the ability of hyaluronan-based nanostructured lipid carriers (HA-Cur-NLCs) to improve the efficacy of curcumin with poor aqueous solubility and deprived bioavailability as an antitumor and antiangiogenic agent in the Jurkat cell line. The nanostructured lipid carriers were characterized for size, zeta potential, and drug release kinetics. Successful cellular uptake was considered by fluorescence microscopy and flow cytometry. The results of cell cytotoxicity studies were measured through MTT assay, flow cytometry, and DAPI staining.

Results: Compared with free curcumin and uncovered NLCs (Cur-NLCs), (HA-Cur-NLCs) demonstrated unique features that piqued our interest. These features include optimized stability, high affinity to CD44, and more potent activity to inhibit ALL cell proliferation. Furthermore, a significant dose-related apoptotic response was observed.

Conclusion: Our results indicated that the development of the HA-Cur-NLCs can reduce the dosage of Curcumin and can be highlighted as a synergic drug delivery system in ALL treatments in combination with other chemotherapy treatments. However, further in vivo studies are crucial to validate the clinical potential of this approach.

Keywords: Acute lymphocytic leukemia, Nanostructured lipid carrier (NLC), Curcumin

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Abstract: A-10-3072-1

Fabrication and Catalytic Activity of Fe3O4 Nanozymes to Induce Oxidative Stress and Apoptosis in Tumor Cells

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Background: a tactic in cancer treatment is oxidative stress, which is a potent mechanism for causing cancer cells to die. Due to their ability to produce reactive oxygen species (ROS) through the breakdown of hydrogen peroxide (H2O2), Fe3O4 nanozymes have shown highly peroxidase mimics activity. The generated ROS can then target and kill tumor cells. In order to cause oxidative stress and encourage apoptosis in cancer cells, we synthesized Fe3O4 nanoparticles and assessed their peroxidase-like activity.

Methods: Fe3O4 nanozymes were synthesized using the co-precipitation method. Initially, (0.1mol/L) FeSO4.7H2O solution was added to (0.1mol/L) FeCl2.4H2O and mixed in 70℃. An ammonia solution of 25% was added to the solution until the pH reached 10. FE-SEM provided a detailed morphological analysis and DLS was utilized to measure the hydrodynamic size. We quantified organic functional groups using ATR-FTIR spectroscopy. The peroxidase-like activity of Fe3O4 was assessed using TMB as a substrate in an acidic pH, simulating the acidic conditions found in tumor microenvironments. The catalytic reaction was monitored by observing the color change of TMB.

Results: Our analyses revealed that the Fe3O4 nanoparticles had an average size of 100-150 nm, FTIR confirmed the successful formation of Fe3O4. The nanoparticles displayed strong peroxidase-like activity at pH 6, indicated by a noticeable color change in the TMB assay, demonstrating their capacity to catalyze H2O2 breakdown and generate free radicals that could induce apoptosis. However, at pH 7.4, the neutral color was consistent and bubble formation was observed, further demonstrating their catalase-like activity. This shows good biosafety in the normal physiologic environment that could produce oxygen and water from H2O2.

Conclusion: The Fe3O4 nanoparticles synthesized in this study mimic peroxidase activity, inducing oxidative stress under acidic conditions. This oxidative stress can cause apoptosis in cancer cells, making these nanoparticles a promising tool for cancer therapy.

Keywords: Nanozyme, Catalytic and enzymatic activity, Fe3O4, Peroxidase mimic, Tumor apoptosis

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3072-2

Synthesis and Characterization of Biomimetic MnO2 Nanozymes with Intrinsic Enzymatic Activity and their ability to Overcome Hypoxia in Tumor Microenvironment

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Background: A major contributing factor to the advancement of cancer and treatment resistance is hypoxia in the tumor microenvironment. By catalyzing the decomposition of H2O2 to produce O2, MnO2 nanozymes provide a solution that can enhance oxygenation in hypoxic tumors. We synthesized MnO2 nanozymes by co-precipitation method, characterized their properties, and assessed their enzyme-like activity at various tumor-relevant pH and temperature levels.

Methods: MnO2 nanoparticles were synthesized via the co-precipitation method. (0.1mol/L) MnSO4.H2O solution was prepared and heated to 40℃. Then (1mol/L) NaOH solution was added to the solution and mixed until the pH reached 12. Finally, the brown product was washed and dried at 150℃ for 2 hours. DLS was used to measure the hydrodynamic size. FE-SEM provided a detailed morphological analysis. We also utilized ATR-FTIR spectroscopy to detect and quantify organic functional groups. The catalase-like activity was evaluated by adding MnO2 to H2O2 solutions at different pH and temperatures, conditions mimicking the tumor microenvironment. The decomposition of H2O2 was monitored by UV-VIS spectroscopy. The oxygen generation was visibly confirmed by bubble formation.

Results: Our results indicated the formation of MnO2 nanoparticles as nanozymes with a size of 80-100 nm. ATR-FTIR indicated successful MnO2 formation. The nanozymes exhibited catalase-like activity by the decomposition of H2O2 and the decrease of the UV-VIS absorbance at 240 to 260 and also the generation of oxygen bubbles with the addition of MnO2 to H2O2. The catalase activity of nanozymes was consistent in both tumor-mimicking and normal physiological microenvironments with a 70% and 50% drop in the amount of H2O2 respectively.

Conclusion: Synthesized MnO2 nanozymes are great candidates for improving the hypoxic condition of the tumor microenvironment due to their facile and low-cost synthesis and great catalase-like activity. Our results suggest that MnO2 nanozymes hold potential as a therapeutic tool for overcoming hypoxia in cancer treatment.

Keywords: Nanozyme, Catalytic and enzymatic activity, MnO2, Catalase mimic, Tumor hypoxia

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Abstract: A-10-3094-1

Investigation of Serum Zinc Status and Its Association with Oxidative Stress Markers in Patients with Metabolic Syndrome

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Background: Metabolic syndrome is a condition characterized by the coexistence of several major risk factors for cardiovascular disease and type 2 diabetes. This study aimed to investigate the serum levels of zinc and its correlation with oxidative stress markers in patients with metabolic syndrome.

Methods: 60 overweight or obese patients with metabolic syndrome (patients group), along with 60 healthy individuals with normal weight of both sexes (control group), were selected. After sampling, serum levels of zinc, insulin, FBS, triglycerides, total cholesterol, LDL-C, HDL-C, MDA, and TAC were measured. HbA1c levels were also measured. The results were analyzed by proper statistical tests.

Results: Serum zinc levels in the patients group were significantly lower compared to the control group. Serum levels of TAC and HDL-C were decreased but serum levels of MDA, FBS, HbA1c, triglycerides, total cholesterol, and LDL-C were significantly increased in patients compared to controls. A significant inverse correlation was observed between serum zinc levels and FBS, and a significant direct correlation was found between serum zinc levels and TAC in patients with metabolic syndrome.

Conclusion: Serum zinc levels decrease in patients with metabolic syndrome who are obese or overweight, and this reduction may be associated with enhanced oxidative stress, and elevated FBS levels. Therefore, zinc levels should be monitored in patients with metabolic syndrome, and any deficiencies should be corrected.

Keywords: Metabolic syndrome, Zinc, Oxidative stress

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Abstract: A-10-3057-1

The Impact of Oxidative Stress Markers on Clinical and Radiological Outcomes in COVID-19 Patients

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Background: The COVID-19 pandemic, resulting from a coronavirus-induced lung infection and systemic disorder, has posed significant challenges to human health. Research primarily focused on the respiratory system has revealed that fundamental biological processes, particularly oxidative stress, play a crucial role in the disease's pathogenesis and complications. This study evaluates oxidative stress biomarkers in COVID-19 patients, examining their relationship with clinical status and other paraclinical findings. The findings suggest that these biomarkers can serve as reliable indicators for assessing disease severity and improving prognosis, thereby enhancing clinical evaluations and treatment strategies for COVID-19 patients.

Methods: This cross-sectional study, was conducted on patients suffering from coronavirus referred to Imam Reza Hospital (AS) and Shahid Hashminejad Hospital in Mashhad from August to February 2020. The patients with COVID-19 who were approved by the relevant specialist were analyzed according to the severity of the disease based on clinical symptoms and hematological-radiological indicators at the beginning of the study and also 5 days after taking the initial sample of the case using statistical and were compared.

Results: The findings of the study showed that the clinical symptoms in the patients decreased significantly ($P<0.05$ to $P<0.001$). The indicators related to oxidative stress were also changed in the direction of improvement. Statistical analysis showed a correlation between indicators related to oxidative stress and clinical, hematological, and radiological symptoms.

Conclusion: The results of the present study show that oxidative stress indicators in patients with corona can be used to investigate and predict clinical symptoms. However, clinical studies with larger sample sizes and different evaluations can support these findings.

Keywords: Corona, clinical symptoms, oxidant, antioxidant

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Abstract: A-10-3096-1

FIB-4 index as a predictor of critical care outcomes in COVID-19-hospitalized patients

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Background: Several comorbidities such as liver disorders worsen the prognosis of coronavirus-19 disease (COVID-19). However, the best strategy to stratify severity and mortality risk according to liver damage has not been established. This study aims to determine the predictive value of the Fibrosis-4 (FIB-4) Index in COVID-19 patients.
Methods: The present study employed a cross-sectional design. A comprehensive electronic medical record including epidemiological, demographic, anthropometric, chronic medical histories, clinical, and laboratory data was created, from people admitted to SHMU hospitals due to a SARS-CoV-2 infection between February 20, 2020, and March 20, 2021. Only data from hospitalized and non-vaccinated cases with a COVID-19 diagnosis confirmed by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) from oro- and nasopharyngeal swab specimens were included in our analysis. A total of 2232 confirmed COVID-19 patients were included in the current research.
Results: Regression models were performed to evaluate the correlation between the FIB-4 and the severity and mortality of COVID-19. The FIB-4 index was significantly higher in the severe patients ($P<0.001$). Also, the FIB-4 level was significantly lower in survivor cases ($P<0.001$). Multivariate logistic regression analysis demonstrated that the FIB-4 was a predictor of the severity and mortality adjusted for age, sex, and BMI (OR=7.4, OR=10.14 respectively).
Conclusion: In summary, the FIB-4 index could be used as an early indicator of mortality in COVID-19 patients. Furthermore, the study revealed that FIB-4 is a biochemical marker of COVID-19 19 severe prognosis.

Keywords: Liver disease, FIB-4, severity, mortality, COVID-19

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Abstract: A-10-2222-1

The role of NLRP3 inflammasome in hepatocellular carcinoma metastasis: a systematic review

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Background: Cancer, the increasing signature disease of the 21st century, is characterized by the rapid uncontrolled division and growth of cells, ultimately proving fatal. The dynamic complex biochemical machinery of cancer remains yet to be fully elucidated. Hepatocellular carcinoma is a prevalent form of cancer with high mortality rates. NLRP3 is a critical regulator of inflammatory processes as well as immune reactions. However, new emerging research demonstrates a critical role for NLRP3 inflammasome in the metastasis of hepatocellular carcinoma which is considered a common hallmark across an extensive range of malignancies.

Methods: In this systematic review, the search strategy and study design were conducted following PRISMA guidelines. Pubmed, Proquest, and Google Scholar were searched until 31 August 2024 using relevant syntax. A total of 2940 relevant articles were identified in our first round of searching. The initial articles were studied and analyzed in terms of relevance according to guidelines. Only Cell culture studies were selected for our study. Consequently, 16 articles were chosen for the current study.

Results: Our findings demonstrated a critical role for NLRP3 inflammasome through regulating several metastasis and angiogenesis-associated genes such as IL-1β, Caspase-1, pyroptosis, MMP3, MMP16, and VEGFA in hepatic cells. Additionally, the knockdown of NLRP3 significantly reduced the genes as mentioned earlier, and demonstrated anti-metastatic properties.

Conclusion: In conclusion, future targeted therapies specifically designed for NLRP3 can prove promising as a way of establishing novel therapies in the treatment of hepatocellular cancer.

Keywords: NLRP3, Hepatocellular cancer, Metastasis

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Abstract: A-10-2594-3

The effect of inflammation and angiogenesis, along with the use of curcumin and nanoparticles on p53 gene expression and the activity of proteins involved in apoptosis on breast cancer

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Background: In the study of factors affecting the incidence of breast cancer in patients, conventional chemotherapy is inadequate in the treatment of BC types. The need for new treatments or drugs such as curcumin has significant potential in inhibiting disease associated with apoptosis, autophagy, inhibition of angiogenesis, cell migration, and metastasis is associated with duplication in this area. Challenges, due to the dynamic and degradable nature, low water solubility, rapid metabolism, and rapid systemic elimination, collectively limit its clinical applications.
Methods: The effect of inflammation and angiogenesis combined with the use of curcumin and nanoparticles on p53 gene expression and the activity of proteins involved in apoptosis on breast cancer, from systematic research according to our criteria From 2024/1/12 to 2024/7/20 several search engines and databases including pubmed..6 keywords: breast cancer, inflammation, curcumin angiogenesis, Apoptosis is P53gen and a comparative study of articles.
Results: According to the purpose of this study, our selection based on entry and exit criteria are as follows: narrative review, systematic comparative, interpretation, case studies in the form of full text/Selection based on the search criteria listed in the international search engine database contains 35 articles from 2013 to 2024 In the first stage, 10 articles were removed due to duplication and waste, the remaining 25 articles were reviewed.
Conclusion: Cancer is an inflammatory disease. Inflammation can alter the expression of oncogenes and tumor suppressor genes to promote neoplastic metamorphosis. A thorough understanding of angiogenesis has led to the identification of new treatments for cancer patients using crocumin in water systems is an insoluble and insoluble analysis of microscopic fluorescence and It also showed that dendrosomes are able to insert insoluble chromins into the tumor cells of MCF-breast 7, This is the same time-dependent nanocortex dendrosome that increases the inhibitory effect of curcumin on breast tumor cells and has a significant potential in inhibiting factors involved in cancer

Keywords: Breast Cancer, Inflammation, Curcumin, Angiogenesis, P53 Gene, Apoptosis

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Abstract: A-10-2971-1

Prevalence of Polycystic Ovary Syndrome (PCOS) Phenotypes in Iranian Women

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Background: Polycystic ovary syndrome (PCOS) is a multifaceted disorder characterized by diverse clinical and metabolic features the diverse nature of PCOS, researchers have increasingly sought to categorize distinct phenotypic subgroups within this condition. This study aimed to examine the prevalence of various PCOS phenotypes in a cohort of Iranian women, with a particular focus on those experiencing infertility and recurrent pregnancy loss (RPL).

Methods: This cross-sectional study included 242 women diagnosed with PCOS, comprising 143 women with infertility and 99 with a history of RPL. The participants were divided into seven phenotypic categories based on the presence or absence of hyperandrogenism, oligo/anovulation, and polycystic ovaries: phenotype A (hyperandrogenism, oligo/anovulation, and polycystic ovaries); phenotype B (hyperandrogenism and oligo/anovulation); phenotype C (hyperandrogenism and polycystic ovaries); phenotype D (oligo/anovulation and polycystic ovaries); phenotype E (hyperandrogenism); phenotype F (polycystic ovaries); and phenotype G (oligo/anovulation).

Results: Phenotype A was the most common PCOS phenotype, both in the overall population and among women with infertil and, comprising 68.6% of the total PCOS population. Phenotypes B, C, E, and F comprised 4.5%, 21.9%, 4.1%, and 0.8% of the PCOS population, respectively. This study found that phenotypes A and C were the most common PCOS presentations among Iranian women. C

Conclusion: These results suggest that the majority of Iranian women with PCOS, including those experiencing infertility or recurrent pregnancy loss, exhibit all three core diagnostic features - hyperandrogenism, oligo/anovulation, and polycystic ovaries - or at least hyperandrogenism and polycystic ovaries.

Keywords: polycystic ovary syndrome, PCOS phenotypes, infertility, recurrent pregnancy loss

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2971-2

Associations between PCOS Phenotypes and Hematological, Biochemical, and Hormonal Parameters in Iranian Women

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Background: Polycystic ovary syndrome (PCOS) is a complex endocrine disorder affecting women of reproductive age. Due to the diverse nature of PCOS, patients have been categorized into distinct phenotypes based on clinical and biochemical characteristics. This study aimed to investigate the relationship between PCOS phenotypes and a range of hematological, biochemical, and hormonal markers, with a particular focus on infertile and recurrent pregnancy loss (RPL) subgroups.

Methods: This study included 242 women diagnosed with PCOS, of whom 143 had infertility and 99 had a history of RPL. Participants were categorized into seven phenotypic groups based on the presence or absence of hyperandrogenism, irregular ovulation, and polycystic ovaries. Blood samples were collected from these women, and their hematological, biochemical, and hormonal profiles were analyzed.

Results: This study found no significant differences in biochemical, hormonal, or hematological profiles among the various PCOS phenotypes. However, women with phenotype F exhibited lower red blood cell counts and hematocrit levels compared to other phenotypes. Within the infertile PCOS subgroup, phenotypes showed significant differences in mean corpuscular volume (MCV). Among PCOS women with a history of RPL, phenotype F demonstrated significantly lower levels of red blood cells, hemoglobin, and hematocrit compared to the other phenotypes.

Conclusion: These findings suggest that most PCOS phenotypes exhibit similar hematological, biochemical, and hormonal profiles except for some distinct variations observed in phenotype F.

Keywords: polycystic ovary syndrome, PCOS phenotypes, infertility, recurrent pregnancy loss

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Abstract: A-10-3108-1

The Role of Saikosaponin b2 in Inhibiting Angiogenesis in Cancer Therapy

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Background: Angiogenesis, the process of new blood vessel formation, is crucial for tumor growth and metastasis in various cancers, including liver cancer. Saikosaponin b2 (SSb2), a natural compound, has been studied for its anti-angiogenic properties, offering a potential new approach to cancer treatment. This review explores the mechanisms by which SSb2 inhibits angiogenesis and discusses its broader implications for cancer therapy.

Methods: According to our data collection criteria, a total of 86 articles were collected using databases such as PubMed, Scopus, and Web of Science from 2014 to 2024 on the anti-angiogenic effects of SSb2 across different cancer types. The review included research on the molecular pathways affected by SSb2, particularly those involving VEGF, ERK, and HIF-1α. Articles that did not specifically address angiogenesis in cancer were excluded from this review.

Results: Saikosaponin b2 has demonstrated significant potential in inhibiting angiogenesis in various cancers by targeting multiple signaling pathways. It has been shown to downregulate VEGF and inhibit the ERK and HIF-1α pathways, which are essential for the proliferation and migration of endothelial cells and the formation of new blood vessels. In studies involving liver cancer, SSb2 effectively reduced tumor growth and metastasis by blocking these angiogenic pathways. Additionally, research in other cancer types, such as colorectal and breast cancers, suggests that SSb2 can suppress angiogenesis by disrupting the tumor microenvironment and reducing the expression of angiogenic factors.

Conclusion: Saikosaponin b2 shows promise as a natural inhibitor of angiogenesis, with potential applications across various cancers. By targeting key pathways involved in blood vessel formation, SSb2 may offer a new avenue for cancer therapy, particularly in tumors that rely heavily on angiogenesis for growth and spread. Further research is needed to fully elucidate its mechanisms and optimize its therapeutic use.

Keywords: Saikosaponin b2, Angiogenesis, Cancer therapy, VEGF, HIF-1α

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Abstract: A-10-3107-1

Biocompatibility, Cytotoxicity, Antimicrobial and Epigenetic Effects of Novel Chitosan-Based Quercetin Nanohydrogel in Human Cancer Cells

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Background: Previous studies have reported that quercetin (Q) has a potential antibacterial and anticancer activity. However, its application is limited by many important factors including high hydrophobicity and low absorption.
Methods: In the current study, we synthesized and characterized (Patent) a novel chitosan-based quercetin nanohydrogel (ChiNH/Q). Encapsulation efficiency was confirmed by UV/VIS spectrophotometer. Physicochemical characterization of ChiNH/Q was assessed by PDI, DLS, SEM, FTIR, and XRD. The toxicity of the ChiNH/Q against five strains of the pathogen and HepG2 cells was examined. Moreover, the quantification of ChiNH/Q on genomic global DNA methylation and expression of DNMTs (DNMT1/3A/3B) in HepG2 cancer cells were evaluated by ELISA and real-time PCR, respectively.
Results: Under the SEM-based images, the hydrodynamic size of the ChiNH/Q was 743.6 nm. The changes in the PDI were 0.507, and zeta potential was obtained as 12.1 mV for ChiNH/Q. The FTIR peak of ChiNH/Q showed the peak at 627 cm−1 corresponded to tensile vibrational of NH2-groups related to Q, and it is the indication of Q loading in the formula- tion. Moreover, XRD data have detected the encapsulation of ChiNH/Q. The ChiNH/Q showed a potent antimicrobial inhibitory effect and exerted cytotoxic effects against HepG2 cancer cells with IC50 values of 100 µg/mL. Moreover, our data have shown that ChiNH/Q effectively reduced (65%) the average expression level of all the three DNMTs ($p<0.05$) and significantly increased (1.01%) the 5-methylated cytosine (5-mC) levels in HepG2 cells.
Conclusion: Our results showed for the first time the bioavailability and potentiality of ChiNH/Q as a potent antimicrobial and anticancer agent against cancer cells. Our result provided evidence that ChiNH/Q could effectively reduce cellular DNMT expression levels and increase genomic global DNA methylation in HepG2 cancer cells. Our results suggest a potential clinical application of nanoparticles as antimicrobial and anticancer agents in combination cancer therapy.

Keywords: chitosan nanohydrogel, quercetin, cytotoxic activity, antimicrobial activity, DNA methylation, gene expression

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The effects of disulfiram on biochemical markers of LPS-induced acute lung injury in rats

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Background: Disulfiram is an FDA-approved medication for alcohol dependence. However, some other pharmacological properties of disulfiram have been shown recently, such as anti-inflammatory and anti-cancer effects. Acute lung injury is one of the diseases with a mortality rate of about 40%, and the treatments used for it are often supportive.

Methods: Eighteen rats were divided into three groups of six: 1. Control, 2. LPS, and 3. LPS+ disulfiram. The control group received normal saline. Acute lung injury was induced using a single intraperitoneal injection of LPS at 10 mg/kg. The third group received disulfiram at 50 mg/kg, three times orally by gavage at 48, 24, and 3 hours before LPS injection. After 20 hours, rats were sacrificed and lung tissue was collected. Biochemical markers of malondialdehyde (MDA), tumor necrosis factor-α (TNF-α), myeloid peroxidase (MPO), and antioxidant enzymes catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GPx) levels were measured in lung tissue samples using ELISA kits.

Results: It was shown that disulfiram increased significantly antioxidant enzyme levels in lung tissues, CAT ($P<0.01$); SOD ($P<0.001$), and GPx ($P<0.05$). It also decreased significantly MPO levels ($P<0.01$). However, its decreasing effects on MDA and TNF-alpha were not significant.

Conclusion: It is concluded that disulfiram has good potential as a preventive agent for LPS-induced acute lung injury with multiple mechanisms, including antioxidant activities. More research is needed to ensure its capability for clinical applications.

Keywords: Disulfiram, Acute lung injury, Biochemical markers

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The regulatory relationship between miR-206 and K-Ras: for understanding the molecular mechanisms in the prevention of gastrointestinal cancer

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Background: Despite progress in developing treatment strategies for gastrointestinal (GI) cancer, which causes more than 2.5 million deaths each year. MicroRNA-206 (miR-206), a member of the miR-1 sequence family, where the coding gene is located on chromosome 6, acts as a tumor suppressor in many human tumor types. K-RAS is a RAS family gene and a major oncogene responsible for one-third of human cancers. This article explores the interaction between miR-206 and K-Ras, aiming to uncover new therapeutic strategies for GI cancer by hindering cancer cell growth and spread.

Methods: This review article was performed within articles published at PubMed, Science Direct, Google Scholar, and Web of Science until May 2024. The keywords were microRNA-206 OR miR-206 AND K-Ras AND GI cancer OR Gastrointestinal cancer AND Treatment. By searching this database, 22 articles were found, and 12 were removed by reading titles and abstracts. 10 articles were selected under the inclusion criteria. All articles were chosen from English articles.

Results: Finally, 10 articles were included in the study. An important strategy in cancer research is inhibiting the cell cycle of tumors. K-Ras is one of the most frequently mutated oncogenes in GI cancer and triggers cancer cells to enter the cell cycle from the G1 to S phase by expressing cyclin D, but miR-206 can inhibit it by directly affecting it. In addition, miR-206 can function as a negative regulator of NF-κB transcriptional activity induced by oncogenic K-Ras.

Conclusion: Further investigation and experimentation into miR-206 with K-Ras is strongly recommended because miR-206 as a negative regulator of gene expression for K-Ras could be the first step in the treatment strategy for GI cancer. However, there needs to be more research done on this topic.

Keywords: MicroRNA-206 (miR-206) / K-Ras / Gastrointestinal cancer (GI cancer) / Treatment

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The Emerging Role of Heat Shock Proteins in Colorectal cancer

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Background: Colorectal cancer (CRC) is one of the most common malignancies worldwide. The metastasis of this cancer poses a severe threat to patients' health. Heat Shock Proteins (HSPs) protect cells against stressful factors, abnormal expression of HSP, a modulator of apoptosis, cell cycle progression, and multidrug resistance in cancers, including CRC. This study aims to review HSPs to find new treatments for CRC with regulation of their expression.
Methods: This review article was performed within articles published at PubMed, Science Direct, and Google Scholar until May 2024. The keywords were Heat Shock Proteins, HSPs, and Colorectal Cancer, or CRC. By searching this database, 19 articles were found, and five were removed by reading titles and abstracts.14 were selected under the inclusion criteria. All articles were chosen from English articles. Finally, 15 Articles were included in the study.
Results: Heat shock proteins (HSPs) play a significant role in colorectal cancer (CRC) prognosis and treatment. HSP70 was associated with a poor prognosis due to its role in promoting tumor growth and metastasis. In contrast, HSP60 (HSPD1) acted as an anti-tumor marker, especially in advanced CRC stages (III/IV). HSP60 served as a valuable prognostic marker when combined with TNM classification. Additionally, HSP90 and HSP110 inhibitors were under investigation for their potential in CRC therapy, particularly in combination treatments. These inhibitors were analyzed for their ability to enhance therapeutic outcomes and overcome resistance. These findings highlighted the role and potential of HSPs in CRC and their potential as therapeutic targets
Conclusion: Further research on HSPs, especially HSP70, HSP60 (HSPD1), and HSP110, could improve the treatment of Colorectal Cancer by enhancing the therapeutic outcomes and overcoming resistance to treatment. However, more studies are needed on this topic.

Keywords: Colorectal Cancer, CRC, Heat Shock Proteins, HSP

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MicroRNA-206 can inhibit the expression of HDAC4 for treatment in gastrointestinal cancer

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Background: Gastrointestinal cancer constitutes over a third of global cancer cases, with a mortality rate above 35%. Its incidence and mortality, including colon and esophageal cancer, are significant in East Asia. MiR-206, a non-coding RNA on chromosome 6p12.2, induces G1 arrest in tumor cells. It inhibits histone deacetylase 4 (HDAC4), by targeting the HDAC4 gene, reducing cancer cell proliferation and metastasis. This article delves into the interaction between miR-206 and HDAC4 to unveil novel therapeutic approaches for gastrointestinal cancer by impeding the proliferation and dissemination of cancer cells.

Methods: This review article was performed within articles published at PubMed, Science Direct, and Google Scholar until May 2024. The keywords were microRNA-206 OR miR-206 AND HDAC4 OR Histone Deacetylase 4 AND GI cancer OR Gastrointestinal cancer AND Treatment. By searching this database, 28 articles were found, and 17 were removed by reading titles and abstracts. 11 articles were selected under the inclusion criteria.

Results: Finally, 11 articles were included in the study. MiRNAs could play an important role in many biological processes, including angiogenesis, proliferation, migration, invasion, and apoptosis in various cancers, and studies showed that HDAC4 correlated with tumorigenesis. The interaction between miR-206 and HDAC4 occurs at the molecular level, where miR-206 binds to the 3-untranslated region (UTR) of the HDAC4 gene, causing its inhibition. This interaction was important for regulating genes and could be used in the development of new treatments for GI cancer.

Conclusion: Further research regarding the role of miR-206 with HDAC4 would be of great help in the Treatment of GI cancer because miR-206 from RNase is well protected by digestion and is enormously stable in plasma/serum, and as HDAC inhibitor has activity against cancer cells via cell cycle arrest.

Keywords: MicroRNA-206, miR-206, Histone Deacetylase 4, HDAC4, Gastrointestinal cancer, GI cancer, Treatment

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The Emerging Role of Heat Shock Proteins in Esophageal Cancer

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Background: Esophageal cancer (EC), the eighth most common cancer globally, has a poor prognosis, often being diagnosed at advanced stages. Heat shock proteins (HSPs) protect cells from stressors, but their abnormal expression can contribute to diseases, including EC. This study aims to review HSPs to identify new treatment methods for EC by regulating their expression.

Methods: This review article was performed within articles published at PubMed, Science Direct, and Google Scholar until May 2024. The keywords were: Heat Shock Proteins OR HPSs AND Heat Shock Response AND Esophageal Cancer OR EC. By searching this database, 21 articles were found, and nine were removed by reading titles and abstracts.12 articles were selected under the inclusion criteria. All articles were chosen from English articles.

Results: Finally, 12 articles were included in the study. Heat shock proteins (HSPs), particularly HSPD1, HSP70, and HSP90, played pivotal roles in esophageal cancer (ESCA). HSPD1 also promoted ESCA progression by affecting cell stemness, metabolism, and immune cell infiltration, making it a potential therapeutic target. Overexpression of HSP70 and HSP90 in irradiated ESCA cells was linked to increased pyroptosis and reduced tumor immunity. HSP90, especially its Kbu modification at lysine 754, contributed to chemotherapy resistance and poor prognosis. Targeting the HSP90 interaction network, specifically through the SDCBP-HSP90 axis, using compounds like V020-9974, offered a promising therapeutic strategy to enhance sensitivity to treatments like 5-FU.

Conclusion: Further research on HSPs, especially HSPD1, HSP70, and HSP90, could improve esophageal cancer treatment by reducing cell proliferation, immune evasion, and therapy resistance. However, more studies are needed on this topic.

Keywords: Esophageal Cancer, ESCA, Heat Shock Proteins, HSP

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Clinical and histological evaluations of low dose administration of silymarin in an EAE mouse model of multiple sclerosis: a pilot study

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Background: Multiple sclerosis (MS) is an inflammatory and demyelinating disease of the central nervous system (CNS). It has been suggested that persistent neurotoxic inflammation may be influenced by elevated iron deposition in the central nervous systems of humans and animal models. Here, we investigated the protective effects of silymarin on clinical scores, as well as inflammation, astrogliosis, demyelination, and iron deposition in the spinal cord of EAE-induced mice.

Methods: C57BL/6 female mice were used in this study and randomly divided into two groups. Experimental autoimmune encephalopathy (EAE) was induced using MOG 35-55 peptide. After EAE induction, mice received 50 mg/kg/day of silymarin intraperitoneally for 20 days. The clinical symptoms of the EAE control group as well as the silymarin-treated group were monitored regularly from the start of the experiment to the last day. After sacrificing, spinal cords were removed, and lumbar sections were stained with Hematoxylin-Eosin (H&E), Luxol Fast Blue (LFB), FluoroMyelin, glial fibrillary acidic protein (GFAP), and Perl staining.

Results: Silymarin at the selected dose could reduce the severity of EAE clinical symptoms but not affect the onset time of the disease. Based on histological evaluations, silymarin could ameliorate inflammation and reduce the extent of demyelination. It also attenuated astrogliosis and spinal cord iron deposition.

Conclusion: It seems that 50 mg/kg/day injection of silymarin had protective effects on EAE progression clinically and histologically with no adverse effects. More experimental research needs to evaluate its impacts at various doses and in different courses of the disease. The obtained results can help researchers determine the optimal dose of silymarin to be used in clinical trials as a co-treatment with glatiramer acetate, a medication that has recently been recommended for the management of multiple sclerosis.

Keywords: MS, CNS, EAE, MOG, Clinical scores, spinal cord

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Abstract: A-10-3112-1

Investigating of the relationship between the expression level of FFAR2 and FFAR3 in peripheral blood leukocytes with the coronary artery stenosis, calcium score and serum concentration of IL-1β in male patients referred to the CT-angiography center of Razieh-Firouz hospital in Kerman

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Background: Cardiovascular disease (CVD) is a public health problem and the main cause of most cardiovascular diseases is atherosclerosis. Atherosclerosis is the accumulation of fat and inflammation in the coronary arteries of the heart, which may eventually lead to complications such as myocardial infarction (MI). The inflammatory process plays an important role in the initiation and progression of atherosclerosis and IL-1β, as a pro-inflammatory mediator, plays an essential role in the development of atherosclerosis. Also, free fatty acids through their receptors (FFARs) affect the severity of inflammation and possibly atherosclerosis. For this reason, in this study, we investigated the relationship between the expression level of FFAR type 2 and 3 as well as IL-1β concentration with atherosclerotic markers obtained from CT angiography in cardiac patients.

Methods: Blood samples were taken from 113 patients referred to the CT angiography center while fasting. After centrifugation at 10000 g, the buffy coat was separated. FFAR-2 and FFAR-3 expression was measured by qRT-PCR and IL-1β concentration by ELISA method. The relationship between these factors with calcium score, percentage of vascular occlusion and CAD risk was determined by linear regression analysis.

Results: The expression of FFAR-2 in the patient group (0.363±0.023) was significantly lower than control group (0.998±0.09), whereas the different of expression level of FFAR-3 in the patient group (1.04±0.06) compared to the control group (1.01±0.088) was not significant. Plasma concentration IL-1β serum concentration in the patient group (210.2436±31.249 pg/ml) compared to the control group (2.24281 ± 35.4371 pg/ml (P=0.045)). Also, a negative and significant correlation was observed between atherosclerotic indices with FFAR-2, however this correlation for IL-1β was positive.

Conclusion: FFAR-2 expression is associated with reduced risk of atherosclerosis and increased IL-1β in humans. It is also possible that specific FFAR-2 ligands have a protective role in the heart and Coronary arteries.

Keywords: FFARs, Atherosclerosis, IL-1β, Calcium Score

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Abstract: A-10-3117-1

Investigation of Serum Magnesium Status and Its Association with Oxidative and Inflammatory Markers in Prediabetic individuals

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Background: Prediabetes is a condition where hyperglycemia is not severe enough to classify the patient as diabetic, but the risk of developing diabetes is high. The importance of magnesium in metabolism has been established. Therefore, in this study, we aimed to evaluate magnesium levels in prediabetic individuals.
Methods: In this study, two groups were examined: 40 prediabetic patients, diagnosed based on ADA criteria, and a control group consisting of 40 healthy individuals. Serum levels of magnesium, FBS, insulin, CRP, MDA, triglycerides, total cholesterol, HDL-C, and LDL-C were measured and compared between the two groups. HbA1c levels were also measured and compared. HOMA-IR index values were calculated and compared between the groups.
Results: Serum levels of magnesium, insulin, HDL-C, and LDL-C, showed no significant differences between the two groups. Triglyceride, total cholesterol, MDA, CRP, and HOMA-IR levels were significantly higher in the patient group compared to the control group. No significant correlation was observed between serum magnesium levels and the study variables, except for HOMA-IR, where a weak inverse correlation with HOMA-IR was found.
Conclusion: Magnesium levels may have an inverse relationship with insulin resistance, but serum magnesium levels in prediabetic individuals do not significantly differ from those in healthy individuals.

Keywords: prediabetes, Insulin resistance, Magnesium

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Abstract: A-10-2865-1

PMS2 Gene and Protein Expression and its Correlation clinicopathological presentations in an Iranian colorectal cancer population

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Background: A significant increase in the incidence of colorectal cancer over the past 20 years has led to more research to find early detection biomarkers. One of the pathways that causes colorectal cancer (CRC) is mutation in the DNA mismatch repair (MMR) genes encoding five families of genes: MLH1, PMS2, MSH6, MSH2, and MSH3. MMR pathways are highly conserved from bacteria to humans, and defects in one of them or their biological pathways can lead to CRC. The purpose of this study was to compare the expression of the PMS2 gene and its protein in the normal and tumoral tissues in CRC, a non-hereditary (sporadic) cancer.

Methods: The study population consisted of 67 patients. Standard biopsies of normal and tumoral tissue were performed under the supervision of a gastroenterologist. All specimens were analyzed for localization of tumor, differentiation, and pathological tumor stage. After extracting mRNA and synthesis of cDNA, real-time PCR was performed to evaluate the expression level of the PMS2 gene. The expression of PMS2 protein in the same tissues was carried out using the immunohistochemistry (IHC) method.

Results: The results of this study indicated that PMS2 gene expression and protein levels in the tumoral tissue were significantly lower compared to that of normal tissue ($p < 0.001$). We found a positive correlation between decreased PMS2 expressions and colorectal cancer.

Conclusion: Low expression of the PMS2 gene in mRNA and protein levels was observed in colorectal cancer. The mutations that occurred in the PMS2 gene resulted in genome instability. This instability is likely to lead to colon cancer. Failure to correctly repair the DNA damage can also contribute to the development of colorectal cancer.

Keywords: sporadic colorectal cancer, PMS2 gene, real-time PCP, mismatch repair

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Abstract: A-10-3112-2

Is There a Relationship Between the Concentrations of Different Types of Free Fatty Acids with Atherosclerosis Indices?

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Background: Atherosclerosis is a complex pathological condition that involves the accumulation of lipid-rich plaques in the arteries. Free fatty acids (FFAs) through their effect on FFARs and based on their length and degree of saturation, act as signaling molecules for inflammation and possibly atherosclerosis. Investigating the relationship between types of fatty acids with atherosclerosis can be effective in guiding patients to control the progress of the disease.

Methods: For this purpose, blood samples were collected from 113 male patients with symptoms of atherosclerosis while fasting. Atherosclerotic indicators were measured by CT angiography. First, lipids were extracted from 500 microliters of plasma by organic solvents. FFAs were separated from lipids by TLC and their concentration of them was measured by the gas chromatography method. The relation between data was analyzed by linear regression test.

Results: We observed in the present study, the concentration of laurate, myristoleate, palmitate, stearate, and oleate in the patients was higher than the control group, and on the contrary, the concentration of caprate, myristate, linoleate, and linolenate showed higher values in the control group. Also, in total, the concentration of saturated and total FFAs was higher in the patient group and unsaturated fatty acids were lower than the control group. A negative and significant relationship was observed between the concentration of long-chain FFA and saturated FFA with atherosclerotic factors, but this relationship was positive with the concentration of total FFA.

Conclusion: Finally, the results of this study showed that the type and concentration of free fatty acids are effective on atherosclerotic indices, such as calcium score and the degree of coronary artery occlusion. An increase in unsaturated fatty acids exerts a protective effect on calcium score and CAD risk.

Keywords: Free Fatty Acids, Atherosclerosis, Gas Chromatography, Calcium Score

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Synthesis of chitosan-alginate nanoparticles with high potential for gene and drug delivery

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Background: Using nanocarriers, especially polymeric nanoparticles, for drug delivery is promising in many aspects, such as protecting drugs against enzymatic degradation, improving drug stability, and improving bioavailability. The excellent performance of polymer nanoparticles can reduce side effects and enhance therapeutic effects. Bio-based polymeric nanoparticles, such as those made from lipids, polysaccharides, and proteins, are highly attractive to medical scientists. Chitosan is a natural polysaccharide with ideal properties, including biodegradability, mucosal adhesion, enhanced penetration, biocompatibility, and non-toxicity in vivo. The physicochemical properties of chitosan contribute to its positive surface charge. Alginate, an anionic polysaccharide composed of guluronic acid and mannuronic acid, can form a gel matrix to preserve the desired gene or drug. Studies have demonstrated that chitosan-alginate nanoparticles can be used as a non-viral vector for gene and drug delivery with maximum transfer efficiency and minimum toxicity.

Methods: To prepare chitosan-alginate nanoparticles: first, a certain amount of alginate powder is dissolved in distilled water with the appropriate viscosity, and then chitosan powder is dissolved in a dilute acetic acid solution for the synthesis of the polymeric nanoparticle. Then chitosan-alginate nanoparticles were synthesized using the gelation method. Prepared nanoparticle investigated using DLS, FESEM, and MTT assay using different concentrations.

Results: The physicochemical properties of chitosan-alginate nanoparticles were evaluated using Field Emission Scanning Electron Microscopy (FESEM) and Dynamic Light Scattering (DLS). These analyses revealed that the average size of the nanoparticles was 45 nm, with a spherical shape and excellent mono disparity. Additionally, the MTT assay results at 24 and 48 hours demonstrated that the nanoparticles exhibited no significant toxicity to normal cells compared to the control.

Conclusion: The results indicate that chitosan-alginate nanoparticles are an effective carrier for gene and drug delivery, due to their properties such as high monodispersity, uniform nanostructure, and low cytotoxicity.

Keywords: Polymeric nanoparticle, chitosan, alginate, drug delivery, gene delivery

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Lithium effect on testosterone levels, pituitary gonadotropins and testis tissue structure in Adult male rats

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Background: Lithium is used to treat bipolar disorder. Considering the importance of sex cells in reproduction and transmitting hereditary traits from generation to generation, in this study, the effects of lithium were investigated on the level of testosterone, gonadotropins, testis tissue, and spermatogenesis.

Methods: An experimental study was performed on 16 rats in each group. The experimental group 180mg/kg/body weight of lithium carbonate solution was injected intraperitoneally for 40 days. The control group did not receive any material. The testis removed and was fixed in 10% formalin. Then staining with hematoxylin - eosin (HE) and the cells were examined. Evaluating hormones FSH, LH, and testosterone were measured by Radioimmunoassay, and the data were analyzed.

Results: Weight, length, and weight testis epidydimis showed a significant decrease in the experimental group compared with controls and reduced the average number of spermatogonia, primary spermatocytes, and spermatid was significant in the experimental group compared with control group P.value<(0001/0). By comparing within testis was observed significant decrease in the experimental and control groups and The mean reduction in the number of Sertoli cells in both experimental and control groups has no difference significant statistic P.value>. (498/0)

Conclusion: It is suggested that lithium will used cautiously for each patient according to the experiments, the dose, and duration of use (Duration of consuming) (Duration of Taking).

Keywords: lithium carbonate, Spermatogenesis, testosterone

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Abstract: A-10-3122-1

Role of efferocytosis in type 2 diabetes mellitus: a systematic review

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Background: Billions of cells undergo apoptosis daily and are efficiently cleared by phagocytes through a process termed "efferocytosis". Efferocytosis plays a crucial role in inflammation resolution and tissue repair that is mediated by receptors and signaling molecules. Defective efferocytosis is associated with the pathogenesis of various diseases such as type 2 diabetes mellitus (T2DM). In this review, we decided to describe the mechanism of efferocytosis and evaluate its association with the progression of T2DM and its complications.

Methods: We searched the keywords "efferocytosis", "diabetes", "obesity" and "apoptotic cell clearance" from databases including PubMed and Google Scholar from 2000 to 2024. A total of 25 articles were included.

Results: The findings of articles showed that impairment efferocytosis may contribute to the progression of T2DM and its resulting complications via limited mechanisms. First, diabetes-induced decrease in miR-126 expression leads to proteolytic cleavage of efferocytic receptor MerTK, indirectly. Second, in obesity-induced diabetes, reduction in erythropoietin level or erythropoietin receptor deficiency leads to impaired efferocytosis through the downregulation of efferocytic molecules. Third, a low level of adiponectin in obesity-induced diabetes results in impairment of apoptotic cell clearance. However, more research is needed to identify the mechanisms of impairment efferocytosis in the pathogenesis of T2DM.

Conclusion: This review indicates that impaired efferocytosis plays a significant role in the progression of T2DM and its complications, contributing to inflammation induction. One of the major manifestations of defective efferocytosis in T2DM is in the form of delayed wound healing. However, the research on efferocytosis in T2DM and its associated complications is still emerging. Indeed, the exploration of efferocytosis in diabetic wound healing is fairly widespread, but research on other diabetic complications, such as diabetic angiopathy, diabetic nephropathy, and diabetic retinopathy, remains rare. However, it is undeniable that efferocytosis has become a promising research direction for T2DM and its complications.

Keywords: efferocytosis, diabetes, obesity, apoptotic cell clearance

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In-Silico Evaluation of Monoterpenoids' Antioxidant and Anticancer Potential: Insights into iNOS Inhibition and DNA Interaction

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Background: Monoterpenoids, including thymol, carvacrol, p-cymene, and γ-terpinene, are natural components found in various plants, known for their potential to inhibit key enzymes such as inducible nitric oxide synthase (iNOS) and NADPH oxidase (NOX), which are involved in oxidative stress and inflammation. Additionally, their interaction with DNA may contribute to their anticancer activity. This study aimed to explore the in-silico interactions of these monoterpenoids with iNOS, NOX, and DNA.

Methods: In-silico analyses were conducted using molecular docking to evaluate the binding affinities of thymol, carvacrol, p-cymene, and γ-terpinene with iNOS, NOX, and DNA.

Results: Molecular docking showed that thymol and carvacrol formed strong interactions within the iNOS active site, with binding energies of −20 and −18 kcal/mol, respectively, indicating significant inhibitory potential. These compounds effectively blocked the l-Arg binding site by forming hydrogen bonds with GLU-371 and interacting with the heme group. In contrast, p-cymene and γ-terpinene exhibited weaker binding energies (−6.3 kcal/mol) and limited interactions with iNOS. For NOX, thymol and carvacrol demonstrated lower affinities (−4.4 and −4.3 kcal/mol) compared to the known inhibitor apocynin (−6.5 kcal/mol). Additionally, both compounds displayed favorable binding to the minor groove of DNA, with carvacrol and thymol showing binding energies of −5.6 and −5.0 kcal/mol, respectively.

Conclusion: The in-silico findings indicate that thymol and carvacrol may be key components with significant antioxidant and anticancer potential. Their strong inhibitory effects on iNOS and ability to interact with DNA suggest a promising therapeutic application, particularly as potential anticancer agents. These results provide a foundation for further studies exploring the development of novel compounds targeting these pathways.

Keywords: Antioxidant activity, anticancer potential, Monoterpenoids, Thymol, Carvacrol, Molecular docking, iNOS, NOX, DNA

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Abstract: A-10-3103-1

Nanocurcumin Provides Protective Effects Against Testicular Torsion Injury in Rats

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Background: Testicular torsion-detorsion is caused by the rotation of the spermatic cord, which first interrupts testicular venous flow and, subsequently, arterial flow, ultimately culminating in testicular ischemia. Reactive oxygen species can lead to apoptosis and cellular dysfunction. This study investigated the protective effect of nanocurcumin on testicular torsion-detorsion injury by focusing on Bax and Bcl2 mRNA expression levels.

Methods: Thirty-six healthy male Sprague-Dawley rats were divided into six groups: group 1: healthy group, group 2: torsion-detorsion (T/D) group, groups 3 and 5: T/D+ nCur (50 and 100 mg/kg thirty minutes before reperfusion, respectively), and groups 4 and 6: T/D + nCur (respectively, 50 and 100 mg/kg thirty minutes before reperfusion and continued for seven days). To induce testicular torsion, the left testis was rotated 720 degrees in a counterclockwise direction. After two hours of ischemia, detorsion was performed. At the end of the treatment, an orchiectomy was carried out. Testicular levels of the Bax and Bcl2 transcripts were assessed using quantitative (q) RT-PCR.

Results: Testicular torsion-detorsion led to a significant increase in Bax expression compared to the control group, while Bcl-2 expression decreased ($p < 0.05$). Treatment with nanocurcumin caused a decrease in Bax level as well as an increase in Bcl2 level compared to the T/D group ($p < 0.05$).

Conclusion: These findings suggest that the administration of nanocurcumin prevents cellular damage in the testicular tissue by regulating the expression of Bax and Bcl-2 transcripts.

Keywords: Spermatic cord torsion, reperfusion injury, nanocurcumin, Bax, Bcl-2

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Abstract: A-10-3124-1

Insulin Resistance Improvement by Vitex agnus-castus Fruit Extract in Polycystic Ovary Syndrome

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Background: Polycystic ovary syndrome is a prevalent endocrine disorder that ranks among the primary causes of female infertility. Oxidative stress is recognized as a potential contributing factor in developing polycystic ovary syndrome. The relationship between oxidative stress and the defining features of polycystic ovary syndrome, such as insulin resistance, hyperandrogenemia, and chronic inflammation, is particularly significant. Aims: This study aimed to investigate the effect of Vitex agnus-castus plant fruit extract on fasting blood sugar and insulin resistance in women with polycystic ovary syndrome.

Methods: The Iranian Registry of Clinical Trials (IRCT20230222057493N1) and the Arak University of Medical Sciences Ethics Committee (IR.ARAKMU.REC.1401.333) approved this randomized, double-blind controlled clinical trial study. Sixty women were diagnosed with polycystic ovary syndrome according to Rotterdam criteria. They were randomly assigned to one of two groups: the Vitex agnus-castus or the placebo group. Fasting blood samples were collected before the intervention. Following this initial assessment, participants received either Vitex agnus-castus or placebo tablets for 12 weeks. Upon completion of the study, blood samples were obtained, fasting blood sugar was evaluated, and insulin resistance was calculated both before and after the intervention.

Results: Daily consumption of 1 tablet containing 5.8 mg of dry extract of Vitex agnus-castus fruit for 12 weeks significantly decreased serum fasting blood sugar level and value of insulin resistance compared to the placebo group.

Conclusion: The results of this study are promising, showing that the Vitex agnus-castus effectively controls blood sugar and reduces insulin resistance. This finding opens up new possibilities for the treatment of polycystic ovary syndrome, offering hope for improved outcomes in the future.

Keywords: Insulin resistance, Vitex agnus-castus, polycystic ovary syndrome, PCOS, IR

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Abstract: A-10-3124-2

The Effect of Vitex Plant on Serum Level of Anti-Mullerian Hormone in Individuals with Polycystic Ovary Syndrome: A Randomized, Double-Blind Controlled Clinical Trial Study

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Background: The anti-mullerian hormone is a product of the granulosa cells of small antral follicles. Increasing serum levels of anti-mullerian hormone in polycystic ovary syndrome are due to growing follicle numbers and excessive anti-mullerian hormone production by each follicle. The fruit extract of the Vitex plant contains several phytoestrogenic compounds. It is used for the treatment of premenstrual syndrome, fertility disorders, and symptoms of menopause. Aims: This study aimed to investigate the effect of Vitex plant fruit extract on the serum level of anti-mullerian hormone in women with polycystic ovary syndrome.

Methods: This randomized, double-blind controlled clinical trial study was approved by the Arak University of Medical Sciences Ethics Committee (IR.ARAKMU.REC.1403.061) and the Iranian Registry of Clinical Trials (IRCT20230222057493N1). Forty women suffering from polycystic ovary syndrome were selected by a specialist according to the Rotterdam criteria. Participants were randomly assigned to either the Vitex group or the placebo group. Fasting blood samples were collected before the intervention. Over 12 weeks, participants received either Vitex or a placebo treatment. After the study concluded, blood samples were collected again, and the level of anti-mullerian hormone was evaluated using an enzyme-linked immunosorbent assay, both before and after the intervention.

Results: Daily consumption of 1 tablet containing 5.8 mg of Vitex plant fruit for 12 weeks significantly decreased serum anti-mullerian hormone level compared to the placebo group.

Conclusion: It seems that the Vitex plant's ability to reduce the serum level of anti-mullerian hormone produced by the granulosa cells is effective in improving polycystic ovary syndrome. Vitex plant improved anti-mullerian hormone in these women, which deserves further exploration in the future.

Keywords: Anti-mullerian hormone, AMH, Vitex, polycystic ovary syndrome, PCOS

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Abstract: A-10-3129-1

Identification of Novel Inhibitors for Nicotinamide Phosphoribosyltransferase through Pharmacophore-Based Screening and Molecular Docking

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Background: Nicotinamide phosphoribosyltransferase (NAMPT) plays a pivotal role as a rate-limiting enzyme in the salvage pathway of nicotinamide adenine dinucleotide (NAD+) synthesis. It catalyzes the incorporation of nicotinamide (NAM) with 5-phosphoribosyl-1-pyrophosphate (PRPP) to produce nicotinamide mononucleotide (NMN), providing a constant source of NAD+ for continuous growth, making it a highly promising target for the development of new cancer therapeutics. This study aimed to generate pharmacophore models as inhibitors of NAMPT enzymatic activity.
Methods: A pharmacophore-based virtual screening technique, followed by molecular docking, was employed to discover potential targets. The potency of the extracted compounds for NAMPT was further validated by molecular dynamics (MD) simulation. This approach of combining multiple pharmacophores into a single lead sets a promising foundation for the design and synthesis of new small molecules with powerful targeting ability and high cytotoxicity.
Results: This study identified two lead compounds, 1 and 2, which exhibited better binding free energy compared to known inhibitors such as FK866 and CHS828. They also demonstrated stable bonding and contact with residues in the active site of NAMPT. Compounds containing these pharmacophores have not previously been reported for NAMPT inhibition, making them novel candidates for future drug development.
Conclusion: We hope that this study provides valuable guidance for the future design, synthesis, and optimization of NAMPT inhibitors.

Keywords: pharmacophore modeling, NAMPT, drug design, Molecular docking, Virtual screening

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Abstract: A-10-2409-3

Polyphenols as Regulators of ER Stress in Metabolic Disorders: A Systematic Review of Mechanisms and Therapeutic Potential

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Background: Endoplasmic reticulum (ER) stress plays a crucial role in the pathogenesis of various metabolic disorders, including obesity, type 2 diabetes, and Metabolic Dysfunction-Associated Fatty Liver Disease (MAFLD). The accumulation of misfolded proteins in the ER triggers the unfolded protein response (UPR), a cellular mechanism aimed at restoring protein homeostasis. This systematic review focuses on the potential of naturally occurring polyphenols in regulating ER stress across key metabolic tissues.

Methods: We conducted a comprehensive literature search to evaluate the effects of selected polyphenols (resveratrol, quercetin, and curcumin) on ER stress in five major metabolic tissues: liver, pancreas, kidney, adipose tissue, and skeletal muscle. We searched PubMed, Scopus, and Embase for peer-reviewed articles (2010–2023) using the terms "polyphenol," "Resveratrol," "Quercetin," "Curcumin," "ER Stress," "UPR," and tissue-specific keywords. Boolean operators refined results.

Results: Out of 161 articles identified, 49 met the inclusion criteria for this review. Our analysis revealed that resveratrol, quercetin, and curcumin exhibited significant capacity to attenuate ER stress in multiple metabolic tissues. These polyphenols appeared to act through various mechanisms, including direct modulation of UPR signaling pathways, enhancement of antioxidant defenses, and improvement of cellular proteostasis. The effectiveness of these polyphenols varied depending on the specific tissue and dosage, underscoring the complex nature of their action in regulating ER stress in metabolic disorders.

Conclusion: This systematic review underscores the potential of polyphenols as natural therapeutic agents for managing ER stress in metabolic disorders. The multifaceted actions of resveratrol, quercetin, and curcumin across different metabolic tissues suggest their promise in developing novel, targeted interventions. Further research is warranted to elucidate optimal dosing strategies and potential synergistic effects among these compounds for maximizing their therapeutic efficacy in metabolic disease management.

Keywords: Endoplasmic reticulum stress, Polyphenols, Metabolic tissue

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Abstract: A-10-3124-3

The Effect of Chasteberry on Inflammatory Markers in Women with Polycystic Ovary Syndrome: A Randomized, Double-Blind Controlled Clinical Trial Study

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Background: Antioxidants are agents that obstruct the oxidation of molecules in the body. These substances prevent cell destruction and inflammation by neutralizing free radicals. As a result, they play an essential role in reducing inflammation. Polycystic ovary syndrome is characterized by a mild chronic inflammatory state, which is considered a contributing factor to the pathogenesis of this syndrome. Chasteberry has potent antioxidant activity. Aims: The purpose of this study is to evaluate Chasteberry's effect on values of inflammatory markers in women with polycystic ovary syndrome.

Methods: This was a randomized, double-blind controlled clinical trial study. Sixty women with polycystic ovary syndrome who were referred to the gynecology clinic of the Arak University of Medical Sciences and whose diseases were confirmed by the Rotterdam criteria were selected by convenience sampling method and randomly allocated to Chasteberry or placebo groups by permuted block randomization method. Fasting blood samples were obtained before the intervention. Patients received either Chasteberry or placebo tablets for 84 days. Upon completion of the study, blood samples were obtained again, serum levels of C-reactive protein and albumin were evaluated, and the ratio of C-reactive protein to albumin was calculated before and after the intervention.

Results: Consuming one tablet containing 5.8 mg of Chasteberry daily for 84 days was associated with a significant decrease in C-reactive protein and the ratio of C-reactive protein to albumin levels as a simple and new inflammatory index, relative to the placebo group.

Conclusion: The results obtained from the present study revealed that treatment with Chasteberry, through its antioxidant properties, provided a beneficial role against inflammation in polycystic ovary syndrome.

Keywords: C-reactive protein, CRP, CRP/albumin ratio, CAR, polycystic ovary syndrome, PCOS, Chasteberry

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Abstract: A-10-3128-1

Investigating Molecular Mechanisms in the Relationship between Endometriosis and Endometrial Cancer; a Bioinformatic Analysis

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Background: Endometriosis and endometrial cancer (EC) are estrogen-dependent female diseases. Although endometriosis is considered a benign female disorder, the pattern of development of this disease is similar to malignant diseases such as EC. Therefore, investigating the relationship between endometriosis and EC has become one of the concerns of researchers in this field.

Methods: In this study, STRING, GEO Profile, GeneCards, and Enrichr databases were used to investigate the genetic changes due to endometriosis and EC. The protein-protein interaction network was obtained by the STRING database. The analysis of this network for endometriosis and EC introduced Tumor Protein P53 (TP53), AKT Serine/Threonine Kinase 1 (AKT1), and Phosphatase and Tensin Homolog (PTEN) as hub genes with high degree. The GEO Profile database showed a decrease in the expression levels of TP53 and PTEN and an increase in the expression level of AKT1 in endometriosis. Articles also confirmed these results for endometriosis and EC. Examining GeneCards and Enrichr databases also confirmed the relationship between the expression of these genes with endometriosis and EC.

Results: TP53 plays a role in cell cycle regulation, apoptosis, cell migration, and proliferation, which is dysregulated in the expression of TP53 in endometriosis and EC. AKT1 is involved in apoptosis, proliferation, migration, and invasion in endometrial stromal cells, which play an important role in the pathogenesis of EC. PTEN is one of the most important tumor suppressors, whose loss of function is considered an early event in endometrial tumorigenesis.

Conclusion: Therefore, according to the role of these genes in the development of endometriosis and EC, it seems that similar molecular mechanisms are involved in the development of these two diseases. As a result, individuals diagnosed with endometriosis may have an increased risk of developing EC, which underscores the importance of regular screening for this population.

Keywords: Endometriosis, Endometrial Cancer, TP53, AKT1, PTEN

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Abstract: A-10-3131-1

The Relationship between Endometriosis and Adenomyosis through the Reduction of TP53 Gene Expression

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Background: Endometriosis and adenomyosis are benign and common conditions in women of reproductive age. These two diseases are often accompanied by each other and their molecular mechanisms remain unclear. Despite the differences between endometriosis and adenomyosis, it is assumed that a common molecular mechanism is involved in the pathogenesis of these diseases. Therefore, identifying the molecular underpinnings of endometriosis and adenomyosis can help to find the relationship between these diseases.
Methods: In this study, data were obtained from GSE7305 and GSE78851 in the GEO dataset, respectively, by comparing women with endometriosis and control groups and women with adenomyosis and control groups. Then, a protein-protein interaction network was drawn for genes with log2FC<-1 and adj.P.Val<0.05. Based on the network obtained from the STRING database, the Tumor Suppressor Gene (TP53) was identified as the high-degree hub gene in both diseases.
Results: According to the GeneCards database, this gene is associated with endometriosis and adenomyosis. TP53 plays a role in cell cycle regulation, DNA repair, angiogenesis, and apoptosis. Studies have shown the effect of TP53 gene polymorphism and its dysregulation in various diseases, especially endometriosis and tumors. It has also been reported that TP53 is decreased in the ectopic endometrium of endometriosis patients compared to eutopic and normal groups.
Conclusion: TP53 is involved in metastasis and regulation of angiogenesis. In conclusion, its decreased expression may be associated with increased migration and angiogenesis for the invasion of endometrial implants during the pathogenesis of adenomyosis and endometriosis. Therefore, it can be assumed that the significant decrease in TP53 expression may be a common molecular feature between endometriosis and adenomyosis. Further studies in this field may help to identify the more precise relationship between these two diseases for diagnosis and treatment.

Keywords: Endometriosis, Adenomyosis, TP53, Angiogenesis, Diagnosis

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Abstract: A-10-2550-3

Liposomes in Chemoimmunotherapy: A New Era of Treatment for Breast Cancer

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Background: In the evolving landscape of cancer therapeutics, the convergence of chemoimmunotherapy stands out as a promising and dynamic approach in the context of breast cancer. This review is dedicated to unraveling the intricate role played by liposomes in amplifying the effectiveness of chemoimmunotherapy. Capitalizing on their distinct attributes, liposomes have become integral carriers for a spectrum of therapeutic agents, encompassing both chemotherapy and immunotherapy. The narrative unfolds through an exploration of diverse studies that leverage liposomal delivery systems for chemoimmunotherapy in breast cancer.

Methods: This review article was performed within articles published at PubMed, Science Direct, Google Scholar, Web of Science until May 2024. The keywords were Chemoimmunotherapy; Breast Cancer Treatment; Liposomal Drug Delivery; Immunogenic Cell Death; Tumor Microenvironment; Immune Checkpoint Blockade; Nanotechnology in Cancer Therapy. By searching this database, 168 articles were found, and 58 were removed by reading titles and abstracts. 110 articles were selected under the inclusion criteria. All articles were chosen from English articles.

Results: These investigations traverse the terrain of dual-targeting liposomes, liposomes enriched with Poly(amidoamine) (PAMAM) dendrimers, and liposomes subject to modification with apolipoprotein A1. Venturing deeper, we immerse ourselves in the concept of immunogenic cell death (ICD) induced by doxorubicin and its far-reaching implications in the realm of chemoimmunotherapy. Moreover, a critical examination unfolds concerning the potential of liposomes to exert influence over the immunosuppressive tumor microenvironment and their pivotal role in orchestrating the sequential release of anticarcinogens.

Conclusion: As the review draws to a close, we engage in a nuanced and comprehensive discussion regarding the prospective trajectory of liposomal chemoimmunotherapy within the overarching treatment paradigm of breast cancer. Our meticulous analysis of the existing literature resonates with a compelling assertion – liposomal chemoimmunotherapy not only holds significant promise but also stands poised to elevate the holistic outcomes of breast cancer treatment.

Keywords: Chemoimmunotherapy, Breast Cancer Treatment, Liposomal Drug Delivery, Immunogenic Cell Death, Tumor Microenvironment, Immune Checkpoint Blockade, Nanotechnology in Cancer Therapy

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Abstract: A-10-2604-1

Ferroptosis in Cancer: Unraveling the Mechanisms and Therapeutic Potential

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Background: Ferroptosis, a distinct form of regulated cell death characterized by iron-dependent lipid peroxidation, has emerged as a critical player in cancer biology. Unlike apoptosis, which is an energy-dependent process involving cell shrinkage, ferroptosis is triggered by oxidative stress. This study aims to elucidate the mechanisms underlying ferroptosis and its role in cancer development and progression.
Methods: The PubMed and Google Scholar databases were searched using keywords such as “ferroptosis,” “cancer,” “lipid peroxidation,” and “oxidative stress” to identify relevant studies published from 2015 to 2024. The search focused on articles investigating the relationship between ferroptosis and cancer, including its mechanisms, regulatory pathways, and therapeutic implications. Duplicate and incomplete studies, conference abstracts, and studies lacking ethical approval were excluded.
Results: After reviewing the selected studies, a total of 214 were investigated. Ferroptosis is characterized by a redox imbalance driven by polyunsaturated fatty acid phospholipid (PUFA-PL) synthesis, lipid peroxidation, and iron toxicity. Key defense mechanisms against ferroptosis include the GPX4 antioxidant system, FSP1/ubiquinol, DHODH, GCH1, MUFA-PL synthesis, and ESCRT-III-mediated membrane repair systems. When the activities promoting ferroptosis exceed the detoxification capabilities of these defenses, it leads to an accumulation of lipid peroxides, resulting in membrane rupture and cell death. Tumor suppressors, such as p53, BAP1, fumarate hydratase, KEAP1, and MLL4, play significant roles in tumor suppression.
Conclusion: Ferroptosis is a multifaceted process with a significant impact on cancer biology. Understanding the mechanisms underlying ferroptosis and its role in cancer development is crucial for developing novel therapeutic strategies. By targeting ferroptosis pathways, it may be possible to selectively induce cell death in cancer cells while sparing normal tissues. Further research is needed to elucidate the complex interplay between ferroptosis and cancer to optimize therapeutic interventions.

Keywords: Ferroptosis, cancer, lipid peroxidation, oxidative stress, tumor suppressor, apoptosis

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Abstract: A-10-2797-1

Isolation and characterization of industrial protease producing bacteria and production optimization

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Background: The use of enzymes in the industry is increasing day by day due to many reasons, including being eco-friendly and not producing harmful, chemical and dangerous waste. Among the industrial enzymes, proteases and especially alkaline proteases are of special importance; So that they have 60% of the enzyme market.
Methods: In this research, 3 samples were isolated from the industrial wastewater of dairy factories and studied to optimize and check the amount of protease production. In order to optimize the growth rate and protease production, the bacteria were subjected to directed mutation, so they were treated with selected substrates and special temperature and pH conditions for more than 3 years in controlled limited culture medium, so that both in terms of substrate consumption, the amount of protease production and also the optimal pH of the enzyme; appropriate amounts for use in the industry are obtained.
Results: During optimization, bacterial growth increased by more than ten times and the enzyme production in different isolated species increased by more than 7 times. Finally, Bacillus subtilis bacterium with protease activity unit equal to 990 U/mL and with optimal pH of 10.5 and temperature tolerance up to 50 degrees was selected as the superior strain. After molecular identification and, this bacterium was registered in the NCBI database under the name Bacillus Subtilis BSA1 and accession number SUB13750996.
Conclusion: Since this enzyme has alkaline activity and is resistant to temperature, it is suitable for use in many industries, including detergent, food, leather and mining industries, and its other potentials should be investigated. Also, the values announced in this article were obtained in a minimal culture medium, and optimization of the culture medium using RSM or Taguchi methods according to the studied articles can increase these values several times (in some cases more than 10 times).

Keywords: directed mutation ،enzyme ،substrate ،bacillus Subtilis BSA1

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Abstract: A-10-2952-2

Liquid Biopsy and its significance on the Early Detection of Breast Cancer

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Background: The screening and early detection of breast cancer helps decrease mortality and improves the quality of life. Liquid biopsy is a novel diagnostic tool that investigates biological biomarkers within blood and other body liquids in order to provide information about the genetic of tumor and treatment response. Liquid biopsy obtained from blood, urine, stool, saliva samples involve components like circulating tumor cells (CTCs), circulating tumor DNA (ctDNA), or circulating tumor RNA (ctRNA), platelets and exosomes. Therefore, the current review study aims to highlight the role of liquid biopsy in breast cancer and precision medicine.

Methods: In the current systematic review study, we attempted to evaluate the recent advancements and innovations in the field of breast cancer diagnosis and personalized medicine through searching using keywords including liquid biopsy, early detection biomarkers, breast cancer, and precision medicine in related databases including Scopus, Web of Science, PubMed and Google Scholar during years 2018 to 2024.

Results: Total number of 10555 published articles were found, of which 58 articles met the criteria and included in the study. Upon investigating the published articles in this filed, it was revealed that the applications of biomarkers in liquid biopsy have significant role in personalized medicine and the early detection of breast cancer as well as other cancers today, many of which have received creditable international approval such as FDA (Food and Drug Association) that highlight they reliability to be used for the personalized medicine.

Conclusion: Liquid biopsy has a great potential to provide diagnosis of the disease in early stages, monitoring the disease progression and recurrence, and predicting treatment response. Biomarkers in liquid biopsy seem to be promising approach in breast cancer early detection and remarkably reduce mortality caused by this disease in the near future.

Keywords: Breast cancer ،Liquid biopsy ،Early detection ،Precision medicine ،Screening

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Abstract: A-10-2828-1

Improving potential of iron oxide-labeled mesenchymal stem cells preconditioned with cardiac myocyte exosomes after myocardial injury

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Background: Cardiovascular diseases (CVDs), despite great advances in medicine, are still the main cause of death in the world, with huge annual costs for governments. Bone marrow progenitor cells (BMPCs) are a group of multipotent stem cells that have properties that make them a suitable source for cell therapy in various diseases. According to the characteristics of mesenchymal stem cells, these cells can differentiate into cardiomyocytes under certain conditions such as co-culture with heart exosomes, preparing the cells for transplantation and restoring heart dysfunction. Tracking these cells by iron oxide nanoparticles is a good alternative due to low cytotoxicity, long-term tracking and safety.

Methods: Mesenchymal stem cells were extracted from rat bone marrow and cultured until the second passage. Human heart cells were cultured in a special culture medium (HCM). The media of cultured heart cells was collected and the exosomes were extracted. Thereafter, the rat mesenchymal stem cells were exposed to these exosomes and later both groups of exposed and non-exposed mesenchymal stem cells, which were labeled with iron oxide nanoparticles were injected to heart failure rat models. Three days after the injection of cells, heart tissue and blood samples of rats were collected and evaluated through histopathology and by real time PCR, respectively.

Results: Mesenchymal stem cells exposed to cardiomyocyte exosomes were labelled with iron oxide nanoparticles as shown by the Prussian blue staining. These cells were able to sharply improve the gene expression of cardiac specific markers troponin and creatine kinase as compared to the control group.

Conclusion: Iron oxide nanoparticles, which are widely used in targeted drug delivery and disease treatment have shown to be a promising tool in increasing the differentiation of mesenchymal stem cells exposed to cardiomyocyte exosomes into cardiac cells.

Keywords: Heart failure, cardiomyocyte exosomes, mesenchymal stem cells, iron oxide nanoparticles

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Abstract: A-10-2822-1

Comparison of differentiation ability of mesenchymal stem cells derived from bone marrow and adipose tissue to cardiac lineage after induction of heart damage in rats

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Background: The global prevalence of Heart failure is estimated to range between 1% and 3% of the total population in 2019. Cardiac tissue approaches depend basically on the application of donor cardiomyocytes and could be an innovation that points to form, repair or supplant cardiac tissues and organs by utilizing combinations of cells, biomaterials and biomolecules. Stem cells have two characteristics, the ability to differentiate along different cell lineages and the ability to self-renew. Mesenchymal stem cells (MSCs) derived from bone marrow and adipose tissue are easily isolated, cultured, immunologically tolerated by the host's immune system, and allow allogeneic transplantation.

Methods: Heart damage in rats was induced by isoprenaline, which was injected intraperitoneally. In the control group, normal saline injection was done in the same way and in the same volume. Occurrence of heart damage was confirmed by the histopathology. Mesenchymal stem cells were isolated from bone marrow and adipose tissue after 5 days and were cultured until the second passage. Cardiac differentiation was induced by 5-azacytidine. After 3 days the cells were collected and cardiac specific markers were measured using real time PCR.

Results: The population doubling time, cell growth curve, cell morphology and the gene expression of cardiac specific markers troponin and creatine kinase did not show any obvious and statistical difference in cardiomyocyte differentiation ability of mesenchymal stem cells derived from bone marrow and adipose tissue.

Conclusion: Both bone marrow and adipose derived mesenchymal stem cells have the same potential in cardiomyocyte differentiation upon heart damage induction, showing a promising impression for providing more extensive sources for heart tissue engineering.

Keywords: Heart failure, Tissue engineering, mesenchymal stem cells, bone marrow and adipose tissue

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Abstract: A-10-2838-1

The effect of exosomes derived from cardiomyocytes on cardiac differentiation of mesenchymal stem cells in culture conditions with and without transfection agent

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Background: The main cause of death in the world is myocardial infarction, which is related to today's lifestyle, urbanization and socio-economic status. Every year, about 1,500,000 people in the world die due to heart attack. Transplanting stem cells to the heart improves heart function by 7-9% by increasing the power of angiogenesis, which in turn leads to the return of the physiological function of ischemic organs. Exosomes are novel intercellular signaling mediators in both homeostasis and pathophysiological conditions, which play a role in cardiac regeneration against stressful factors; they also have protective and regenerative effects in the heart.

Methods: Human heart cells were cultured and exosomes were extracted from their cultured media. Mesenchymal stem cells were exposed to exosomes derived from heart cells in 4 groups as follows: 1-in the presence of transfection agent 5-azacytidine in culture media, 2-without the presence of transfection agent, 3- in the presence of iron nanoparticles, and 4-a control group that only includes the MSCs. Thereafter, on the third and seventh days after exposure, the cells were photographed and the growth curve and the time required for cell doubling were drawn and calculated for all four groups. Cardiac markers were measured using real time PCR.

Results: The population doubling time and the cell growth curve of the mesenchymal stem cells did not show any difference in the proliferation pattern between heart-cell-exosome-treated mesenchymal stem cells either in presence or absence of the transfection agent. However, iron nanoparticle exposure was able to specifically decline the population doubling time and improve the growth curve of cells and also promote the expression of cardiac specific markers troponin and certain kinase.

Conclusion: MSCs labelled with iron nanoparticles showed promising results in both proliferation and differentiating towards cardiomyocyte cells, as compared to the stimulating effect of a transfection agent.

Keywords: Heart failure, cardiomyocyte exosomes, mesenchymal stem cells, 5-azacytidine

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Abstract: A-10-3099-1

Effect of oleuropein on apoptosis, miR-149-3p expression and PI3K/AKT signaling pathway in acute myeloid leukemia cells treated with azacitidine.

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Background: Acute myeloid leukemia (AML) is the most common type of acute leukemia in adults and is typically managed with high doses of chemotherapy medications. The abnormal expression of miRNAs is related to the pathogenesis and progression of AML. Oleuropein, a natural polyphenol known for its anticancer effects, can be utilized either on its own or in combination with other chemical agents. Azacytidine is a hypomethylating drug used in AML.

Methods: This study was carried out to evaluate the therapeutic effect of oleuropein by enhancing the expression of miR-149-3p, which serves as a tumor suppressor and one of the factors that reduce the response to Azacitidine and its effect on the PI3K/AKT as an important pathway in multiple biological processes. Human leukemia (HL-60) cells were categorized into the following groups: control (untreated HL-60 cells), HL-60 cells treated with oleuropein, HL-60 cells treated with azacitidine, and HL-60 cells receiving a combination of both treatments. A bioinformatics analysis was performed to examine the connection between miR-149-3p and the proteins PI3K and AKT. The MTT assay was used to assess cell proliferation and calculate the IC50 value, while flowcytometry was utilized to study apoptosis. RT-PCR for detection of miR-149-3p, PI3K, and AKT expression, and Western blot was used to detect PI3K and AKT protein expression.

Results: Treatment with oleuropein and azacitidine, whether individually or in combination, led to an increase in miR-149-3p expression while reducing the levels of PI3K and AKT in comparison to the untreated cells. In addition, apoptosis increased with up-regulation of Bcl-2 expression and down-regulation of Bax expression. Besides enhancing apoptosis, oleuropein inhibits the PI3K/AKT pathway in azacitidine-treated cells by up-regulation of miR-149-3p.

Conclusion: In summary, our study revealed that oleuropein can enhance the response to azacitidine and improve the drug's effectiveness by raising miR-149-3p levels and inhibiting the PI3K/AKT pathway.

Keywords: leukemia, oleuropein, Azacytidine, miR-149-3p, PI3K/AKT pathway

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Abstract: A-10-2863-2

The relationship between chronotype and lifestyle with some biochemical factors based on Sabzevar Cohort Center data

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Background: Personality traits have been categorized into various types by psychologists, with individuals being placed into different groups based on these traits. One such classification is the morning and evening chronotype model. Chronotypes refer to individual differences in activity and sleep-wake patterns. This study aimed to investigate the relationship between chronotypes and certain biochemical factors, with a particular focus on morning and evening personality types.

Methods: A cross-sectional survey was conducted, targeting participants from the Sabzevar Cohort Center. After obtaining informed consent, data were collected using the Morningness-Eveningness Questionnaire (MEQ), which assessed participants' daily habits, sleep-wake cycles, and other life patterns to classify their circadian rhythm. Venous blood samples were collected following the cohort center's protocol. Serum was isolated from the blood samples for biochemical analysis, which measured variables such as blood urea nitrogen (BUN), creatinine (CERAT), serum glutamic-oxaloacetic transaminase (SGOT), and alkaline phosphatase (ALP). Data were entered into SPSS software and analyzed using descriptive and inferential statistics. The Chi-square test was used to compare qualitative variables, and ANOVA was employed for group comparisons. Additional analyses, such as regression and correlation coefficients, were performed as necessary. A significance level of 5% was set.

Results: The analysis revealed a significant association between morning chronotype scores and several biochemical markers, including BUN, CERAT, SGOT, and ALP. The triglyceride (TG) variable showed a positive correlation, while other factors demonstrated negative correlations. Additionally, age-related demographic characteristics significantly influenced chronotype distribution.

Conclusion: The findings suggest that individuals with a morning chronotype tend to exhibit healthier biochemical profiles and a lower incidence of disease. These results highlight the potential health benefits associated with morningness and suggest further investigation into chronotypes' role in disease prevention and health promotion.

Keywords: Chronotypes, Personality Types, Biochemical Factors

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Abstract: A-10-3156-1

Clinical Relevance of Circulating Biomarkers in Breast Cancer Metastasis Detection: "Insights from Liquid Biopsy Technology"

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Background: Breast cancer (BC) is a significant global issue, particularly because of the high mortality rates associated with advanced stages of the disease. Metastasis can occur at an early stage; however, current diagnostic methods often fail to identify small metastatic cells. Non-invasive liquid biopsies, including circulating miRNA, ctDNA, and cfDNA, offer a promising approach for the screening and monitoring of breast cancer. This study aimed to evaluate the clinical significance of serum level of cfDNA in patients with metastatic and non-metastatic breast cancer. Additionally, we sought to investigate the relationship between this biomarker and clinical stage as well as distant metastasis.
Methods: The study included 17 patients with metastatic breast cancer and 29 patients with non-metastatic breast cancer, from whom 10 ml blood samples were collected prior to surgery. The level of cfDNA was quantified using fluorometric methods.
Results: The results indicated significantly elevated level of cfDNA in women with metastatic breast cancer when compared to those with non-metastatic breast cancer ($p < 0.05$). This biomarker was correlated with advanced clinical stages and larger tumor sizes. Increased level of cfDNA was associated with a higher risk of lymphatic metastasis, as well as cfDNA linked to distant metastasis ($p < 0.05$).
Conclusion: The analysis of this biomarker will improve the accuracy of predicting metastatic breast cancer and will provide clearer insights into the relationship between biomarker level and the characteristics of metastatic versus non-metastatic patients, utilizing liquid biopsy technology.

Key words: metastatic breast cancer, liquid biopsy, biomarkers, cfDNA

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Abstract: A-10-3146-1

Investigating the effect of the serum of people with polycystic ovary syndrome on the induction of oxidative stress factors in cancer cells

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Background: Polycystic ovary syndrome or PCOS is one of the most common endocrinopathy gland disorders in women. Patients are exposed to serious complications such as increased risk of endometrial and breast cancer, dyslipidemia, hypertension, cardiovascular diseases and diabetes. In PCOS, the amount of apoptosis-inducing factors and oxidative stress in the serum of people increases and caspase-3 deficiency or defects can lead to PCOS. The aim of the present study is to investigate the effect of serum from people with polycystic ovary syndrome on the induction of oxidative stress factors in cancer cells.

Methods: AMH and Zinc were measured in two groups of minimum 30 samples in normal and PCOS sera by quantitative luminescence immunoassay. Thereafter, ELISA test was conducted for IL6 and Caspase 3 measurement in the selected sera. Finally, one serum of each group was chosen to be added to HapG2 cell culture microenvironment for 24h and 48h.

Results: After 24h and 48h of exposure to specific-serum-containing media, generally, the level of caspase 3 production and induction of oxidative stress by the HepG2 cells were also highly proportional to the produced IL6 serum level.

Conclusion: PCOS is slightly associated with increased IL6 serum levels. Considering the relationship between AMH and PCOS, and AMH and cancer, and also considering that oxidative stress induces more cell damage and apoptosis; the results of this research showed that the presence of more AMH hormone is related to induced amount of inflammatory cytokine IL6 in the tumor microenvironment around the cells which might generally lead to an increase in the production of caspase 3.

Keywords: polycystic ovary syndrome, caspase 3, Oxidative Stress, Cancer

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Abstract: A-10-3100-1

Pyroptosis in Fatty Liver Disease: A Systematic Review

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Background: Fatty liver disease (FLD), particularly non-alcoholic fatty liver disease (NAFLD), has emerged as a significant global health concern due to its high prevalence and risk of progression to severe liver conditions, including steatohepatitis and cirrhosis. Pyroptosis, a form of programmed cell death characterized by inflammatory responses, has been implicated in liver inflammation and injury. This systematic review aims to evaluate the role of pyroptosis in the pathogenesis of FLD.

Methods: A comprehensive systematic search was conducted in PubMed, Scopus, and Google Scholar using keywords such as "pyroptosis," "fatty liver disease," and "inflammation." Studies published from 2010 to 2023 that investigated the mechanisms and effects of pyroptosis in liver cells were included.

Results: A total of 20 studies were analyzed, showing that pyroptosis is activated in hepatocytes due to lipid accumulation and inflammatory signals. Studies have demonstrated that inhibiting the NLRP3 inflammasome significantly reduced hepatic inflammation in NAFLD models. Additionally, some research highlighted the connection between gut microbiota dysbiosis and pyroptosis in liver cells, suggesting a potential link between the gut-liver axis and liver inflammation.

Conclusion: This review indicates that pyroptosis plays a crucial role in the pathogenesis of fatty liver disease, contributing to hepatocyte injury and exacerbating inflammation. Targeting pyroptosis may represent a promising therapeutic approach for managing FLD and its complications. Future research should focus on elucidating the intricate mechanisms that connect pyroptosis with liver inflammation to develop effective interventions.

Keywords: pyroptosism,inflammation,fatty liver disease

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Abstract: A-10-3127-1

Nano Alum Adjuvant Enhances Anti-Tumor Efficacy of E7 Epitope of HPV16 in a Mouse Model of Cervical Cancer

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Background: Human papillomavirus (HPV)-induced cervical cancer is a major health concern in women and therapeutic vaccines can overcome the challenge. Although peptide-based vaccines are a promising strategy for developing therapeutic vaccines, insufficiency to generate robust immunity limits their application. In the current study, we coated the surface of negatively- charged aluminum phosphate (AlPO4), nano alum, with positively-charged HPV16 E7 epitope to develop an effective regimen with therapeutic effects on a TC-1 mouse model.

Methods: To prepare AlPO4 nanoparticles, AlPO4 powder was dissolved in Milli-Q water to form the white, opaque 2% AlPO4 - suspension at pH 7.4. The suspension was sonicated while cooling on ice for 15 min. To construct an Alum/pep regimen, 20 µg of AlPO4 and 20 µg of HPV16 E7 epitope were mixed for 15 minutes at room temperature. Its surface charge and particle size were characterized by zeta potential and dynamic light scattering. The developed construct was administrated into the TC-1 mouse model, and finally, the levels of IFN-γ, IL-10, and CTL responses as well as inhibition of tumor growth, were measured.

Results: Incubation of positively-charged HPV16 E7 epitope with alum changed the negative charge of the nanoadjuvant to a positive one, without significant changes in its size, indicating that the E7 epitope coated on the surface of nano alum. Compared with naked alum, homologous administration of E7-coated nano alum exhibited significant anti-tumor activities characterized by higher levels of IFN-γ, IL-10, and CTL responses, as well as inhibition of TC-1 tumor growth in vivo.

Conclusion: We introduced a versatile and rapid immunotherapy platform based on nano alum that elicits potent anti-tumor immune responses.

Keywords: Human papillomavirus, Cervical cancer, Nanoadjuvant, Aluminum phosphate

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Abstract: A-10-2241-1

Biosynthesis of Gold Nanoparticles and Assessment of Their Cytotoxic Effects on MDA-MB-231 Breast Cancer Cell Line

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Background: Cancer, especially breast cancer, is a major global health issue. Due to the severe side effects of chemotherapy, nanoparticle-based treatments are gaining attention for their targeted delivery and lower toxicity. Green synthesis of nanoparticles, using natural materials like plant extracts, is preferred for being eco-friendly and simple, offering an effective alternative to chemical methods.

Methods: In this study, gold nanoparticles were synthesized using Pimpinella affinis extract. The hydroalcoholic extract was prepared, and nanoparticles were formed at various concentrations. UV-Vis spectroscopy confirmed their formation, and TEM was used to analyze their size. Cytotoxicity on MDA-MB-231 breast cancer cells was evaluated using the MTT assay.

Results: Gold ions (Au^{3+}) were reduced to gold nanoparticles (Au^{0}) using Pimpinella affinis leaf and stem extract, accompanied by a visible color change from yellow to red/purple, indicating nanoparticle formation. Different extract concentrations (0.07, 0.14, and 0.28 mg/mL) were tested, and UV-Vis spectroscopy revealed a peak between 500-550 nm, with 0.28 mg/mL showing the sharpest peak, confirming this as the optimal concentration. TEM analysis at this concentration showed spherical nanoparticles of 12-14 nm. MTT assay results demonstrated that higher nanoparticle concentrations increased cytotoxicity, with 65% cell inhibition at 1000 µg/mL and an IC50 of 676 µg/mL.

Conclusion: Pimpinella affinis extract effectively facilitated the green synthesis of gold nanoparticles, confirmed by UV-Vis spectroscopy and TEM analysis. The optimal concentration for synthesis was 0.28 mg/mL, producing spherical nanoparticles with an average size of 12-14 nm. Cytotoxicity studies using the MTT assay demonstrated significant inhibition of MDA-MB-231 breast cancer cells, with an IC50 of 676 µg/mL, suggesting the potential of these nanoparticles as a promising anti-cancer agent.

Keywords: Breast cancer therapy, gold nanoparticle, green synthesis, Pimpinella affinis

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Abstract: A-10-3111-1

Whole-genome sequencing of Salmonella phage vB_SenS_TUMS_E15 for bio-control in the food chain

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Background: Understanding the genetic makeup of bacteriophages through genome analysis is vital for ensuring their effectiveness and safety when used in clinical settings for treating bacterial infections and in biocontrol settings for controlling pathogenic bacteria in various environments.
Methods: Samples of untreated municipal and hospital wastewater were gathered and examined. A host range determination was carried out using standard strains. The morphology of the phage w:as char:acterized through transmission electron microscopy. Subsequently, the phage's genomic DNA was extracted, sequenced, and analyzed.
Results: Morphologic, genomic and phylogenetic analysis indicated that E15 is a member of the Jersyvirus genus in the subfamily Guernseyvirinae. Complete genome analysis revealed that vB_SenS_TUMS_E15 had circularly permuted double-stranded DNA of 43,048 base pair (bp), with a G+C content of 49.7%. Sixty coding sequences (CDSs) were predicted in the genome, with 44 CDSs encoding known proteins in different modules, including the packaging, structure, replication and metabolism, and lysis modules, and there were no tRNA genes in the genome. No antibiotic-resistance genes, toxins, virulence factors, or lysogen-forming genes were observed in the genome.
Conclusion: The genome analysis of phage E15 provides valuable insights into its genetic composition and potential applications in both clinical and biocontrol settings. By understanding the molecular mechanisms underlying its lytic activity, researchers can further optimize phage therapy strategies and develop novel solutions for combating antibiotic-resistant bacterial infections.

Keywords: Bacteriophage, Salmonella, Jersyvirus, Guernseyvirinae, Biocontrol

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Abstract: A-10-3106-1

Computational de novo design of mini-protein binder against PD-1 receptor involved in cancer

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Background: Programmed cell death 1 (PD-1) is an immune checkpoint protein expressed on activated T cells that modulate immune responses in different conditions. Cancer cells often take advantage of the PD-1/PD-L1 pathway by overexpressing the PD-1 ligand PD-L1 to escape the immune system detection and destruction. In recent years, protein-based drugs have been utilized to downregulate the function of the PD-1 pathway, resulting in normalization of antitumor responses. This study aimed to de novo design mini-protein binders with high specificity and potency that did not previously exist in nature. Mini-protein binders are derived from various protein scaffolds that can be used to block or mask protein function.

Methods: In silico methods based on specialized software such as Rosetta and new Python code development were used to enhance the design process. Thousands of mini-protein binders (< 65 aa) with diverse topologies have been designed for the two binding sites on PD-1. Subsequently, designs using fast predictor xml and machine learning methods with exceptional stability and affinity were selected. Molecular dynamics (MD) simulations and MM-PBSA were used to measure the dynamics and binding affinities of the final designs.

Results: The obtained receiver operating characteristic (ROC) values of 0.83 and 0.79 for binding sites 1 and 2 indicated that the relative ranking of the designs is generally accurate. The results from MM-PBSA demonstrated that designed mini-protein binders selectively and potently bind to the PD-1 receptor, with a success rate of 65%.

Conclusion: Our findings indicate that mini-protein binders with a three-helix topology had a more favorable orientation and binding energy than the other scaffolds. Furthermore, the existence of hydrophobic cavities on the protein surface plays a crucial role in enhancing the attachment of mini-protein binders that possess an α-helical structure.

Keywords: De novo design, Mini-protein binder, Immune checkpoint

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3088-1

Advances in Tumor-Infiltrating Lymphocyte-Based Therapies for Cancer Immunotherapy

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Background: Tumor-infiltrating lymphocytes (TILs) play a crucial role in the immune response within the tumor microenvironment. Unlike peripheral blood lymphocytes (PBLs), TILs better reflect host-tumor interactions and have shown significant therapeutic potential, especially in adoptive cell therapy for cancer. This review provides an overview of recent advances in TILs-based therapies and their impact on cancer immunotherapy.

Methods: A systematic review was conducted to assess the role of TILs in cancer therapy, focusing on their interactions within the tumor microenvironment. We searched PubMed, Scopus, and Web of Science using keywords including Tumor-infiltrating lymphocytes, Immunotherapy, Cancer therapy, TIL therapy, and tumor microenvironment. The search covered studies published between 2014 and 2024, and 93 studies were selected for in-depth analysis. Articles were included based on predefined criteria, such as TIL functionality in tumor progression and immunotherapy response. Studies lacking sufficient data on TIL characterization or clinical outcomes were excluded.

Results: From the 93 studies reviewed, TILs were found to exhibit enhanced anti-tumor activity compared to PBLs, notably in their ability to directly interact with tumor cells and modulate immune responses within the tumor microenvironment. Clinical studies showed that TIL therapy, particularly when combined with interleukin-2 (IL-2), can induce significant tumor regression in metastatic melanoma and other cancers. Advances in single-cell sequencing have provided deeper insights into TIL heterogeneity and functional states, revealing distinct activation and exhaustion patterns that correlate with therapeutic outcomes.

Conclusion: TIL-based therapies hold great promise in cancer immunotherapy due to their unique ability to target tumor cells directly. Despite challenges from the tumor microenvironment, TIL therapy has shown success in clinical settings, warranting further research to optimize its use across various cancers.

Keywords: Tumor-infiltrating lymphocytes, Immunotherapy, Cancer therapy, TIL therapy, Tumor microenvironment

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Abstract: A-10-3137-1

An investigation on the impact of silver nanoparticles on the oxidative stress experienced by blue swimmer crabs (Portunus pelagicus)

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Background: Metallic nanoparticles likely induced significant oxidative stress in aquatic creatures, which increased reactive oxygen species and damaged the antioxidant defense system. Blue swimming crab Portunus pelagicus, one of the most economically valuable species, is a major component of commercial crustacean fisheries in the Indo-Pacific region and one of the most important cultured species in China. This benthic carnivore can accumulate contaminants from the water and be used as indicator organisms for environmental pollution.

Methods: The LC50 value was calculated by employing the standard method developed by the OECD, and crabs were subjected to a range of concentrations over a period of fourteen days. Catalase, glutathione superoxide dismutase, glutathione peroxidase, total antioxidant capacity, and malondialdehyde were all evaluated for their levels of activity. The amount of AgNPs that had a 96-hour LC50 value was 13.65 mg/L.

Results: The levels of catalase, superoxide dismutase, and total antioxidant capacity were significantly lower in the crabs that were subjected to 50% LC50 of AgNPs as compared to the group that served as the control. In crabs that were subjected to 50% LC50 of AgNPs, the levels of MDA in the hepatopancreas increased considerably in comparison to all of the concentrations that were examined and the control group. However, the levels of MDA in the muscle did not rise.

Conclusion: Silver nanoparticles are harmful to Portunus pelagicus based on LC50. The hepatopancreas tissue plays a key function in Portunus pelagicus' antioxidant defense since it possessed greater antioxidant enzyme activity than muscle. Catalase (CAT), superoxide dismutase (SOD), and TAC levels were significantly reduced in crabs exposed to AgNPs at 50% LC50, indicating that crabs' hepatopancreatic antioxidant ability was impaired. MDA levels also increased at this concentration. Insignificant GPx and GSH increases suggest glutathione-based antioxidant defense enzymes have little effect on AgNP-induced oxidative stress.

Keywords: Silver nanoparticles, Toxicity, Oxidative stress, blue swimmer crabs

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Acta Biochimica Iranica

Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3125-1

Investigating the toxicity of biosynthesized gold nanoparticles on breast cancer cells

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Background: This study focuses on the green synthesis of gold nanoparticles using the aqueous extract of Eryngium caeruleum an eco-friendly and cost-effective alternative to conventional chemical methods.

Methods: Various concentrations of plant extract were tested, with 0.1 mg/mL identified as the optimal concentration for synthesizing stable nanoparticles. The produced nanoparticles were characterized using UV-Visible spectroscopy and TEM analysis was used to measure the dimensions of synthesized gold nanoparticles. Finally, MTT analysis was used to investigate the effects of these gold nanoparticles synthesized by green synthesis on breast cancer cells.

Results: The produced nanoparticles were characterized using UV-Visible spectroscopy and Transmission Electron Microscopy (TEM), revealing spherical nanoparticles with a size range of 20 to 22 nm. In measuring the toxicity of nanoparticles on cancer cells through MTT analysis, it was observed that there is appropriate toxicity in the concentration ranges. IC50 was calculated as 4369 ng/mL.

Conclusion: Transmission Electron Microscopy (TEM), revealed spherical nanoparticles with a size range of 20 to 22 nm. Cytotoxicity tests on breast cancer cells were conducted using the MTT assay, showing minimal toxicity at lower nanoparticle concentrations. However, a significant increase in toxicity was observed with higher concentrations, with 60% cytotoxicity at 5000 ng/mL. The IC50 value was determined to be 4369 ng/mL. These findings suggest that gold nanoparticles synthesized via green methods have promising potential for use in cancer treatment, though further research is needed to explore their full therapeutic capabilities and safety profiles.

Keywords: Green synthesis, gold nanoparticles, breast cancer

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Abstract: A-10-3139-1

The effect of blood serum exosomes of patients with coronary artery disease on cardiac differentiation of bone marrow mesenchymal stem cells

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Background: Coronary artery disease is the main cause of death and ailments related to heart and blood vessels in different countries. In the cardiovascular system, mesenchymal stem cells can protect the myocardium by reducing the level of inflammation, differentiating myocardial cells around the infarcted and angiogenic areas, increasing resistance to apoptosis, and inhibiting fibrosis, which are ideal strategies for repairing the cardiovascular system. Exosomes are one of the types of membrane vesicles that are secreted into the extracellular space by most types of cells. They play an important role in cellular communication and epigenetic regulation by transporting protein and vital genetic material such as miRNA, mRNA and DNA.

Methods: Serum of three people with coronary artery disease and three healthy ones were collected and using a special kit, their exosomes were extracted. Human bone marrow mesenchymal stem cells were cultured and treated in the following 5 groups, by adding: 1-exosome of patients' sera with coronary artery disease, 2-exosome-free serum of patients with coronary artery disease, 3-exosome of healthy people and 4- exosome-free serum of healthy people, and 5-the control group with non-treated cells. Later, the expression of cardiac specific genes was measured in different groups by Real Time PCR method.

Results: The extracted exosomes could induce the proliferation of mesenchymal stem cells, which was shown both in the population doubling time and the cell growth curve. As compared to the control group, the treated cells with exosomes also showed higher expression of cardiac specific markers Troponin and creatine kinase.

Conclusion: Although patients with coronary artery disease might have deficiencies in their heart tissue, but the exosome extracted from their blood serum might promote the cardiac differentiation of bone marrow mesenchymal stem cells in a promising way.

Keywords: coronary artery disease, cardiomyocyte exosomes, mesenchymal stem cells, cardiac differentiation

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Abstract: A-10-3149-1

Targeting vimentin: a multifaceted approach to combatting cancer metastasis and drug resistance

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Background: Vimentin is a type III intermediate filament protein that plays a critical role in maintaining cellular integrity, facilitating cell migration, and regulating various signaling pathways. Primarily associated with mesenchymal cells, vimentin is upregulated during the epithelial-to-mesenchymal transition (EMT), a crucial process in cancer metastasis. Its overexpression correlates with aggressive tumor behavior and poor prognosis in several cancers, including breast, lung, and gastrointestinal cancers. Given its significant involvement in tumor progression and drug resistance, vimentin has emerged as a promising therapeutic target in cancer treatment.

Methods: This review analyzed 50 articles published from 1998 to 2023, sourced from databases including PubMed, Scopus, Embase, Web of Science, and the Cochrane Library. The search specifically targeted studies examining vimentin's role in cancer progression, particularly concerning metastasis and therapy resistance. Inclusion criteria focused on relevance to vimentin in cancer, study type (both experimental and review), publication date (with an emphasis on the last decade), and peer-reviewed status. Articles that did not concentrate on vimentin or were from non-peer-reviewed sources were excluded.

Results: The review categorized various strategies for inhibiting vimentin to mitigate its pro-tumorigenic effects. These strategies included precision tools such as antibodies and nanobodies that specifically target vimentin, alongside DNA and RNA aptamers designed to disrupt vimentin-related signaling pathways. Additionally, innovative approaches like vimentin-targeted vaccines and microRNAs (miRNAs) were discussed for their potential to activate the immune system and regulate post-transcriptional processes in vimentin-expressing cancer cells. The findings underscore the growing recognition of vimentin as a vital target in cancer therapy and highlight diverse therapeutic approaches aimed at enhancing treatment efficacy.

Conclusion: This systematic review emphasizes vimentin's critical role as a therapeutic target in cancer treatment, particularly concerning metastasis and drug resistance. The diverse strategies explored—including antibodies, aptamers, vaccines, and miRNAs—demonstrate significant promise for improving outcomes in cancer therapy. Further studies are warranted to optimize targeted approaches against vimentin to enhance therapeutic effectiveness.

Keywords: Vimentin, Metastasis, Plasticity, Drug resistance, Inhibitor, EMT

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Abstract: A-10-2568-1

Recombinant Listeriolysin O as a Potentiator of Cisplatin and Carfilzomib Chemotherapy: Apoptotic Induction and Gene Expression Alterations in A2780S and A2780CisR Ovarian Cancer Cells

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Background: Ovarian cancer's high mortality is largely due to resistance to chemotherapy agents like cisplatin. This study explores the use of recombinant listeriolysin O (LLO) as an adjuvant to enhance the effectiveness of cisplatin and carfilzomib in both cisplatin-sensitive and resistant ovarian cancer cell lines. The research highlights LLO's potential to induce apoptosis and modify the expression of key genes linked to drug resistance and survival.
Methods: This study evaluated the effects of cisplatin (Cis) and carfilzomib (CFZ) on ovarian cancer cell viability, with a focus on their potential synergistic effects after 72 hours. Listeriolysin O (LLO) was used to enhance drug delivery, and apoptosis was assessed via flow cytometry. Gene expression changes and NFκB p65 protein level were measured using real-time PCR and ELISA, respectively, with significant results determined by ANOVA and Tukey tests ($p < 0.05$).
Results: The MTT assay revealed that A2780S cells were more sensitive to cisplatin and carfilzomib than A2780CisR cells. Combination treatment showed a synergistic effect, especially in A2780S cells after 72 hours. Flow cytometry indicated higher apoptosis rates with drug combinations, particularly with listeriolysin O (LLO). Carfilzomib significantly reduced the expression of MDR1, Bcl-2, and Bax genes, with LLO enhancing this effect. ELISA results confirmed that carfilzomib also significantly decreased NFκB p65 levels, with greater reductions seen in LLO-containing combinations.
Conclusion: This study demonstrates that carfilzomib, a second-generation proteasome inhibitor, effectively enhances cisplatin's antiproliferative effects even in drug-resistant ovarian cancer cells. Additionally, recombinant listeriolysin O significantly improves drug loading and accumulation. Future research should explore the combined use of new proteasome inhibitors and pore-forming proteins on drug transporter activity.

Keywords: listeriolysin O, Apoptotic, Cisplatin, carfilzomib, Gene Expression, ovarian cancer

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Abstract: A-10-2959-1

Synthesis of Nano silver@oleuropein,Taurine for Skin healing with antibacterial characteristics

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Background: Silver nanoparticles (AgNPs) have been widely studied for their antibacterial properties, but there is growing interest in enhancing their biocompatibility and reducing their toxicity for human cells. In this study, oleuropein, known for its antioxidant and anti-inflammatory properties, and Taurine, an amino acid with cell-protective functions, were incorporated into AgNPs to assess their potential as safe and effective antibacterial agents for applications in dermatology.

Methods: The nanoparticles were synthesized using green chemistry methods, avoiding the use of toxic reagents. The structural and morphological characteristics of the synthesized nanoparticles containing Oleuropein and Taurine (Ag@-O,T) were characterized using UV-Vis spectrophotometry, FTIR, SEM, and XRD techniques. To evaluate the antibacterial efficacy, the Ag@-O,T was tested against Staphylococcus aureus, a common bacterial strain that causes skin infections, using the disk diffusion assay. Toxicity on human skin cells was assessed using the MTT assay, which measures cell viability after exposure to varying concentrations of the nanoparticles.

Results: The synthesized Ag@O,T demonstrated significant antibacterial activity against Staphylococcus aureus, showing a strong inhibition zone in the disk diffusion assay. In terms of toxicity, the MTT assay results indicated that at lower concentrations, the nanoparticles exhibited minimal toxic effects on human skin cells, suggesting a high level of biocompatibility. At higher concentrations, slight toxicity was observed, but within acceptable safety margins for topical applications.

Conclusion: The incorporation of Oleuropein and Taurine on the silver nanoparticles coat enhances their antibacterial activity while reducing toxicity to human skin cells. This suggests that these nanoparticles could be developed into a potential topical antibacterial agent with minimal side effects.

Keywords: Taurine, SilverNano, Skin, Antibacterial, S.aureus

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Abstract: A-10-3090-1

Enhancing Cancer Radiotherapy with Gold Nanoparticles and Natural Radiosensitizers: A Promising Approach

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Background: Radiosensitizers are agents that enhance the effectiveness of radiotherapy by increasing the sensitivity of cancer cells to radiation. This review focuses on the potential of gold nanoparticles (GNPs) and natural compounds, such as resveratrol, as novel radiosensitizers in cancer treatment. GNPs have shown promise in enhancing radiation dose absorption in cancer cells while minimizing damage to healthy tissues, and natural compounds offer a complementary approach by overcoming tumor resistance to radiotherapy.
Methods: A comprehensive literature review was conducted using databases such as PubMed, Scopus, and Web of Science from 2014 to 2024 to identify studies on the use of gold nanoparticles (GNPs) and natural compounds as radiosensitizers in cancer treatment. Studies were selected based on their relevance to the mechanisms of action, clinical applications, and efficacy in enhancing radiotherapy outcomes. A total of 93 articles were reviewed. Articles that lacked sufficient detail or were not directly related to radiosensitization were excluded from this review. The keywords used for this search included: Radiosensitizers, Gold nanoparticles, Radiotherapy, and Cancer treatment.
Results: The 93 reviewed studies demonstrate that GNPs can significantly enhance the effectiveness of radiation therapy through both passive and active targeting strategies, as well as surface modifications like PEGylation and albumin-coating. These modifications improve the biocompatibility and accumulation of GNPs in tumor tissues, enhancing their radiosensitizing effects. Combination therapies using GNPs and chemotherapeutic drugs or immunoadjuvants have also shown synergistic effects in preclinical studies.
Conclusion: Both gold nanoparticles and natural compounds present promising opportunities as radiosensitizers in cancer radiotherapy. Their ability to enhance radiation effects while minimizing side effects suggests significant potential for improving treatment outcomes. Further research, including clinical trials, is necessary to optimize these strategies and fully realize their therapeutic benefits.

Keywords: Radiosensitizers, Gold nanoparticles, Radiotherapy, Cancer treatment

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Abstract: A-10-2836-1

Comparing effect of saffron carotenoids crocin and crocetin treatment on PI3K/AKT/NRF2 signaling pathway of Alzheimer's disease

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Background: Alzheimer's disease is a progressive neurodegenerative disorder. It is the most common cause of dementia. Saffron (Crocus sativus L.) as a medicinal plant has been used in traditional medicine for many years. Its bioactive compounds, crocin and crocetin, show promise in protecting against aβ-induced neurotoxicity and may affect the PI3K/AKT/GSK-3β pathway.

Methods: In this study, PC12 cells were differentiated using nerve growth factor (NGF), followed by transfection of neuron like PC12(nPC12) cells with Aβ1-42 oligomers. Cell viability assessed under two treatment approaches: pretreatment (where crocin and crocetin was added to nPC12 cells for 24 hours before Aβ1-42 exposure) and posttreatment (where nPC12 cells were first incubated with Aβ1-42 to establish an Alzheimer's model and then continuously incubated with crocin and crocetin for another 24 hours). Neural differentiation of PC12 cells and the translocation of Nrf2 to nuclei assessed by using immunocytochemical analysis. Additionally, key markers in the AKT/GSK-3β pathway were evaluated by Western blot. Also, cell cycle arrest and apoptosis were evaluated by flowcytometry.

Results: The data indicated that Crocin (Cro) and Crocetin (Crt) significantly decreased the AβO toxicity against nPC12 cells in both preventive and therapeutic modalities. While Crocin promotes cell growth at the highest tested concentrations, Crocetin's highest concentration poses a risk to cell viability. Cro and Crt Crt significantly reduced Tau phosphorylation levels. In addition, it was found that Cro and Crt might modulate oxidative stress induced by AβO by activating the PI3K/Akt signaling pathway, facilitating the translocation of NRF2 into the cell nucleus, and enhancing the expression of the antioxidant enzyme NQO1. The Cro groups exhibited higher antioxidant activity compared to the Crt groups.

Conclusion: Cro(potentially) and Crt they showed a neuroprotective effect against Aβ1-42 infection of dPC12 cells in both preventive and therapeutic manners. This function was through PI3K/AKT pathways.

Keywords: Neurodegenerative Disease, crocin, crocetin, Prevention, Therapeutic, Apoptosis, Signaling Pathway.

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Abstract: A-10-3155-1

Optimizing hyaluronic acid and investigating its effect on fibroblast (skin) cells

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Background: Hyaluronic acid is a natural biopolymer that has multiple functions in the body, including wound healing, cell migration, and cell signaling. Due to its versatility, hyaluronic acid has been used in many fields such as tissue engineering, treatment of various diseases including cancer through various forms. Therefore, in the present study, the optimization of hyaluronic acid and its effect on human skin fibroblast cells (HGF grade) is discussed.
Methods: In the present study, after extracting hyaluronic acid by chemical hydrolysis from the tissue of the cock's crown, FTIR analysis was used to check and confirm the obtained composition. Then, in order to evaluate the cytotoxicity effects of extracted hyaluronic acid on fibroblast cells, MTT assay was performed in different buffers.
Results: The obtained results indicated that human HGF skin fibroblast cells treated with hyaluronic acid in water buffers and pH=7 buffers had no toxic effects. However, placing the cells in DMEM buffer in some concentrations of the filtered hyaluronic acid sample has shown a significant decrease in the survival rate of fibroblastic cells compared to the control. However, in the rest of the concentrations in the above buffer, the percentage of cell survival did not show a significant decrease.
Conclusion: Therefore, it seems that the clinical use of the above combination is suitable for therapeutic purposes due to the lack of induction of cytotoxicity in fibroblastic cells.

Keywords: Hyaluronic acid, Fibroblast, Cytotoxicity.

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Abstract: A-10-2572-1

The effect of ginseng plant extract on ALT and AST levels in blood serum of rats after aerobic exercise

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Background: AST and ALT index is a valuable marker used in assessing liver health. Ginseng is an antioxidant that can affect oxidative stress parameters. This study aims to investigate the effect of ginseng plant extract on ALT and AST parameters in rat blood serum after aerobic exercise.

Methods: In this study, we used 30 Wistar rats. The animals were divided into six groups. The Control (without exercise and ginseng supplement) young, Control (without exercise with ginseng supplement(200mg/kg)) old, Aerobic exercise (without taking ginseng supplement(200mg/kg)) old, Ginseng (without aerobic exercise) old, Aerobic exercise + ginseng (aerobic exercise with ginseng supplement (200 mg/kg)) old. We evaluated the performance of rats on a treadmill for 8 weeks, supplemented with 200 mg/kg of ginseng supplement 5 days a week as a gavage injection. After the tests animals were sacrificed and their blood serum was separated after blood collection. The basis of the ALT, alanine reacts with 2-oxoglutarate, and pyruvate and glutamate are produced, while the basis of the AST, aspartate reacts with 2-oxoglutarate and oxoglutarate and glutamate are produced. Data were analyzed using repeated measures of One-Way ANOVA.

Results: The results showed that there was a significant difference between the groups in the level of AST. The level of AST in the Control (without exercise and ginseng supplement) young was significantly higher compared to Aerobic exercise+ginseng (aerobic exercise with ginseng supplement (200 mg/kg)) old($p<0.05$). However, the level of ALT is not significant($p>0.05$).

Conclusion: The reduction of AST in rat blood indicates a reduction in cell damage and cell death due to ginseng consumption during aerobic exercise. Ginseng can be effective in reducing enzymes, but more parameters should be measured and the result can be different according to the type of protocol performed.

Keywords: effect, ALT, AST, ginseng plant, blood serum, aerobic exercise

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Abstract: A-10-3150-1

Cancer inhibition through altered exosome content rather than drugs

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Background: Cancer is one of the most important causes of death in human society. Drug resistance in cancer cells is an important issue that the existence of limitations in the number of drugs in the field of oncology and the need to curb cancer due to the high epidemic demands new methods to be invented along with conventional methods. Exosomes as a suitable carrier without creating antibodies is a new method that if it changes its content in the direction of increasing the expression of miRNAs related to the increase of tumor suppressors and inhibition of oncogenes, it will be the practical goal of this research.
Methods: For this purpose, in this article, a systematic review of the latest articles (2020-2024) in the Exocarte Database, Google Scholar, PubMed, with the keywords Exosome, change content, differential miRNAs expression was done according to the research hypothesis.
Results: From the 165 articles obtained in the initial search, 35 final articles were selected by removing duplicate articles, and their results showed that using exosomes as a carrier and engineering its contents by inducing binding to oncogenes seems to be a suitable solution for transferring the drugs into the cells.
Conclusion: The use of exosomes extracted from the same category under the influence of inhibitory treatment as drugs can break drug resistance in the same category.

Keywords: Exosome, Drug resistance, Cancer, Exosome content engineering.

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Abstract: A-10-3154-1

Premature Aging Occurs Through the Mitochondria in Cuprizone Demyelinating Model of Multiple Sclerosis

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Background: Multiple sclerosis (MS) is a chronic neuroinflammatory disease primarily affecting young adults, but its severity tends to increase with age. While MS typically manifests early in life, research indicates that as patients age, both the progression of the disease and the myelin repair decrease. One possible explanation for this could lie in the energy production capabilities of oligodendrocytes and neurons, cells essential for myelin repair and neural function. Mitochondrial dysfunction in these cells may play a crucial role in this decline. Understanding how mitochondrial health influences the repair process could be key to addressing the worsening outcomes seen in MS patients and also investigating aging incidence in demyelinating condition.

Methods: To induce the cuprizone (CPZ) demyelinating model, 8-week-old mice were fed 0.2% CPZ-supplemented chow for 12 weeks. Then we analyzed mitochondrial activity by assessing oxidative stress and mitochondrial DNA copy number and its ultrastructure. Telomere length and the expression of senescence-associated β-galactosidase (SA-βgal) were also measured as biomarkers of aging.

Results: Our analysis also revealed increased oxidative stress and reduced mtDNA copy number. We also characterized a decreased telomere length and increased presence of SA-β-gal in the corpus callosum section of the CPZ mice model compared to the control group.

Conclusion: This study aimed to elucidate the white matter alteration and aging incident in demyelinating conditions. Our data strongly suggested the presence of aging biomarkers in demyelinating conditions. We also demonstrated mitochondrial disruption and increased oxidative stress in the brain of the CPZ group. Since mitochondrial dysfunction is a pivotal director of aging, it seems mitochondria might conduct accelerated aging in demyelinating mice models.

Keywords: Demelination, aging, mitochondria

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Abstract: A-10-3063-1

Protein trafficking pathways in the eukaryote cells: a systematic review

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Background: Regulation of protein trafficking inside the cell is one of the main biochemistry topics. Newly synthesized proteins in the cytoplasm of mammalian cells must be delivered to appropriate cellular destinations to prevent human diseases.
Methods: A systematic literature search was done using the Web of Science, and Scopus covering articles from 1998 to 2024. Articles were selected that describe the movement path of proteins and important factors in the secretory and non-secretory pathways of the cell. The following search terms were used: protein trafficking, secretory pathway of proteins, vesicular transport, ER-Associated Degradation (ERAD), anterograde traffic of proteins, late secretory pathway, clathrin, caveolae, peroxisomal targeting signal, importin, sorting signals of proteins.
Results: To examine our purpose, 200 publications were downloaded. Of these, 76 studies were excluded after a review of the abstracts. Finally, 64 papers were included after a review of the full text. Based on the literature, defects in the transport system of cargo proteins from the endoplasmic reticulum to the Golgi have been mentioned in the combined deficiency disease of coagulation factors 5 and 8. In Menkes disease, the disturbance in normal copper homeostasis occurs due to a defect in the ATP7A gene. The importance of protein traffic from the Trans Golgi Network to the lysosome has been shown in lysosomal storage diseases. The proteins targeted to enter the peroxisome matrix have a peroxisome (PTS1 and PTS2) signal in their amino acid sequence. Two classical routes for proteins to enter mitochondria include presequence and carrier. The signal of nuclear proteins is recognized in the cytoplasm by the superfamily of Importins (IMPs), which have different types of α and β.
Conclusion: An adequate understanding of the proteins involved in the secretory and non-secretory pathways will help correctly understand many genetic diseases.

Keywords: Protein trafficking, COPI, COPII, Clathrin

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Abstract: A-10-2909-1

Evaluating The Effectiveness of Quercetin Nanoparticles in The Prevention and Treatment of Oral Mucositis During Radiotherapy for Head and Neck Cancers

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Background: Oral mucositis is a debilitating side effect of head and neck radiotherapy, impacting up to 85% of patients. Quercetin, a flavonoid with significant antioxidant and anti-inflammatory properties, has yet to be thoroughly investigated for its potential in mitigating radiation-induced oral mucositis. This study aims to evaluate the preventive and therapeutic efficacy of quercetin and quercetin nanoparticles on radiation-induced oral mucositis in a murine model.

Methods: Thirty Wistar rats were subjected to a single 13 Gy dose of radiation to induce mucositis. The rats were then divided into six groups (n=5/group): non-irradiated control, vehicle control, 10 mg/kg quercetin, 10 mg/kg quercetin nanoparticles, and dexamethasone. Treatments were administered from day 7 to day 13 post-irradiation. Outcome measures included daily oral injury scoring, serum TNF-α levels, total antioxidant capacity, weight changes, and scar area. Additionally, histological examination of oral mucosal samples was performed using hematoxylin and eosin (H&E) staining to assess the extent of tissue damage after the treatment period.

Results: Administration of 10 mg/kg quercetin significantly reduced TNF-α levels and increased antioxidant capacity compared to the vehicle group ($p<0.001$). Both quercetin and quercetin nanoparticles significantly attenuated the progression of oral injury scores compared to other treatments ($p<0.01$). Additionally, quercetin nanoparticles and dexamethasone effectively protected against weight loss compared to the vehicle ($p<0.001$). Dexamethasone also significantly reduced scar area compared to the control group ($p=0.0438$). Histopathological evaluation revealed that eight days post-radiation, untreated groups exhibited significant tissue damage and endothelial cell apoptosis, whereas treated groups showed marked improvement.

Conclusion: Quercetin nanoparticles at a 10 mg/kg dose demonstrated significant protective effects against radiation-induced oral mucositis, likely through antioxidant and anti-inflammatory mechanisms. These findings suggest that quercetin, particularly in nanoparticle form, warrants further investigation as a potential adjuvant therapy for radiotherapy induced mucositis in head and neck cancer patients.

Keywords: Antioxidant, Quercetin, Head and Neck Cancer, Oral mucositis, Radiotherapy

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Abstract: A-10-2563-2

Effects of lncRNAs on Wnt/β-catenin signaling pathway in colorectal cancer

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Background: LncRNAs are one of the most important influencing factors in the formation or prevention of various cancers, including colorectal cancer. Therefore, we performed a systematic review to investigate the effects of lncRNAs on Wnt/β-catenin signaling pathway; the main signaling pathway in colorectal cancer biogenesis.
Methods: The Google Scholar and PubMed databases was systematically searched for trials in English language published between 2015 and 2024 that examined the effects of lncRNAs on Wnt/β-catenin signaling pathway in colorectal cancer.
Results: In total, 134 related articles were reviewed. After removing irrelevant articles to the subject, 34 articles fulfilled the inclusion criteria. According to the conducted researches, there are a large number of lncRNAs like H19, CRNDE, HOTAIR are over-expressed in CRC cells and tissues. Another group of lncRNAs like RMST, CTD903, GAS5 are under-expressed in colorectal cancer cells.
Conclusion: The available evidence supports the role of lncRNAs as an inducer, enhancer or inhibitor genetic factors in Colorectal cancer. Also, the advances on mechanism of understanding lncRNAs in Wnt/β-catenin signaling might bring novel candidates as biomarkers and therapeutics for CRC.

Keywords: LncRNA, Colorectal Cancer, β-catenin, Target Therapy

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2594-3

The effect of inflammation and angiogenesis, along with the use of curcumin and nanoparticles on p53 gene expression and the activity of proteins involved in apoptosis on breast cancer

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Background: The study of factors affecting the incidence of breast cancer in patients like conventional chemotherapy is inadequate in the treatment of breast cancer (BC) types. New treatments or drugs such as curcumin has significant potential in inhibiting disease associated parameters such as apoptosis, autophagy, angiogenesis, cell migration, and metastasis.

Methods: The effect of inflammation and angiogenesis combined with the use of curcumin and nanoparticles on p53 gene expression and the activity of proteins involved in apoptosis on breast cancer were studied in this systematic research according to our criteria from 2013 to 2024. Several search engines and databases including Pubmed and Google Scholar were searched using 6 keywords: breast cancer, inflammation, curcumin, angiogenesis, Apoptosis is P53gen and a comparative study of articles.

Results: According to our search 35 articles from 2013 to 2024 were found. Then, 10 articles were removed due to duplication and the remaining 25 articles were reviewed.

Conclusion: Cancer is an inflammatory disease. Inflammation can alter the expression of oncogenes and tumor suppressor genes to promote neoplastic metamorphosis. These findings suggest that curcumin, particularly in nanoparticle form, warrants further investigation as a potential adjuvant therapy for treatment of breast cancer.

Keywords: Breast Cancer ،Inflammation ،Curcumin ،Angiogenesis ،P53 Gene ،Apoptosis

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2978-1

A Novel Approach for Detecting Colorectal Cancer MicroRNA Through Au-Graphene quantum dot nanostructure

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Background: Colorectal cancer is a significant global health issue, and its early detection is crucial for improving treatment outcomes. Despite the traditional methods for detecting miRNAs have limitations, researchers are exploring the microRNAs (miRNAs) potential as a novel strategy for early cancer detection. Smart Nanostructured biosensors, using nanomaterials such as Au-NPs and graphene quantum dots, have shown promise for improving the detection of miRNAs. Here, we have developed a nano-biosensors, that offers enhanced sensitivity, selectivity and stability, making it useful for a wide range of diagnostic purposes.

Methods: In order to synthesize the graphene quantum dots (GQDs), glucose powder was dissolved in deionized distilled water and then placed in an autoclave reactor where it was heated at 160° C for 6 hours. After that, the autoclave reactor was left to cool down to room temperature. The next process involved cleaning electrodes, electrodeposition of GQDs, and then gold nanoparticles. At last process of cap-223 (SH-ssDNA) was immobilized on the surface of nanostructured biosensor. Finally, the sensitivity and selectivity of the nanostructured electrode was evaluated by electrochemical approaches through different concentrations of miR-223.

Results: FTIR, Raman, and UV analyses have shown that graphene quantum dots were successfully synthesized. The FE-SEM characterization results of fabricated biosensor showed a nanostructure mixing of graphene quantum dots and Au-nanoparticles on the surface of electrodes. Finally, the electrochemical analyses confirmed the successful fabrication of this nanostructured biosensor and possessing an extensive surface area and high electrical conductivity, followed by accurate quantification of miR-223 detection even in real sample.

Conclusion: This study introduced a highly sensitive, and selective nanostructured biosensor for early detection of colorectal cancer biomarker, miR-223. By using graphene quantum dot (GQDs) and gold nanostructure, this biosensor overcomes the stability issues and improved detection limit compared previous researches.

Keywords: Nano-biosensor, graphene quantum dot, micro RNA, gold nanostructure, colorectal cancer.

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Abstract: A-10-3091-1

Low hemoglobin level is associated with an elevated risk of osteoporosis in individuals exposed to lead and cadmium: A Systematic Review and Meta-Analysis of Observational Studies

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Background: Cadmium and lead exposure is linked to osteoporosis and anemia. Nonetheless, the relationship between these outcomes has not been thoroughly elucidated. This systematic review and meta-analysis investigated the association between hemoglobin levels and osteoporosis in adults exposed to lead and cadmium.
Method: This analysis retrieved all publications and research published till September 2024 from the databases PubMed, SID, Magiran, Google Scholar, Science Direct, and Scopus. The investigation for publications utilized the keywords hemoglobin, osteoporosis, lead, and cadmium. The correlation coefficients from all studies were aggregated in a random effects meta-analysis. The risk of bias was evaluated utilizing the GRADE system.
Results: We identified a substantial inverse correlation between hemoglobin levels and osteoporosis in people exposed to lead ($r = -0.230$, 95% CI = -0.179 to -0.259, $p < 0.001$) and cadmium ($r = -0.069$, 95% CI = -0.049 to -0.082, $p < 0.001$). 16 articles related to the topic were found, 8 articles were excluded due to lack of proper quality and 8 articles were included in the study.
Conclusion: This meta-analysis reveals that low hemoglobin levels are correlated with an elevated risk of osteoporosis in individuals exposed to lead and cadmium. Consequently, in these patients, addressing anemia may effectively mitigate the heightened risk of osteoporosis.

Keywords: hemoglobin, osteoporosis, lead, and cadmium

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Abstract: A-10-2251-1

Investigating the effect of quercetin in increasing the expression of BDNF and SIRT1 genes in the brain of diabetic rats

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Background: Diabetes Mellitus is a complex metabolic disorder with multifactorial etiology. BDNF gene is one of the genes responsible for memory and learning in the brain. In addition, BDNF has a key role in protecting nerve cells and cognitive processes. It has been found that BDNF gene expression is significantly reduced in the group of patients with diabetes. Decreased expression of this gene in diabetics is associated with increased cognitive impairment. SIRT1 enzyme is also a vital enzyme in the survival and death of cells under conditions of oxidative stress caused by diet. The reduction of SIRT1 activity causes the death of nerve cells and the reduction of cognitive functions. Quercetin is a biologically active compound belonging to a group of plant compounds called flavonoids. Conjugation of quercetin with superparamagnetic iron oxide nanoparticles (QCSPION) affects a wide range of genes related to diabetes and cognitive impairment.

Methods: In this article, the techniques of electrophoresis, PCR, real-time PCR, electrophoresis, extraction of total RNA from the brain of rats, measurement of quality, concentration and purity of RNA and primer design have been used.

Results: The results of the investigations showed that the expression of BDNF gene and SIRT1 gene increased in the treatment group with diabetes after treatment with quercetin conjugate with iron oxide nanoparticles. In the present study, following the previous study, real-time PCR technique was used to investigate the expression of SIRT1 and BDNF genes in the above groups.

Conclusion: Real-time PCR data analysis showed that the use of quercetin in diabetic patients leads to a significant increase in the expression of SIRT1 and BDNF gene compared to the control group.

Keywords: Diabetes Mellitus ،Cognitive Disorders ،BDNF ،Quercetin ،SIRT1

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2286-1

Exosomes Isolated from Metabolically Unhealthy Normal Weight and Overweight Phenotypes Deteriorated the Er/pr Positive Breast Cancer Behavior

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Background: Obesity has been linked to an increased risk of postmenopausal breast cancer, but interestingly, it has been inversely associated with premenopausal breast cancer risk. Metabolic health status, which varies across different obesity phenotypes, might play a key role in these associations. This study aimed to evaluate the effects of plasma exosomes obtained from women with different obesity phenotypes on the migration, matrix metalloproteinase-2 (MMP-2) activity, and apoptosis of MCF-7 breast cancer cells.

Methods: Exosome isolation, characterization, and their internalization into MCF-7 cells were conducted. MCF-7 cells were treated with exosomes isolated from various obesity phenotypes, and their effects on migration, MMP-2 activity, mRNA expression of Bax and Bcl-2, protein expression of p-53 and Thr55 p-p53, and apoptosis were evaluated.

Results: Exosomes isolated from unhealthy obese individuals significantly enhanced MCF-7 cell migration. Additionally, exosomes from unhealthy normal weight, overweight, and healthy obese groups increased MMP-2 activity compared to their counterparts. Exosomes from these same groups also decreased apoptosis in MCF-7 cells compared to those from their respective counterparts.

Conclusion: Overall, plasma exosomes from unhealthy normal weight, overweight, and unhealthy obese individuals worsened the behavior of estrogen/progesterone receptor-positive breast cancer cells by promoting migration and reducing apoptosis. These findings suggest that metabolic health, in addition to obesity status, may influence breast cancer progression.

Keywords: Obesity, breast cancer, exosomes, the metabolic phenotype

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2405-2

A2β1 Integrin Specific Inhibitor Btt-3033 Promotes Paclitaxel-Induced Apoptosis in Human Ovarian Cancer Cells

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Background: The use of molecular targeted agents combined with cytotoxic drugs is emerging as a promising approach to enhance the effectiveness of chemotherapy. This study aimed to investigate whether the α2β1 integrin-specific inhibitor, BTT-3033, could increase the sensitivity of ovarian cancer cells, OVCAR3 and SKOV3, to the chemotherapeutic agent paclitaxel (PTX).

Methods: OVCAR3 and SKOV3 ovarian cancer cell lines were treated with BTT-3033 and various concentrations of PTX. The combined effect of BTT-3033 and PTX on cell death mechanisms was assessed by evaluating cell viability, apoptosis, reactive oxygen species (ROS) production, mitochondrial membrane potential (MMP), and caspase-3 activity. The goal was to determine whether BTT-3033 could enhance the antiproliferative and apoptotic effects of PTX.

Results: Both BTT-3033 (≥ 1 µM) and PTX (≥ 0.01 µM) inhibited the proliferation of OVCAR3 and SKOV3 cells in a concentration-dependent manner. Pretreatment with 1 µM BTT-3033 followed by PTX led to synergistic antiproliferative effects, significantly lowering the IC50 values of PTX from 0.45 µM to 0.03 µM in OVCAR3 cells and from 0.35 µM to 0.02 µM in SKOV3 cells. All coefficients of drug interaction for PTX/BTT-3033 combinations were below 1, indicating strong synergy. Additionally, the PTX/BTT-3033 combination induced a significant increase in the percentage of apoptotic cells, from 4.2% to 87.0% in OVCAR3 and from 2.4% to 88.5% in SKOV3 cells, compared to PTX treatment alone.

Conclusion: The combination of BTT-3033 and PTX not only enhanced apoptosis but also reduced mitochondrial membrane potential and increased caspase-3 activity. Moreover, this combination therapy stimulated greater ROS production in both OVCAR3 and SKOV3 cells, further promoting cancer cell death.

Keywords: Paclitaxel, BTT-3033, apoptosis, drug interaction, ovarian cancer

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Abstract: A-10-2412-1

Investigating the Comparative Effect of 5-Fu on the Expression Level of Glycotic Genes in High Glucose and Normal Glucose Mediums in Human Colorectal Cancer Cells (ht-29) Under Hypoxic Conditions

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Background: Colorectal cancer (CRC) is the third most common cancer worldwide, and chemotherapy remains a central treatment modality. Among various chemotherapeutic agents, 5-fluorouracil (5-FU) is particularly effective in treating CRC. However, while the antiproliferative effects of 5-FU on CRC have been extensively studied, the impact of 5-FU on the expression of glycolytic genes under different glucose conditions, especially in a hypoxic tumor microenvironment, remains unexplored. This study aimed to investigate the effects of 5-FU on glycolytic gene expression in human colorectal cancer cells (HT-29) cultured under high and normal glucose conditions in hypoxia.
Methods: HT-29 cells were cultured in DMEM medium with 10% FBS and 1% antibiotics. The cells were treated with 6.5 µM and 28.5 µM of 5-FU and 150 µM CoCl2 to simulate hypoxic conditions in both high (28.5 mM) and normal (6.5 mM) glucose mediums for 72 hours. Gene expression levels of key glycolytic components such as hypoxia-inducible factor 1-alpha (HIF-1α), glucose transporters (GLUT1 and GLUT3), and glycolytic enzymes (hexokinase II (HKII) and pyruvate kinase M2 (PKM2)) were measured using qRT-PCR.
Results: The qRT-PCR analysis showed that 5-FU treatment significantly downregulated the expression of HIF-1α, GLUT1, GLUT3, HKII, and PKM2 in both high and normal glucose mediums. However, the suppression of these glycolytic genes was more pronounced in high glucose conditions compared to normal glucose.
Conclusion: This study reveals that 5-FU differentially affects the expression of glycolytic genes in HT-29 colorectal cancer cells under varying glucose levels and hypoxic conditions. The findings suggest that glucose concentration in the tumor microenvironment can influence the therapeutic efficacy of 5-FU by altering glycolytic pathways, potentially affecting cancer cell survival and metabolic adaptability under hypoxia. These results underscore the importance of considering glucose levels in the tumor microenvironment when optimizing chemotherapeutic strategies for CRC. Further research is needed to clarify the mechanisms underlying these effects and explore therapeutic approaches targeting cancer metabolism.

Keywords: Colorectal Cancer,5-FU, high and normal glucose, Cocl2, glycotic genes

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Abstract: A-10-2459-1

Investigation Methylation Status of Tumor Suppressor Genes Nr4a1 and Nr4a3 in Patients with Acute Myeloid Leukemia

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Background: Acute myeloid leukemia (AML) is the most frequent type of leukemia among adults, accounting for almost 80% of all cases. Investigating AML heterogeneity based on DNA methylation can be clinically informative and improve clinical diagnosis and prognosis. This study was conducted to investigate NR4A1 and NR4A3 gene methylation in AML patients.

Methods: The study involved fifty newly diagnosed AML patients and fifty healthy controls. The frequency of methylation of the NR4A1 and NR4A3 genes in patients with AML was investigated using Methyl specific PCR (MSP). The association between methylation of studied genes and some prognostic marker including mutation of FLT3 and NPM genes, as well as some hematological factors of patients was evaluated. The results were analyzed using SPSS-16 software using Chi-square test and Fisher's exact test.

Results: According to the findings, individuals with AML have a significantly higher prevalence of methylated NR4A1 and NR4A3 genes than those without AML ($P<0.05$). AML patients with un-methylated NR4A3 gene had significantly higher frequency of FLT-ITD positivity than AML patients with methylated NR4A3 gene ($P=0.009$). The Association between methylation of NR4A1 and NR4A3 genes and NPM mutation was not statistically significant.

Conclusion: The results of the present study indicated that NR4A1 and NR4A3 were hyper-methylated in AML patients. Future studies should consider other mechanisms that may be effective in the role of NR4A1 and NR4A3 hypermethylation in AML.

Keywords: Acute myeloid leukemia, Methylation, Tumor suppressor genes

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Abstract: A-10-2552-1

Evaluation of Autophagy Related Atg4b Gene, Protein and miR-655-3p Expression Levels in Endometrial Cancer and Hyperplasia

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Background: The pathogenesis of endometrial cancer (EC) and hyperplasia is complex and not fully understood. Autophagy, a cellular degradation process, has emerged as a key factor in this pathology. This study aims to investigate the role of autophagy in EC and hyperplasia by examining the expression of the ATG4B gene, its corresponding protein levels, and miR-665-3p in patients compared to a control group.
Methods: This cross-sectional case-control study included a total of 90 endometrial tissue samples, consisting of 30 tumors, 30 hyperplasia cases, and 30 normal controls. The expression of ATG4B gene and protein levels was assessed using qRT-PCR and Western blotting, respectively, to evaluate differences across the three groups.
Results: The analysis revealed that ATG4B gene expression was significantly higher in the endometrial tissues of EC patients compared to hyperplasia patients and controls. Similarly, ATG4B protein levels were elevated in both EC and hyperplasia patients in comparison to the control group. A positive correlation was observed between ATG4B gene expression and protein levels in EC patients. However, miR-665-3p exhibited a significant negative correlation with ATG4B gene and protein levels in EC patients.
Conclusion: The elevated expression of the ATG4B gene and protein in EC tissue suggests that ATG4B may act as a tumor promoter in endometrial cancer.

Keywords: endometrial cancer, endometrial hyperplasia, ATG4B, miR-665-3p

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Abstract: A-10-2460-1

Investigation of the Effects of A New Thiophene Carboxamide Quinazoline Derivative on Cell Toxicity and Apoptosis Induction in the K562 Chronic Myeloid Leukemia Cell Line

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Background: Chronic myeloid leukemia (CML) is a significant blood malignancy associated with high mortality rates. A major challenge in treating CML is the emergence of drug resistance, prompting the need for new cytotoxic agents that can effectively induce apoptosis in resistant cancer cells. The quinazoline core has been recognized for its diverse biological activities, including its potential as an anti-cancer agent.

Methods: In this study, K562 cells were treated with varying concentrations of N-(4-ethyl-4'-oxo-1'H-spiro[cyclohexane-1,2'-quinazoline]-3'(4'H)-yl) thiophene-2-carboxamide (4e-QTC) for 24, 48, and 72 hours in a final volume of 200 µL. The cytotoxic effects of 4e-QTC were assessed using the MTT assay, while apoptosis induction was evaluated through flow cytometry. The percentage of apoptotic cells was analyzed using FlowJo software version X.0.7.

Results: The results indicated a significant reduction in the viability of K562 cancer cells after treatment with 4e-QTC, demonstrating a time-dependent effect. Additionally, the Annexin V/PI double staining technique revealed a marked increase in the percentage of apoptotic cells following treatment with 4e-QTC.

Conclusion: The findings of this study suggest that the novel quinazoline derivative 4e-QTC effectively induces apoptosis in K562 chronic myeloid leukemia cells. These results highlight the potential of 4e-QTC as a promising therapeutic agent to combat drug resistance and enhance treatment efficacy in CML patients. Further investigations are warranted to explore its mechanisms of action and clinical applications.

Keywords: Cancer, Chronic myeloid leukemia, Quinazoline, Apoptosis

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Abstract: A-10-2682-1

Comprehensive Analysis of Heavy Metals and Essential Elements in Colorectal Cancer

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Background: Colorectal cancer (CRC) ranks as the third most common cancer worldwide. The relationship between heavy metals (HMs) and CRC progression is complex, as HMs can replace essential elements in the body, disrupting cellular and enzymatic functions. Thus, investigating the changes in profiles of HMs and essential metals is crucial for understanding their roles in malignancies.

Methods: This study involved a 3.5-year case-control analysis with 322 participants divided into CRC, advanced adenoma (AA), and control groups at the Poursina Hakim Gastroenterology Research Center in Isfahan, Iran. Serum levels of 18 metals were assessed using Inductively Coupled Argon Plasma Optical Emission Spectroscopy. The analyzed metals included essential nutritional elements (calcium, zinc, copper, magnesium, manganese, iron, boron, sodium), heavy/toxic metals (nickel, lead, cadmium, arsenic, aluminum, antimony, tungsten), and trace elements (selenium, cobalt, chromium).

Results: The analysis revealed significantly elevated levels of arsenic and cadmium in the CRC group compared to both the AA and control groups. Furthermore, lead and antimony levels were also higher in the CRC group relative to controls. In contrast, zinc levels were notably higher in the AA group compared to the CRC group. Serum copper levels exhibited a similar trend to zinc across the groups, although the difference was not statistically significant ($p=0.084$).

Conclusion: This study demonstrates a clear association between elevated levels of certain heavy metals, specifically arsenic, cadmium, and lead, and the occurrence of CRC. These findings imply that disturbances in HM homeostasis may play a role in the development and progression of CRC. Insights gained from these metal profiles could facilitate the development of targeted diagnostic and preventive strategies to mitigate CRC incidence. Further research is needed to elucidate the underlying mechanisms of these associations and to assess the potential for clinical applications in cancer prevention and management.

Keywords: Colorectal cancer, heavy metals, essential elements, advanced adenoma

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Abstract: A-10-2518-1

Molecular Insights into Colorectal Cancer Stem Cells: A Path To Targeted Therapies

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Background: Colorectal cancer (CRC) is a malignant tumor associated with a poor prognosis, particularly in advanced cases due to high rates of recurrence and metastasis. These challenges are largely attributed to a subset of cancer stem cells (CSCs), specifically colorectal cancer stem cells (CCSCs), which exhibit high tumorigenic potential and resistance to conventional therapies. Current treatment strategies aim to target stem cell genes and key signaling pathways, such as Notch, Hedgehog, and WNT, to suppress CCSCs. However, these approaches may inadvertently affect normal stem cells in the colon and other tissues.

Methods: This study employed in silico techniques to compare normal colorectal stem cells and CCSCs. We analyzed microarray data from the GEO database using the Transcriptome Analysis Console (TAC). Tools such as STRING, Cytoscape, and Gephi were utilized to construct and analyze the protein-protein interaction (PPI) network of significant differentially expressed genes (DEGs). Additionally, enrichment analysis was conducted using the Enrichr platform to explore the functional roles of the identified clusters. This integrated approach, combined with the prediction of miRNAs associated with critical nodes in the PPI network, sheds light on the molecular distinctions between normal colorectal stem cells and CCSCs, potentially informing more effective therapeutic strategies.

Results: Our microarray analysis identified CXCL5, RPS4Y1, CD177, PRAC1, and XIST as the genes with the highest fold changes. The PPI network analysis highlighted IL6, CXCL8, IL1A, KIT, FN1, MMP9, AGT, and COL1A1 as the most significant nodes within the network. Three functional clusters were identified: the first cluster is associated with cytokine-cytokine receptor interactions; the second is involved in the PI3K-Akt, MAPK, and Ras signaling pathways; and the third cluster is linked to extracellular matrix organization and collagen fibrils. Furthermore, miRNA analysis predicted hsa-miR-29b-3p, hsa-miR-1-3p, hsa-miR-32-5p, hsa-miR-4267, and hsa-miR-149-5p for genes exhibiting positive fold changes.

Conclusion: The identification of these molecular criteria provides potential targets for more precise therapeutic interventions. By elucidating the differences between normal colorectal stem cells and CCSCs, this study aims to improve targeted therapy and enhance treatment outcomes for colorectal cancer.

Keywords: Colorectal cancer, cancer stem cells, differentially expressed genes, protein-protein interaction, miRNAs

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2252-1

Testosterone, B-Estradiol and Hepatocellular Carcinoma: Stimulation or Inhibition? A Comparative Effect Analysis on Cell Cycle, Apoptosis and Wnt Signaling of Hepg2 Cells

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Background: Unlike breast and prostate cancers, which are specifically affected by estrogens or androgens, hepatocellular carcinoma has been reported to be influenced by both sex hormones. High androgen level is conventionally considered carcinogenic for the liver; however, the effect of estrogens in the development stages of liver cancer is still controversial. Given the incidental differences of hepatocellular carcinoma in males and females, to understand the sex hormonal-derived etiology, we investigated the effects of β-estradiol and testosterone on the cell cycle, apoptosis and molecular mechanisms involved in the occurrence of carcinoma in liver cells.
Methods: To determine the effective concentration of both hormones, an MTT assay was performed. The effects of β-estradiol and testosterone on cell proliferation and death were evaluated by specific staining and flow cytometry. In addition, gene expression levels of estimated factors involved in GPC3-Wnt survival signaling were analyzed using quantitative real-time polymerase chain reaction.
Results: Both hormones inhibited hepatic cell proliferation through arresting the cell cycle at S/G2 and increased the apoptosis rate in HepG2 cells. Both hormones dose-dependently decreased GPC3, Wnt, and DVL expression levels as activators of the Wnt-signaling pathway. In the case of Wnt-signaling inhibitors, the effects of both hormones on WIF were negligible, but they increased DKK levels in a dose-dependent manner. In each of the effects mentioned above, β-estradiol was notably more potent than testosterone.
Conclusion: In contrast to the primary hypothesis of the project, in which testosterone has been considered a stimulatory carcinogenic factor in HCC pathogenesis, testosterone inhibited the occurrence of HCC similar to β-estradiol. This inhibitory effect was still weaker than that of β-estradiol and required more elaborating studies.

Keywords: Hepatocellular carcinoma, Wnt/β-catenin pathway, β-estradiol, Testosterone

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2561-1

Synthesis, Characterization, and Cytotoxic Effects of Gallic Acid-Based Carbon Dots

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Background: Colorectal cancer (CRC) is a leading cause of cancer-related deaths worldwide, highlighting the urgent need for novel therapeutic strategies. Carbon dots (CDs) have emerged as promising nanoparticles for biomedical applications due to their unique properties. Additionally, gallic acid (GA) is recognized as an effective anticancer agent against various tumor cells. This study investigates the potential of gallic acid-derived carbon dots (GA-CDs) as an innovative anticancer agent against HCT-116 colorectal cancer cells.

Methods: GA-CDs were synthesized using a one-pot hydrothermal method. Characterization was conducted through transmission electron microscopy (TEM), Fourier transform infrared (FT-IR) spectroscopy, and ultraviolet-visible (UV-Vis) absorption spectroscopy. The cytotoxicity of GA-CDs on HCT-116 cells was evaluated using the MTT assay at different concentrations of GA and GA-CDs over 24 and 48 hours. Cellular uptake was assessed via fluorescence microscopy.

Results: Characterization techniques confirmed the successful synthesis of GA-CDs. TEM analysis revealed a spherical morphology, while FT-IR spectroscopy validated the synthesis process. UV-Vis analysis indicated the presence of aromatic and carbonyl functional groups in the GA-CDs. Cell viability assays demonstrated a dose- and time-dependent decrease in cell viability, with IC50 values of 192.2 µg/mL for GA and 88.55 µg/mL for GA-CDs after 24 hours of incubation. Fluorescence microscopy confirmed the efficient uptake of GA-CDs by cancer cells, which correlated with enhanced cytotoxicity.

Conclusion: This study shows that GA-CDs possess potent anticancer properties, significantly inducing cytotoxic effects in HCT-116 cells. These findings suggest the potential of GA-CDs as a novel therapeutic agent for colorectal cancer treatment, warranting further exploration of their mechanisms of action and in vivo efficacy.

Keywords: Gallic acid, Carbon dots, Colorectal cancer, HCT-116 cell line, Cell viability

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Abstract: A-10-2578-1

DNA Methylation of Foxn3 and Foxo3 Genes and Its Association with Dnmt3a Rs2289195 Polymorphism and Clinicopathological Features in Acute Myeloid Leukemia Patients

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Background: The Forkhead box (FOX) transcription factors represent a large gene family that may influence cancer development, yet their specific roles remain largely unknown. Leukemia, a type of blood cancer affecting white blood cells, encompasses various subtypes, including acute myeloid leukemia (AML), which specifically targets immature myeloid cells. A frequent mutation found in AML patients is in the DNMT3A gene, which may impact the course of the disease. However, the influence of the DNMT3A gene variant rs2289195 on AML patient outcomes is not well understood.

Methods: In our study, we employed a case-control design. Initially, 50 patients diagnosed with AML (the patient group) were selected, alongside 50 individuals without AML (the control group). Blood samples were collected from all participants, and DNA was extracted from these samples. We utilized methylation-specific PCR and ARMS-PCR Tetra-primer techniques to assess the methylation status and genetic variation of the DNMT3A gene in both AML patients and healthy individuals. The resulting data were analyzed using statistical tests via the SPSS software package.

Results: Our findings revealed significant hypermethylation of the FOXO3 and FOXN3 genes in AML patients compared to healthy individuals, suggesting their potential involvement in the occurrence of AML. Despite the tumor suppressor functions of these genes, hypermethylation may reduce their activity. Additionally, no significant correlation was found between DNMT3A gene polymorphism and mutations in the NPM and FLT3 genes with the methylation status of FOXO3 and FOXN3.

Conclusion: These findings underscore the potential of FOXO3 and FOXN3 methylation as diagnostic biomarkers for AML and highlight their viability as targets for therapeutic interventions utilizing demethylation or hypomethylating agents.

Keywords: Methylation, acute myeloid leukemia, tumor suppressor genes, FOXN3, FOXO3, polymorphism

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Abstract: A-10-2562-1

Investigation of Melatonin Protective Effects on FGF Tumor Induction of Breast Cancer

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Background: Breast cancer is among the most prevalent types of cancer affecting women globally. Fibroblast growth factors (FGFs) have been implicated in enhancing cancer cell invasion, growth, and migration. Conversely, the inhibitory effects of melatonin on various cancer types have been well-documented. This study aimed to investigate the interaction between melatonin and epidermal growth factor (EGF) in the proliferation of breast cancer cells.
Methods: MDA-MB-231 and MCF-7 breast cancer cell lines were cultured, and the effects of melatonin and FGFs on cell viability were assessed using the MTT (3-(4, 5-Dimethylthiazol-2-yl)-2, 5-Diphenyltetrazolium Bromide) assay. Additionally, a cell proliferation assay was conducted to evaluate Ki-67 protein expression, and a cell apoptosis assay was performed to investigate apoptotic induction resulting from the interaction between melatonin and FGF.
Results: The IC50 values for melatonin were determined to be 2.06 mM for the MCF-7 cell line and 3.80 mM for the MDA-MB-231 cell line after 48 hours of incubation. Treatment with FGF (50 ng/ml) significantly increased cell viability in both MCF-7 and MDA-MB-231 cells ($p<0.05$). In contrast, melatonin effectively countered the effects of FGF, reducing cell viability in MCF-7 cells ($p<0.05$). However, melatonin treatment did not significantly affect the viability of the MDA-MB-231 cell line ($p>0.05$). Ki-67 expression was elevated in both cell lines treated with FGF ($p<0.05$), whereas melatonin significantly decreased Ki-67 levels in the MCF-7 cells ($p<0.05$). Furthermore, FGF treatment reduced the apoptotic cell population by 12% in MDA-MB-231 cells and 20.6% in MCF-7 cells, while melatonin treatment increased the apoptotic population to 41% in MCF-7 cells, though no significant change in apoptosis was observed in MDA-MB-231 cells.
Conclusion: The findings of this study suggest that melatonin has the potential to counteract the tumor-promoting effects of FGF in breast cancer.

Keywords: Breast Cancer, FGF, Melatonin

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Abstract: A-10-2520-3

Discovering New Pancreatic Adenocarcinoma Pathogenesis Biomarkers Using Three-Way Interaction

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Background: Pancreatic ductal adenocarcinoma (PDAC) is one of the deadliest cancers, with a poor prognosis. High-throughput gene expression data provide valuable insights into gene interactions, improving our understanding of disease mechanisms. While co-expression analysis is a commonly used approach for studying gene interactions, it alone cannot fully capture the complexity of these interactions. To address this, we applied a three-way interaction model to uncover more intricate connections between genes.

Methods: This study utilized the liquid association approach to identify statistically significant triplet gene interactions involved in PDAC development. Gene set enrichment analysis (GSEA) and gene regulatory network (GRN) analyses were then performed to explore the biological relevance of these triplets.

Results: Our findings suggest that the biological processes "response to estradiol" and "regulation of T-cell proliferation" may play critical roles in PDAC development. Additionally, we identified six potential switch genes—Lamc2, Klk1, Nqo1, Aox1, Tspan1, and Cxcl12—that could be involved in driving PDAC progression.

Conclusion: This study is the first to apply a three-way interaction model to investigate the key genes and pathways involved in PDAC. We identified two crucial biological processes and six potential biomarkers that may contribute to PDAC initiation. Importantly, existing literature provides strong support for the biological significance of our findings.

Keywords: Pancreatic ductal adenocarcinoma, Liquid Association analysis, Three-way Gene Interaction, Gene Set Enrichment Analysis, Therapeutic Targets.

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Abstract: A-10-2655-2

Evaluation of Drug Resistance in the Tamoxifen-Treated Mkn-45 Gastric Cancer Cell Line Via the Epithelial-Mesenchymal Transition Signaling Pathway

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Background: One of the major obstacles in treating gastric cancer (GC) is the development of multi-drug resistance (MDR), which is often associated with the epithelial-mesenchymal transition (EMT). EMT is driven by key molecules such as transforming growth factor-β (TGFβ) and SMAD2, both of which contribute significantly to the occurrence of MDR.

Methods: Tamoxifen (TAM), a triphenylethylene derivative, has been shown to counteract MDR in human gastric cancers. This study aimed to evaluate the effect of TAM on 5-FU resistance in GC by inhibiting the TGFβ1/SMAD2 signaling pathway and EMT. The MKN-45 GC cell line was treated with 5-FU, TAM, or a combination of both. The cytotoxic effects of the treatments were assessed using the MTT assay, while DNA fragmentation and apoptosis were examined through DNA laddering. Real-time RT-PCR was performed to investigate the expression of EMT-related genes (SNAI2, VIM, TGFβ1, and SMAD2).

Results: The study revealed that TAM significantly reduced the IC50 of 5-FU in MKN-45 cells ($P \leq 0.05$) and enhanced 5-FU-induced apoptosis. Furthermore, the combination of TAM and 5-FU effectively inhibited the expression of TGFβ1 and EMT markers (VIM and SNAI2) in the MKN-45 cell line ($P \leq 0.05$). The downregulation of TGFβ1 targets in the SMAD2 pathway reversed EMT and increased the sensitivity of the MKN-45 cells to 5-FU.

Conclusion: These findings suggest that TAM may reverse EMT-mediated MDR by targeting the TGFβ1/SMAD signaling pathway, offering a potential new therapeutic strategy to overcome chemoresistance to 5-FU in gastric cancer treatment.

Keywords: Epithelial-mesenchymal transition, gastric cancer, drug resistance, Tamoxifen, TGFβ1/SMAD2 signaling pathway

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Abstract: A-10-2621-1

Investigating the Effects of Separate and Concomitant Use of Salinomycin and Mk-2206 on Viability, Apoptosis, and Gene Expression of Human Gastric Adenocarcinoma Cells

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Background: Human gastric adenocarcinoma (AGS) is a significant health concern globally. This study aimed to investigate the individual and combined effects of salinomycin and MK-2206 on the viability, apoptosis, and gene expression of AGS cells.
Methods: The AGS cell line was utilized to evaluate the potential anticancer effects of salinomycin and MK-2206. Various assays were conducted to explore key molecular pathways, focusing on the induction of apoptosis, cancer cell viability, and gene expression rates.
Results: The results indicated a significant decrease in cell viability ($P<0.001$), Akt expression levels ($P<0.001$), and NF-κB expression levels ($P<0.001$) in all groups treated with salinomycin, MK-2206, and the combination of both, compared to the negative control group. Furthermore, treatment with salinomycin, MK-2206, and their combination led to a marked increase in apoptosis rates in AGS cells compared to the negative control. Notably, the concurrent administration of salinomycin and MK-2206 resulted in synergistic effects, enhancing AGS cell viability and the expression levels of Akt and NF-κB more significantly than either agent alone (all $P<0.05$).
Conclusion: The findings from this study suggest that the combination of salinomycin and MK-2206 may enhance treatment efficacy for AGS.

Keywords: Salinomycin, MK 2206, Gene Expression, Neoplasms

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Abstract: A-10-2659-1

Relationship Between FGFR2 Expression and Clinicopathological Features in Oral Squamous Cell Carcinoma Tumors

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Background: Oral squamous cell carcinoma (OSCC) constitutes over 90% of malignancies affecting the oral cavity. Cervical lymph node metastasis is a critical clinicopathological prognostic factor in oral cancer, contributing to the poor prognosis of OSCC, which has a 5-year survival rate of approximately 50%. This highlights the need for improved diagnostic and treatment strategies, underscoring the importance of elucidating the molecular mechanisms underlying OSCC pathogenesis. This study aims to explore the relationship between FGFR2 expression and various clinicopathological features in OSCC tumors.

Methods: Biopsy samples of OSCC tumors (n=30) and normal gingiva (n=25) were collected and processed. RNA was extracted to assess FGFR2 expression at both mRNA and protein levels using real-time PCR and immunohistochemistry (IHC) analysis. Statistical analyses were performed to determine potential correlations between FGFR2 expression and clinicopathological features, including age, gender, smoking habits, lymph node metastasis, tumor size, and tumor site.

Results: The expression of FGFR2 mRNA was significantly elevated in OSCC tissues compared to normal tissues (3.5-fold increase). Statistical analysis revealed no significant correlation between FGFR2 mRNA expression and the aforementioned features, except for lymph node metastasis (LNM). OSCC tumors with positive LNM exhibited significantly higher FGFR2 mRNA levels. IHC data demonstrated differential expression of FGFR2 protein in the normal tissue biopsies (negative), tumor tissues with negative LNM (++) and tumor tissues with positive LNM (+++).

Conclusion: Previous studies indicate that the presence of even a single positive cervical lymph node is associated with a 50% reduction in overall survival. The differential expression of FGFR2 mRNA and protein in OSCC tumor biopsies with varying LNM status suggests that FGFR2 may serve as a valuable prognostic and diagnostic marker in the progression of OSCC.

Keywords: FGFR2, Oral squamous cell carcinoma, Lymph node metastasis

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Abstract: A-10-2203-1

Evaluation of Gene and Protein Expression Profiles of IGF-1 Axis Mediators and Mmp-9 in Patients with Primary Malignant and Benign Bone Tumors

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Background: Primary bone tumors, classified as sarcomas, can be categorized into benign and malignant types based on their genetic and histological characteristics, exemplified by giant cell tumors (GCT) and Ewing sarcoma. The insulin-like growth factor-1 (IGF-1) axis, a crucial component of the endocrine system, comprises ligands (such as IGF-1), receptors (such as IGF-1R), and binding proteins (including IGFBP-1 and IGFBP-3). Various studies have highlighted the role of the IGF-1 axis in both normal physiology and pathological conditions. This study aims to investigate the involvement of the IGF-1 axis in primary bone tumors.

Methods: A total of sixty patients with primary bone tumors, including Ewing sarcoma and GCT, were enrolled, along with thirty healthy control subjects. Enzyme-linked immunosorbent assay (ELISA) was utilized to measure circulating levels of IGF-1, IGFBP-1, and IGFBP-3. Furthermore, local gene and protein expressions of IGF-1R and MMP-9 were evaluated using quantitative reverse transcription polymerase chain reaction (qRT-PCR) and immunohistochemistry in tumor tissues and adjacent non-cancerous margins.

Results: Significant elevations in serum levels of IGF-1, IGFBP-1, and IGFBP-3 were observed in patients with Ewing sarcoma and GCT, with these increases correlating with indicators of tumor severity, including high tumor grade, metastasis, chemotherapy treatment, and tumor recurrence. Gene and protein expression analyses revealed markedly increased levels of IGF-1R and MMP-9, particularly in Ewing sarcoma patients, which were positively associated with severe tumor conditions. Additionally, receiver operating characteristic (ROC) curve analyses demonstrated the remarkable potential of components of the IGF-1 axis and MMP-9 to differentiate between bone neoplasms and normal tissues, as well as between malignant and benign tumors.

Conclusion: The findings indicate that IGF-1, IGFBP-1, IGFBP-3, IGF-1R, and MMP-9 levels are elevated in primary bone tumors and correlate with tumor aggressiveness. Collectively, these results suggest that mediators of the IGF-1 axis hold promise as biomarkers for Ewing sarcoma and GCT and may serve as therapeutic targets in the management of primary bone tumors.

Keywords: Primary bone tumor, IGF-1 axis, MMP-9

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Abstract: A-10-2686-1

Regulatory Effects of Catalytic Inhibitors of IMPDH on Its Expression and Cytoophidia Dynamics in K562 Cells

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Background: Inosine 5'-monophosphate dehydrogenase (IMPDH) is a critical enzyme in the guanine nucleotide biosynthesis pathway, and its dysregulation has been associated with various cancers. Cytoophidia, the filamentous structures formed by IMPDH, serve as regulatory elements and are involved in multiple cellular functions; however, their modulation is not yet fully understood. While mycophenolic acid (MPA) and ribavirin (RIBA) are known inhibitors of IMPDH, the comprehensive effects of these compounds on IMPDH protein expression and cytoophidia dynamics in K562 cells remain unclear. This study aimed to investigate how MPA and RIBA influence IMPDH protein levels, enzymatic activity, and the formation and size of cytoophidia in K562 cells to enhance our understanding of the regulatory mechanisms affected by these compounds.

Methods: K562 cells were treated with MPA (2 µM) and RIBA (2.5 µM). Following treatment, IMPDH protein expression was assessed using Western blotting. The enzymatic activity was measured by monitoring NADH formation at 340 nm. Additionally, cytoophidia formation and sizes were evaluated using immunofluorescence imaging techniques.

Results: Treatment with MPA and RIBA resulted in a significant increase in IMPDH protein levels while simultaneously reducing its enzymatic activity. Both compounds significantly enhanced the formation of IMPDH cytoophidia but reduced their sizes.

Conclusion: MPA and RIBA markedly elevate IMPDH protein levels while diminishing its enzymatic activity, leading to substantial changes in cytoophidia dynamics in K562 cells. These findings reveal a complex regulatory mechanism and provide new insights into the modulation of IMPDH, a crucial enzyme in cancer, by MPA and RIBA. This modulation may have therapeutic implications for cancer management.

Keywords: Cytoophidia, IMPDH, Mycophenolic acid, Ribavirin

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Abstract: A-10-2690-1

Sex Hormone-Dependent Modulation of Nrf2 and Its Association With Apoptosis, Metastasis and Drug Resistance in Hepatocellular Carcinoma

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Background: Cancer cells adapt to oxidative stress by increasing the expression of nuclear factor erythroid 2-related factor 2 (Nrf2), which is linked to enhanced metastasis, drug resistance, and evasion of apoptosis. This study aimed to examine the impact of sex hormones, specifically testosterone and β-estradiol, on Nrf2 levels in relation to factors associated with metastasis, apoptosis, and drug resistance in the HepG2 cell line, a model for hepatocellular carcinoma (HCC). This focus arises from the higher prevalence of HCC in men compared to women.

Methods: The study utilized testosterone and β-estradiol hormones alongside the HepG2 cell line. The MTT assay was employed to determine the optimal hormone concentration for treatment (IC50). The oxidative stress status was assessed by measuring total antioxidant capacity (TAC), total oxidant status (TOS), and malondialdehyde (MDA) levels. Flow cytometry was used to investigate apoptosis, and the expression levels of Nrf2, MRP-1, MMP-9, Bcl-2, and Sirt1 genes in HepG2 cells were evaluated using real-time PCR.

Results: β-estradiol exhibited a more potent effect in inducing apoptosis and demonstrated a greater capacity for reducing oxidative stress markers compared to testosterone in the HepG2 cell model. Treatment with β-estradiol significantly decreased the expression of Nrf2, MRP-1, MMP-9, and Bcl-2 genes associated with cell survival and metastasis, whereas testosterone did not significantly affect these genes.

Conclusion: The findings of this research highlight the hepatoprotective effects of β-estradiol in contrast to testosterone, as it reduces oxidative stress and modulates key genes associated with cancer cell survival, apoptosis, invasion, and drug resistance.

Keywords: Non-alcoholic fatty liver, Lipid droplets, Sex hormones

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Abstract: A-10-2699-1

Augmentation of Arl13b-IMPDH Interaction Is Linked To IMPDH-Based Cytoophidia formation in Ribavirin-Treated MCF-7

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Background: Inosine monophosphate dehydrogenase, IMPDH, is the rate-limiting enzyme in de novo biosynthesis of guanine nucleotide. IMPDH can form cytoophidium, an organelle-like macrostructure consisting of filamented IMPDH, which makes it more productive. On the other hand, IMPDH interaction with ADP-ribosylation factor-like protein 13B, ARL13B, directs purine biosynthesis toward the de novo pathway essential for highly proliferative cells.

Methods: Here, we investigated the correlation between the cytoophidia formation ability of IMPDH, ARL13B-IMPDH interaction, and cell viability in MCF-7 cells treated with different concentrations of Ribavirin, an IMPDH inhibitor, using Immunofluorescent, Co-Immunoprecipitation, and MTT assays respectively.

Results: The results showed that at a Ribavirin concentration of 4 µM with the highest amount of cytoophidia, the ARL13B-IMPDH interaction increases approximately two-fold over control. This interaction decreased in Ribavirin IC50, proportional to the cytoophidia formation ability of IMPDH. The positive correlation between ARL13B-IMPDH interaction and cytoophidia formation was further confirmed using two other IMPDH inhibitors, Mycophenolic acid and Mizoribine, as well as in mitogen-activated T cells.

Conclusion: Setting up the correlation between the induction of cytoophidia, de novo purine biosynthesis, and cell growth at low concentrations of IMPDH inhibitors, would certainly be useful in the dose management of IMPDH inhibitors for more efficient cancer therapies.

Keywords: IMPDH, Cytoophidia, ARL13B, Purine metabolism, Cancer

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Abstract: A-10-2162-1

Serum Levels of Oxidative Stress, IL-8, and Pepsinogen I/ii Ratio in Helicobacter Pylori and Gastric Cancer Patients: Potential Diagnostic Biomarkers

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Background: Helicobacter pylori (H.pylori), is a gram-negative bacterial pathogen that is associated with an increased risk of gastric cancer. This study investigates potential factors in the incidence of gastric cancer in patients with H.pylori, including oxidative stress, inflammatory biomarkers, serum pepsinogens (PGs), and PG-I/PG-II ratio.
Methods: The study comprised individuals with Helicobacter pylori (H.pylori) infection, gastric cancer patients, and healthy individuals. Biochemical parameters like FBS, triglycerides, cholesterol, and HDL were assessed using enzymatic techniques. Oxidative markers such as total oxidant status (TOS) and malondialdehyde (MDA) were quantified through colorimetric methods. Additionally, IL-8, PG-II, and PG-II levels were determined using the ELISA technique.
Results: Elevated IL-8 and oxidative stress levels were noted in individuals with H.pylori compared to those with gastric cancer. Although gastric cancer patients exhibited lower levels of oxidative stress and inflammation than H.pylori patients, they showed higher levels of MDA. H.pylori patients displayed higher levels of PG-I, PG-II, and PG-I/PG-II compared to gastric cancer patients. The study group established three threshold values for IL-8, PGI, PGII, and PGI/PGII parameters. The findings were substantiated using various data analysis platforms such as Gene Expression Profiling Interactive Analysis (GEPIA), UALCAN, cBioPortal, and TIMER. Based on the cut-off values derived from ROC curves for IL-8, PGI, PGII, and PGI/PGII across the three groups, these parameters could serve as potential diagnostic biomarkers for screening and therapeutic interventions.
Conclusion: IL-8, PGI, PGII, and PGI/PGII parameters could serve as potential diagnostic markers for the screening and treatment of gastric conditions.

Keywords: Helicobacter pylori, Gastric cancer, Pepsinogen-I, Pepsinogen-I, PG-I/PG-II Interleukin-8

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2636-1

Non-coding RNAs Correlated to Hepatoma-Derived Growth Factor in Ovarian Cancer Patients

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Background: Ovarian cancer is the most lethal gynecological malignancy, with a dismal 5-year survival rate of only 30%, primarily due to late-stage diagnosis. With 80% of cases detected at advanced stages, there is an urgent need for novel biomarkers to improve early detection. Hepatoma-derived growth factor (HDGF) is known to play a significant role in cancer progression; however, its dysregulation in ovarian cancer remains poorly understood. This study aims to investigate HDGF expression in ovarian cancer and to develop a competing endogenous RNA (ceRNA) network to elucidate the underlying regulatory mechanisms, with the goal of establishing HDGF as a novel biomarker for improved diagnosis and treatment.

Methods: Fifty ovarian cancer tissue samples and fifty normal ovarian tissue samples were collected from patients at Rasool-e-Akram Hospital, with histopathological verification. Preoperative serum samples were also obtained. HDGF-targeting miRNAs were predicted using the miRDB database, and a gene-miRNA-lncRNA network was constructed using the LNCipedia and GEPIA2 databases. RNA was extracted and analyzed via quantitative RT-PCR (qRT-PCR), while serum levels of HDGF, HE4, and CA125 were measured using ELISA. Statistical analysis was performed with SPSS and GraphPad Prism, with significance set at $P < 0.05$.

Results: HDGF expression was significantly upregulated in ovarian cancer tissues compared to normal ovarian tissues ($p < 0.001$). A negative correlation was observed between HDGF expression and miR-345-5p, while a positive correlation was noted with LINC00839, indicating that LINC00839 may function as a ceRNA for miR-345-5p. Receiver operating characteristic (ROC) analysis suggested that although HDGF has potential as a diagnostic marker for ovarian cancer, it is less effective than CA-125 or HE4.

Conclusion: This study is the first to investigate HDGF expression in ovarian cancer tissues and proposes its serum level as a potential diagnostic biomarker. Further research is required to explore the cellular and molecular mechanisms by which HDGF contributes to carcinogenesis and tumor progression, as well as to validate its efficacy as a biomarker in larger patient cohorts.

Keywords: Ovarian cancer, Hepatoma-derived growth factor, LINC00839, miR-345-5p, miR-384

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Abstract: A-10-2766-1

Ndufs8: Specific Potential Gene Based on TCGA Datasets in Acute Myeloid Leukemia and Bioinformatics Analysis of Its Cerna Network

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Background: Acute myeloid leukemia (AML) is a heterogeneous hematological malignancy characterized by diverse genetic alterations. This study aimed to investigate crucial miRNAs, transcription factors (TFs), and circular RNAs (circRNAs) associated with hub genes involved in AML survival, focusing on identifying potential biomarkers for diagnosis and treatment.

Methods: The TCGA LAML dataset from GEPIA2 was utilized to identify differentially expressed genes (DEGs) associated with AML through high-throughput RNA sequencing data. A protein-protein interaction (PPI) network of significant genes was constructed using STRING and analyzed in Cytoscape. Hub genes with higher connectivity were selected, and pan-cancer analysis using GEPIA2 and UALCAN revealed NDUFS8 as a key gene. The hTFtarget database was employed to identify transcription factors associated with NDUFS8, relevant to blood and bone marrow. Additionally, miRNAs regulating NDUFS8 were identified using miRTarBase, TargetScan, miRDB, and miRWalk, while circRNAs were sourced from the circBank database. A competing endogenous RNA (ceRNA) network encompassing selected genes, their TFs, miRNAs, and circRNAs was established in Cytoscape, with hub nodes identified for further analysis.

Results: From the 7,965 genes obtained from the TCGA RNA-seq data, 843 genes were considered significant. Eight hub genes were identified, with pan-cancer analysis showing that NDUFS8 was significantly downregulated compared to normal samples and other cancers. A total of 93 transcription factors associated with blood and bone marrow were identified, along with 25 miRNAs from three databases (16 from TargetScan, eight from miRWalk, and one from miRTarBase), and seven circRNAs (including hsa_circ_0023138, hsa_circ_0023139, hsa_circ_0096261, hsa_circ_0023140, hsa_circ_0023141, hsa_circ_0023142, and hsa_circ_0023143). The ceRNA network was designed, and hub nodes were identified.

Conclusion: This study highlights NDUFS8 as a differentially expressed gene in AML, demonstrating a significant negative impact on overall survival. The diagnostic potential of NDUFS8 and its involvement in the ceRNA network suggest that it may serve as a reliable biomarker for diagnosing AML and monitoring treatment responses. Furthermore, NDUFS8 represents a promising target for future AML therapies.

Keywords: Acute myeloid leukemia, TCGA, bioinformatics, miRNA, circRNA, transcription factors

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Abstract: A-10-2824-2

Thymoquinone Reversed Doxorubicin Resistance in U87 Glioblastoma Cells Via Targeting PI3K/AKT/mTOR Signaling

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Background: Natural compounds like Thymoquinone (TQ) have garnered increasing interest in treating Glioblastoma (GBM), one of the most aggressive brain cancers. However, the role of TQ in reversing drug resistance in GBM, particularly resistance to Doxorubicin (DOX), remains incompletely understood. This study aimed to investigate the effects of TQ on DOX-resistant GBM cells and its involvement in modulating the PI3K/Akt/mTOR pathway, a key signaling pathway in cancer progression and drug resistance.
Methods: GBM cell lines, U87 (sensitive to DOX) and U87/DOX (DOX-resistant), were treated with DOX and TQ, either individually or in combination. Cell proliferation was measured using the MTT assay, while apoptosis was evaluated by ELISA. Expression levels of apoptotic mediators (Caspase-3, Bax, Bcl-2) and key components of the PI3K/Akt/mTOR signaling pathway, along with P-gp and PTEN, were assessed via qRT-PCR and western blot analysis.
Results: TQ enhanced the cytotoxic effects of DOX in a dose-dependent manner, suppressing cell proliferation in both U87 and U87/DOX cells. In resistant U87/DOX cells, TQ significantly increased DOX-induced apoptosis, as evidenced by modulation of pro-apoptotic markers (Caspase-3, Bax) and downregulation of the anti-apoptotic protein Bcl-2. Furthermore, TQ combined with DOX upregulated PTEN expression while downregulating PI3K, Akt, and mTOR levels, effectively inhibiting the PI3K/Akt/mTOR signaling pathway, which is commonly associated with drug resistance.
Conclusion: Thymoquinone significantly potentiates the antiproliferative and pro-apoptotic effects of Doxorubicin in DOX-resistant glioblastoma cells by targeting and suppressing the PI3K/Akt/mTOR signaling pathway. This suggests that TQ could serve as an effective adjuvant therapy in overcoming drug resistance in GBM treatment.

Keywords: Glioblastoma, Thymoquinone, Doxorubicin resistance, Apoptosis PI3K/Akt/mTOR pathway

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Abstract: A-10-2793-1

Investigating the Anticancer Effects of the NAPRT Inhibitor on Breast Cancer Cells

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Background: Breast cancer is the most common malignancy and the leading cause of cancer-related death among women worldwide. A hallmark of cancer cells is altered metabolism, including persistent NAD biosynthesis, which supports the increased proliferation, invasion, and metastasis of malignant cells. The Preiss-Handler pathway, a key route for NAD production, is regulated by the enzyme nicotinate phosphoribosyl transferase (NAPRT). This study aims to explore the effects of 2-hydroxy nicotinic acid (2-HNA), an inhibitor of NAPRT, on breast cancer cell survival, apoptosis, and metastasis.

Methods: Breast cancer cell lines MCF-7 and MDA-MB-231 were cultured and treated with 2-HNA. Cell viability was measured using the MTT assay to determine the IC50 values of the inhibitor and assess its effects. Apoptosis was analyzed by flow cytometry using Annexin V staining. Real-time PCR was employed to examine the expression of pro-apoptotic genes (p21, BAX, and p53) after RNA extraction and cDNA synthesis using specific primers. Cell migration was evaluated using scratch assays, while invasion capability was tested through Matrigel penetration assays.

Results: Treatment with 2-HNA significantly decreased cell viability in both MCF-7 and MDA-MB-231 breast cancer cell lines in a dose-dependent manner. The compound induced apoptosis in the treated cells, with an increase in the expression of pro-apoptotic genes p21, BAX, and p53. Furthermore, 2-HNA effectively reduced the invasion and migration capacities of the breast cancer cells.

Conclusion: The NAPRT inhibitor 2-HNA shows promising potential in reducing cell viability, inducing apoptosis, and inhibiting metastasis in breast cancer cells.

Keywords: Keywords: Breast cancer, NAD, NAPRT, 2-HNA, Apoptosis, Real Time PCR.

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Abstract: A-10-2712-1

Distinctive Effect of Obeticholic Acid on the McF-7 Cell Line

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Background: Obeticholic acid (OCA) is a semi-synthetic bile acid and a specific ligand for the farnesoid X receptor (FXR), playing a key role in lipid metabolism. FXR, particularly expressed in hepatobiliary tissues, regulates lipid homeostasis by decreasing lipogenesis and increasing lipolysis upon activation. However, studies suggest that OCA may exert effects on other cellular receptors beyond FXR. This study aimed to investigate FXR activation in the MCF-7 breast cancer cell line following treatment with OCA.

Methods: MCF-7 cells were treated with 0.1 µM OCA for 24 hours. The effects of OCA on cell viability were assessed using the MTT assay. Protein levels of FXR and the small heterodimer partner (SHP) were evaluated by western blot analysis. Additionally, gene expression levels of SHP, sterol regulatory element-binding protein-1c (SREBP1C), fatty acid synthase (FAS), and acetyl-CoA carboxylase (ACC) were measured using real-time PCR.

Results: The MTT assay demonstrated that OCA concentrations exceeding 75 nM significantly reduced MCF-7 cell viability. Western blot analysis revealed that OCA treatment decreased the protein levels of FXR by 37.35% and SHP by 47.89%. However, real-time PCR results showed no significant changes in the transcript levels of SHP, SREBP1C, FAS, and ACC genes.

Conclusion: The findings suggest that OCA's effects on MCF-7 breast cancer cells may be independent of FXR activation. The observed reduction in FXR and SHP protein levels might be linked to OCA-induced changes, though further investigation is needed to clarify the underlying mechanisms.

Keywords: Obeticholic acid, MCF-7, FXR

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Abstract: A-10-2850-1

Exosomal Delivery of Mir-155 Inhibitor Can Suppress Migration, Invasion, and Angiogenesis Via PTEN and Dusp14

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Background: Triple-Negative Breast Cancer (TNBC) is the most aggressive subtype of breast cancer, often lacking effective treatment options. Angiogenesis, the process of new blood vessel formation, plays a key role in TNBC progression by supporting tumor growth and metastasis. MicroRNA-155 (miR-155) has been implicated in promoting angiogenesis, tumor invasion, and metastasis in TNBC. Exosomes, nano-sized vesicles that transport molecular cargo like miRNAs, offer a promising therapeutic vehicle for targeting specific genes. This study aimed to investigate the effect of exosomal delivery of miR-155 antagomir (an inhibitor of miR-155) on TNBC cell migration, invasion, and angiogenesis.

Methods: Exosomes were isolated from MDA-MB-231 TNBC cells, characterized, and loaded with miR-155 antagomir using electroporation. RT-qPCR was performed to evaluate the expression of miR-155 and its target genes, phosphatase and tensin homolog (PTEN) and dual specificity phosphatase 14 (DUSP14). Cell migration and invasion were assessed using wound-healing and transwell assays, while angiogenesis was evaluated through tube formation and chorioallantoic membrane (CAM) assays.

Results: Exosomal delivery of miR-155 antagomir to human umbilical vein endothelial cells (HUVECs) significantly reduced miR-155 expression and upregulated its target genes PTEN and DUSP14. The tube formation capacity of HUVEC cells, an indicator of angiogenesis, was significantly impaired by exosomes containing miR-155 antagomirs, and these results were further confirmed in the CAM assay. Additionally, the migration and invasion of MDA-MB-231 cells were substantially reduced following treatment with miR-155 antagomir-loaded exosomes.

Conclusion: This study demonstrates that the exosomal delivery of miR-155 antagomir can effectively inhibit tumor migration, invasion, and angiogenesis in TNBC by regulating key genes such as PTEN and DUSP14.

Keywords: Exosome, miR-155, PTEN, DUSP14, TNBC

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Abstract: A-10-2550-1

Synthesis of SLN Nanoparticles Containing Naringenin Decorated with Folate-Conjugated Chitosan to Evaluate Its Anticancer Effects

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Background: This study aimed to encapsulate naringenin in lipid nanoparticles and investigate the toxic effects of solid lipid nanoparticles containing naringenin compared to surface-modified nanoparticles with chitosan-folate and the free drug.

Methods: Nanoparticles composed of SLN and naringenin were coated with chitosan folate, and their physical and chemical properties were evaluated using DLS, FTIR, and electron microscopy. Drug encapsulation and folate binding were measured using the spectrophotometric absorption method. The toxicity and inhibitory pathways in cancer cells were examined.

Results: The results of this investigation revealed a higher toxic effect of chitosan folate-coated nanoparticles on breast cancer cells, which may be attributed to the transfer and internalization of nanoparticles into breast cancer cells as they possess positive folate receptors. Evaluation of the effects of nanoparticles on angiogenesis using the CAM method demonstrated a decrease in the average number and length of blood vessels, as well as a decrease in embryo height and weight. Increased expression of p53, decreased expression of NFKB, and the results of AO/PI staining, along with an increased level of ROS in cells treated with nanoparticles, confirmed the induction of apoptosis by nanoparticles. The antibacterial test results also confirmed the inhibitory effects of nanoparticles on various strains of bacteria.

Conclusion: These findings highlight the potential of nanoparticle-based treatments in preclinical research and demonstrate their effectiveness in suppressing cancer cells and combating bacterial strains.

Keywords: Naringenin, Breast cancer cells, Angiogenesis, CAM method, Reactive Oxygen Species, Apoptosis

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Abstract: A-10-2550-2

The Anticancer Role of Cerium Oxide Nanoparticles by Inducing Antioxidant Activity in Esophageal Cancer and Stem Cell-Like Cell Lines

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Background: Esophagus squamous cell carcinoma (ESCC) has a poor prognosis, a high rate of metastasis, and rapid clinical progression. One hypothesis is that therapeutic failure is due to the presence of cancer stem cells (CSC). Previous studies showed the anti-cancer effect of Cerium oxide nanoparticles (CNP) in different cancer cells. In this study, we aim to evaluate the effect of cerium oxide nanoparticles on cell antioxidant level, toxicity, as well as cell oxidant level in esophageal cancer (YM1) and cancer stem cell-like (CSC-LC) cell lines.

Methods: YM1 and CSC-LC cell lines were treated with CNP at different concentrations. The cell viability was assessed by using the MTT test. Antioxidant levels including, SOD (superoxide dismutase, CAT (catalase), thiol, and TAC (total antioxidant capacity) expression, ROS (reactive oxygen species), and MDA (malondialdehyde) levels were assessed in both cell lines.

Results: CSC-LC had significantly elevated SOX4 and OCT4 pluripotency genes. The ROS and MDA levels were significantly reduced in both YM1 and CSC-LC cell lines after treatment with CNP. Also, the anti-oxidant levels and expressions were elevated significantly in both cell lines after CNP treatment.

Conclusion: These results suggest the potential anti-cancer effect of CNP by elevating antioxidant levels and expression, and reducing oxidant levels.

Keywords: Antioxidant, Cancer stem cell, Cerium oxide, Esophageal cancer

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Abstract: A-10-2525-2

Curcumin Loading on Graphene Oxide and Chitosan Nanoparticles to Evaluate the Induction of Cytotoxicity and Apoptosis in Esophageal Squamous Cell Carcinoma

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Background: Esophageal cancer (EC) is a highly malignant gastrointestinal malignancy with a poor prognosis and high mortality rates. Conventional anti-cancer drug delivery techniques have limitations, prompting the exploration of novel drug delivery systems such as nanoparticles (NPs). Curcumin, extracted from the rhizomes of turmeric (Curcuma longa L.), is a natural polyphenol with potent pharmacological effects. Curcumin has shown significant anti-cancer properties in vitro and in vivo through various mechanisms of action.
Methods: The particle size of Cur-BCD-MGO-CS NPs was on average 250 nm, with a negative surface charge, an Index of dispersion of 0.2, and also showed high loading capacity toward Curcumin. In this context, loading curcumin onto graphene oxide nanoparticles (a single layer of carbon atoms arranged in a hexagonal lattice) and chitosan (a biodegradable and biocompatible natural polymer) presents a novel strategy to target esophageal cancer cells, induce cytotoxicity, and promote apoptosis. We carried out the Resazurin assay to assess nanoparticle toxicity, identified apoptosis using real-time PCR, and measured the antioxidant properties of nanoparticles through TAC and CAT assays.
Results: The 50% cell growth inhibition (IC50) of nanoparticles against two Esophageal cancer cell lines including KYSE-30 and YM1 were obtained as 65 µg/mL and 89 µg/mL respectively. Cancer Cell treatment with nanoparticles at 40 and 20 µg/mL increased the expression genes encoding BAX, BCL2, and p53 in prostate cancer cells.
Conclusion: By utilizing these nanoparticles, there is potential to improve the treatment outcomes for esophageal cancer patients. Future research and development in this area could lead to more effective and personalized treatment options for this challenging disease.

Keywords: Esophageal cancer, drug delivery, nanoparticles, curcumin, graphene oxide, chitosan

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Abstract: A-10-2381-1

Selenium Nanoparticles Influence Astaxanthin Production in Haematococcus Lacustris

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Background: Haematococcus lacustris, a microalga of significant interest, produces the valuable pigment astaxanthin under stress conditions. Factors like heavy metals and culture conditions impact its growth and astaxanthin synthesis. In this study, we investigated the effects of selenium nanoparticles (SeNPs) on H. lacustris biomass and astaxanthin content.

Methods: We cultured H. lacustris in BBM medium at 25±1°C, with 100 µmol photons m−2 s−1 illumination (16 h light/8 h dark). SeNPs were inoculated at the end of the log phase, with concentrations of 0 (control), 40, and 80 mg L-1 (three replications). Growth rate was assessed through cell counting and culture absorbance over 15 days. We measured chlorophyll a and b, total carotenoids, and astaxanthin content using the method from Azizi et al. (2019)[1].

Results: SeNPs significantly reduced growth rate, chlorophyll levels, total carotenoids, and astaxanthin content in both 40 and 80 mg L-1 treatments. Astaxanthin content decreased by 50% and 65%, respectively. Interestingly, microalgae proliferation rebounded after a week of SeNP inoculation.

Conclusion: Our study highlights the negative impact of SeNPs on H. lacustris biomass and astaxanthin production. While other nanoparticles enhance astaxanthin accumulation, our results differ from those with zinc oxide nanoparticles. We recommend using lower SeNP concentrations to achieve higher astaxanthin content. A distinctive nutrient design, combined with a statistical approach and a light-feeding strategy, is suggested to improve Haematococcus pluvialis growth performance and astaxanthin accumulation.

Keywords: Haematococcus lacustris, astaxanthin, selenium, nanoparticl

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Abstract: A-10-2301-1

Colorimetric Detection and Determination of Glucose in Human Serum by Peroxidase Mimic Activity of Pt@MOF-808

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Background: Blood sugar or diabetes is one of the chronic diseases that can be encountered at any age and is a concern of a significant number of developed countries today. HRP is an enzyme that is widely used in biosensors, especially in glucose diagnostic kits. Many patients with diabetes use this type of kit to determine their blood sugar level. Unfortunately, enzymes also have limitations that prevent their widespread use, such as limited stability and denaturation with increasing temperature. They are also affected by poisons and drugs. Therefore, the main goal in this study was to overcome the mentioned problems, and use enzyme-like substances that have peroxidase-like properties in glucose detection kits. In this project, the peroxidation effect of Pt@MOF-808 was innovatively used in the preparation of glucose detemination kit.

Methods: Pt@MOF-808 was first synthesized using a hydrothermal and simple stirring method, then FT-IR, SEM, and XRD were used to confirm characteristics of MOF-808 and Pt@MOF-808. The peroxidation property of Pt@MOF-808 was tested using a TMB+H2O2 system in an acetate buffer. Subsequently, effective factors in the peroxidation property, including time, pH, TMB concentration, hydrogen peroxide concentration, and amount of Pt@MOF-808, were investigated to optimize the measurement conditions. Ultimately, glucose was measured experimentally and in real samples of human serum using Pt@MOF-808 peroxidation property. To achieve this, a calibration curve was created, and the linear range, LOD, LOQ, and recovery values were computed.

Results: Pt@MOF-808 was synthesized and characterized successfully. The method demonstrated a linear range of 0-0.5 µM with a detection limit of 0.82 nM and detection quantification of 2.467 nM. Analysis of glucose in human serum samples yielded acceptable and excellent recovery values.

Conclusion: In summary, Pt@MOF-808 exhibited strong peroxidase activity and was able to successfully develop a sensitive colorimetric method for glucose detection.

Keywords: colorimetry, measurement, MOF-808, Pt@MOF-808, glucose

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Abstract: A-10-2544-1

Fabrication, Optimization, and Biochemical Characterization of Biomimetic Hybrid Cartilage-Polymer Scaffold for Cartilage Tissue Engineering Application

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Background: Osteoarthritis (OA) is a widespread chronic disease defined by the gradual deterioration of articular cartilage, resulting in reduced quality of life and social expenses. No conventional method has proven its ability to restore the injured hyaline cartilage. Decellularized ECM has achieved interest as a potential scaffold for cartilage tissue engineering approaches. The decellularized cartilage-derived matrix (CDM) scaffold retains the native architecture and composition of hyaline cartilage tissue, providing a conducive microenvironment for cellular growth and differentiation but revealing restricted mechanical support.

Methods: Our investigation involved the fabrication of a hybrid CDM-polyvinyl alcohol (PVA) hydrogel scaffold, followed by a comprehensive characterization of the construct's physicochemical, mechanical, and biological properties such as histological analysis, compressive test, FESEM, EDX, FTIR, DSC, XRD, and viability assay to elucidate its potential in cartilage regeneration applications.

Results: Our results showed that hybridizing the CDM with PVA improved the mechanical properties besides appropriate biocompatibility and cell attachment.

Conclusion: Our data has confirmed that our hybrid CDM-PVA scaffold mimics the native cartilaginous matrix, making it a promising candidate for future cartilage tissue engineering investigations.

Keywords: Osteoarthritis, Cartilage, Tissue engineering, Decellularized, CDM

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Abstract: A-10-2560-1

Application of Alginate/Chitosan Hydrogel to Loading of Platelet-Rich Plasma-Derived Exosomes for Wound Healing Purposes

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Background: The management of skin wounds comprises attaining hemostasis of the injury, maintaining a high moisture of the wound bed, absorbing wound exudate and providing oxygen diffusion, and eventually accelerating cutaneous wound healing. During the last decade, attention has been focused on Platelet-rich plasma extracellular vesicles (PRP-Exo), which have the potential to favor proliferation and migration in different cell types. A therapeutic strategy is based on a combination of PRP-Exo with biocompatible materials such as Alginate (Alg) /Chitosan (CS) hydrogel, which acts as a vehicle for sustained application of PRP-Exo and has a positive impact on the speed and quality of wound healing. This study aimed to investigate the effect of PRP-Exo in the process of wound healing and identify whether Alg/CS hydrogel can achieve the high efficiency of PRP-Exo.

Methods: PRP-Exos were successfully isolated by ultracentrifugation method and subsequently characterized by TEM, DLS, and western blotting analysis. Then, we developed Alg/CS hydrogel as the wound dressing to incorporate different concentrations of PRP-Exos and evaluated their morphology, swelling properties, weight loss, and cytocompatibility. Finally, the scratch assay was carried out to test the impact of Alg/CS hydrogel containing PRP-Exo on the migration of fibroblasts.

Results: Our data provided that the fabricated hydrogel was highly porous with interconnected pores. Weight loss assessment confirmed that the prepared hydrogels have suitable biodegradability within 8 days. MTT assay revealed that the hydrogels have no toxicity effect on fibroblasts. Coculturing of cells with Alg/CS hydrogel containing PRP-Exo resulted in a faster wound closure compared with that observed in the hydrogel without PRP-Exo, as shown using scratch assay.

Conclusion: To the best of our knowledge, this study substantiated the synergistic effects of Alg/CS hydrogel loaded with PRP-Exo and suggested the probability of using Alg/CS/PRP-Exo hydrogel as the material of choice for the treatment of skin injuries.

Keywords: Wound healing, Fibroblast, Alginate, Chitosan, Hydrogel, Platelet Rich Plasma, Exosome

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Abstract: A-10-2606-1

Detection of Superoxide Anion Based on the Cytochrome c Immobilization onto Carboxylated Carbon Nanotube Field Effect Transistor

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Background: Detecting superoxide anion is crucial for understanding oxidative stress in biological systems. Therefore, developing superoxide anion biosensors with enhanced sensitivity and specificity is needed. The immobilization of cytochrome c (Cyt c) onto carboxylated multi-wall carbon nanotube field effect transistors (cMWCNT-FETs) provides a suitable strategy for superoxide anion detection.
Methods: The initial stage involved the functionalization of MWCNT through acid treatment with 35% nitric acid. Then, a suspension of carboxylated MWCNT (cMWCNT) in dimethyl formamide was prepared and used to modify the surface of FET. In the next step, a Bio-FET was fabricated utilizing Cyt c immobilization onto cMWCNT modified FET (Cyt c/cMWCNT-FET). The performance of the Cyt c/cMWCNT-FET was examined and the output current was recorded under various conditions such as different concentrations of cMWCNTs and pH using a linear sweep voltammetry technique. To detect the superoxide anion, different concentrations of superoxide anion were made using a solution of potassium superoxide salt in dimethyl sulfoxide and added to the surface of Cyt c/cMWCNT-FET, then output currents were recorded using the amperometric technique.
Results: Carboxylation of carbon nanotubes was confirmed through Fourier-transform infrared spectroscopy (FT-IR). To determine the electrical characteristics of Bio-FET, the (I-V) curves were recorded under the various gate biases (0.5, 1, 1.5, 2, 2.5 V). The Bio-FET showed typical behavior of a P-type FET. Field-emission scanning electron microscopy (FE-SEM) was used to evaluate the surface morphology of cMWCNT-FET and Cytc/cMWCNT-FET. Immobilized Cyt c, as a biological recognition element, was used to detect the superoxide anion due to its heme group and oxidation ability in the presence of superoxide anion, which resulted in changes related to the current flowing through the Bio-FET channel.
Conclusion: Here, a novel and cost-effective Bio-FET biosensor (Cyt c/cMWCNT-FET), with high sensitivity and specificity was developed for detecting superoxide anions.

Keywords: Biosensor, Superoxide anion, Cytochrome c, Field effect transistor, Carboxylated carbon nanotube.

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Abstract: A-10-2622-1

Investigating the Cytotoxic Effects of Synthesized Green Cerium Oxide Nanoparticles on Glioma and Normal Fibroblast Cells: Separation of Nanoparticles by A Different and New Method

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Background: Glioblastoma, the most common and malignant type of brain tumor, is a major challenge for the health system. This tumor has several treatment methods, one of which is the targeted delivery of drugs with the help of nanoparticles. Recently, cerium oxide nanoparticles (CONPs) have gained great fame in biomedicine due to their cytotoxicity and distinct therapeutic potential. For the first time, this study performs the process of separating these nanoparticles using a different extract and then evaluates the antioxidant and pro-oxidant effects of green nanoparticles on normal and cancer cell lines.

Methods: CONPs were synthesized from flax seed extract (Linum usitatissimum L.) and characterized using UV-Vis, FT-IR, FESEM/PSA, EDAX, and XRD techniques. MTT assay and DCFH-DA dye were used to measure cytotoxicity and intracellular reactive oxygen species (ROS) levels, respectively. Finally, by performing bioinformatics studies, the possibility of the drug passing through the blood-brain barrier was investigated.

Results: FESEM/PSA analysis showed spherical nanoparticles with an average size of 52.51 nm. FT-IR analysis showed that the synthesized CONPs have a pure and crystalline structure. CONPs showed no cytotoxic effect on human normal fibroblast (HFF) cells while inhibiting the growth of glioblastoma multiforme (U87) cells. Furthermore, CONPs significantly increased the intracellular ROS levels in U87 cells compared to the control group. Also, bioinformatic analyses showed that this nanoparticle can effectively cross the blood-brain barrier.

Conclusion: CONPs prevented the growth of U87 cancer cells by increasing ROS levels, while they did not affect intracellular ROS levels in HFF cells at the same concentration. Additionally, the ability of this nanoparticle to pass through the blood-brain barrier was shown. This drug has the potential to be used in targeted drug delivery methods. Finally, this nanoparticle has significant anti-cancer effects and can be effective in the delivery of various drugs.

Keywords: Cerium oxide nanoparticles, Glioblastoma, Green synthesis method, Reactive oxygen species

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Abstract: A-10-2674-1

The Design and Synthesis of An Antibacterial Composite Hydrogel Based on Gelatin/amniotic Membrane/aminophylline and the Evaluation of Its Biocompatibility in the Presence of Mesenchymal Stem Cells

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Background: Hydrogel scaffolds have shown great promise in various biomedical applications, particularly in tissue. engineering and regenerative medicine. This study aimed to synthesize novel antibacterial hydrogels using a combination of gelatin (Gel), amniotic membrane extract (AME), and aminophylline (AMP) drug. Additionally, the study sought to investigate the survival of human Wharton's jelly mesenchymal stem cells (hWJMSCs) on these composite hydrogels.

Methods: Hydrogel was synthesized using the freeze-drying method and crosslinked with glutaraldehyde (Glu). The physicochemical properties of hydrogels were evaluated by various methods and techniques, including Fourier transform infrared spectroscopy (FTIR), field emission scanning electron microscopy (FESEM), biodegradability, water uptake ability, and antibacterial activity. The biocompatibility of hWJMSCs seeded on the hydrogels was evaluated by the MTT assay and acridine orange/ethidium bromide (AO/EB) staining.

Results: The FTIR results showed that all polymers are present in the composite hydrogels. The FESEM results showed that the hWJMSCs have suitable attachment and growth on surface hydrogels and that the average pore size of hydrogels was 153.92 µm. Additionally, after 96 hours, the rate of water uptake and biodegradation of the hydrogels was 54.70% and 86.97%, respectively. The results of the minimum inhibitory concentration (MIC) assay demonstrate that the hydrogels exhibit antibacterial activity against Pseudomonas aeruginosa (P. aeruginosa) and Staphylococcus aureus (S. aureus) due to the presence of penicillin and streptomycin (Pen-Strep) antibiotics in the hydrogels. Furthermore, the MTT assay results show that the hydrogels are biocompatible and do not have a cytotoxic effect on the cell viability of hWJMSCs. The AO/EB staining data confirmed the MTT assay results and showed that hWJMSCs seeded on surface hydrogels have a normal morphology with a clear nucleus and cytoplasm.

Conclusion: In conclusion, the study suggests that antibacterial composite hydrogels with water uptake, biodegradability, and biocompatibility properties could be promising candidates for tissue repair applications, especially neural tissue.

Keywords: Composite hydrogel, Gelatin, Amniotic membrane extract, Aminophylline, Wharton's jelly mesenchymal stem cells.

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Abstract: A-10-2689-1

The Synthesize, Characterize, and Determination of Biological Properties of Gelatin/chitosan Based Composite Hydrogel Containing Diprophylline for Tissue Engineering

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Background: Hydrogel scaffolds have emerged as a promising tool in neural tissue engineering due to their biocompatible properties. Biocompatible scaffolds can enhance cell adhesion, proliferation, and differentiation, ultimately leading to improved neural tissue regeneration outcomes. This study aims to synthesize a new biodegradable and hydrophilic composite hydrogel scaffold based on gelatin (GE), chitosan (CS), umbilical cord serum (UCS), and diprophylline (DPI) drugs. Additionally, this study examined the biocompatibility of the composite hydrogel on human Wharton's jelly mesenchymal stem cells (WJMSCs).
Methods: We synthesized the composite hydrogel scaffold using glutaraldehyde (GLU) as a cross-linking agent. The chemical structure properties of the composite hydrogel scaffold were characterized with various techniques and methods, including X-ray diffraction (XRD), biodegradability, water contact angle, and porosity. The biocompatibility of the composite hydrogels was analyzed with MTT assay and Acridine Orange/ethidium bromide (AO/EB) staining.
Results: The XRD patterns of the composite hydrogel containing DPI showed a semi-crystalline structure. After 72 hours, the result of the biodegradability rate of composite hydrogel containing DPI was 54.67%. The water contact angle result showed that the composite hydrogel containing DPI was categorized as a hydrophilic group. The porosity rate of composite hydrogel containing DPI was 92.47%. Additionally, the MTT assay result showed that the composite hydrogel containing DPI was biocompatible and had no cytotoxic effect on the survival of human WJMSCs. The AO/EB staining results approved MTT assay data and demonstrated that human WJMSCs seeded on composite hydrogel containing DPI had a normal morphology with a clear nucleus and cytoplasm.
Conclusion: This study suggests that the GE-CS-based composite hydrogel containing DPI can be used as an ideal candidate in neural tissue engineering due to its biodegradability, hydrophilicity, and biocompatibility properties.

Keywords: Hydrogel, Gelatin, Chitosan, Umbilical cord serum, Diprophylline, Tissue engineering

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2662-1

Effects of Nano Cerium on Antioxidant Markers in Rats Undergoing Withdrawal

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Background: Drug addiction is a challenging health problem in many countries. Opium is the second most consumed substance in the Middle East and in many Asian countries. Today, opium use is the most common substance abuse in Iran. In this respect, many subjects try to stop opium use. Opium withdrawal refers to the symptoms faced by subjects who are stopping opium use. It has been reported that Nano cerium has mimetic properties of multi-enzymes such as catalase, superoxide oxidase, and oxidase, and is known as an exceptional material in biological fields of drug delivery, biomedicine, and bioanalysis. Hence, this experiment aimed to evaluate the useful effects of Nano cerium in opium withdrawal rats.

Methods: In this experiment, male rats were randomly divided into 3 groups: control, group2: withdrawal, and group3: withdrawal+ Nano cerium. At the end of the experiment, the animals were sacrificed and the liver was removed and used for experiments. The activity of antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase, and catalase were determined by ELISA. The gene expression of SOD, glutathione peroxidase, and catalase were measured by real-time PCR. Antioxidant capacity (TAC), malondialdehyde (MDA), and total oxidation capacity (TOS) were determined. The histological changes were evaluated by a light microscope.

Results: TAC, glutathione, SOD, glutathione peroxidase, and catalase were significantly decreased in withdrawal rats, while the concentration of MDA, and TOS significantly increased in withdrawal rats compared to the control ($p<0.05$). Gene expression and activity of SOD, glutathione peroxidase, and catalase also increased in withdrawal rats ($p<0.05$). However, treatment with Nano cerium significantly increased the Gene expression and activity of SOD, glutathione peroxidase, and catalase in withdrawal rats ($p<0.05$). Nano cerium also normalized histological changes.

Conclusion: This study showed that Nano cerium normalized liver function and histology in withdrawal rats.

Keywords: Antioxidant, glutathione peroxidase, addiction

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2231-3

Biosynthesis of Silver-Doped Zinc Oxide Nanoparticles Using Juniperus Sabina Extract and Their Anticancer Efficacy on Ht29 Colorectal Cancer Cells

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Background: Zinc oxide nanoparticles (ZnO NPs) are notable in cancer research for their unique properties and biocompatibility. Doping ZnO NPs with silver (Ag) enhances their effectiveness as anticancer agents. This study examines the biosynthesis of Ag-doped ZnO NPs using Juniperus sabina extract (JSE@ZnO/Ag NPs) and their cytotoxic effects on HT29 colorectal cancer cells.
Methods: ZnO NPs were synthesized through the coprecipitation method. JSE@ZnO/Ag NPs were synthesized through a green synthesis approach using Juniperus sabina extract, which acted as both a reducing and stabilizing agent. The NPs were characterized by X-ray diffraction (XRD) to assess crystallinity, Fourier-transform infrared spectroscopy (FTIR) to identify functional groups, and transmission electron microscopy (TEM) to examine morphology and size. The anticancer activity was evaluated in HT29 colorectal cancer cells through MTT assays to determine cytotoxicity, with IC50 values calculated for both ZnO and JSE@ZnO/Ag NPS.
Results: The XRD confirmed the crystalline nature of the synthesized ZnO NPs and JSE@ZnO/Ag NPs. FTIR spectra indicated the presence of bioactive compounds from Juniperus sabina involved in JSE@ZnO/Ag NPs stabilization. TEM analysis showed well-dispersed, spherical NPs with a size range of 60-80 nm, and Ag NPs uniformly distributed on the ZnO surface. The MTT assays showed that JSE@ZnO/Ag NPS had an IC50 value of 611 µg/mL, which was significantly lower than the IC50 value of 1024 µg/mL for ZnO NPs alone, indicating enhanced cytotoxicity.
Conclusion: The biosynthesized JSE@ZnO/Ag NPs exhibited superior anticancer activity against HT29 colorectal cancer cells compared to ZnO alone, highlighting their potential as an effective, eco-friendly therapeutic option. Further studies are needed to validate these findings in vivo.

Keywords: Anticancer, Nanoparticles, Zinc oxide, Silver, Juniperus sabina

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Abstract: A-10-2739-1

Separation and Purification of Hyaluronic Acid by Fe_3O_4 Nano and Micro Particles Coated with Chitosan and Silica

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Background: Hyaluronic acid (HA), a glycosaminoglycan, is comprised of alternating units of D-glucuronic acid and N-acetylglucosamine. This compound harbors numerous biomedical applications, including its use in pharmaceuticals, wound healing, osteoarthritis treatment, and drug delivery. Its unique composition and exceptional features, such as its high water-absorbing and retaining capacity, have also led to its use in the cosmetics industry. The employment of this biopolymer has given rise to an escalation in the request for its manufacture
Methods: The present investigation explored the correlation between hyaluronic acid and chitosan and silica for separation. Consequently, iron oxide magnetic nanoparticles and microparticles were produced via the co-precipitation method and were layered with chitosan and silica to purify the hyaluronic acid from the fermentation broth that was generated by Streptococcus Zooepidemicus.
Results: The maximum HA adsorption capacity, under optimal pH conditions of 4, was determined to be 87 mg/g, 112 mg/g, 51 mg/g, and 44 mg/g for Fe_3O_4 -chitosan nanoparticle, Fe_3O_4 -chitosan microparticle, Fe_3O_4 -silica microparticle, and Fe_3O_4-silica nanoparticle, respectively.
Conclusion: The issue of protein contamination, which poses a significant challenge in the purification process of HA, was observed to be significantly reduced by almost 10 times. The findings of this study suggest that the particles coated for HA purification were specific, low-cost, and potentially more compatible with biological systems.

Keywords: Hyaluronic Acid, Purification, Magnetic Particles, Separation, Protein Contamination

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2211-1

Effects of N-Butyl-Deoxynojirimycin on Calreticulin, Calnexin, and Rabies Virus

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Background: N-butyl-deoxynojirimycin, as an iminosugar, inhibits the α-glucosidase enzyme that removes the last glucose from the amino end of the nascent glycoprotein. NB-DNM can block rabies virus glycoprotein binding to calnexin and calreticulin chaperones in the endoplasmic reticulum by omitting the last glucose. Therefore, it prevents the proper folding of rabies virus by chaperones and releasing new viruses. This action stops the maturation of the glycoprotein by chaperones and impedes the packaging of the newly replicated virus.

Methods: Stable serial dilutions of NB-DNM were made in DMSO. MTT assay was performed on BHK cells- that were cultured in standard conditions, and exposed to different concentrations of the NB-DNM until the effective and non-toxic concentration of NB-DNM was obtained. BHK cells were infected with CVS-11(one strain of rabies virus) and the effect of a non-toxic concentration of NB-DNM was investigated in a time-lapse by collecting supernatants. Then rabies virus proliferation was tested by FFA. NB-DNM treatment effects on rabies-infected cells' relationship with glycosylation, calnexin, and calreticulin were investigated by confocal microscopy.

Results: NB-DNM effects (in the non-toxic concentration 10-5) on rabies-infected BHK cells were studied at different times. By comparing virus-infected cells (control) with infected cells treated with NB-DNM, it was observed that the number of viruses attached to calreticulin and calnexin chaperones decreased with the increase in time of NB-DNM treatment. Also, FFA carried out on the supernatant of NB-DNM-treated infected cells showed a significant decrease in the virus titer.

Conclusion: The treatment of Virus-infected cells with NB-DNM at different times showed a decrease in virus titer by FFA. A decrease in rabies virus connection to chaperones was revealed by confocal microscopy. This is related to the reduction of assembly of newly produced viruses due to the reduction of glycoprotein production.

Keywords: N-butyl-deoxynojirimycin, calreticulin, calnexin, rabies virus, Virus Titer

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Abstract: A-10-2618-1

Comprehensive Assessment of Mineral and Inflammatory Markers in Hemodialysis Patients

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Background: This study investigates biochemical profiles of individuals at various stages of kidney disease, including kidney disease (KD) without hemodialysis (HD), chronic kidney disease (CKD) without HD, and kidney failure undergoing HD. The primary objectives were to assess and compare key biomarkers related to mineral status, inflammation, and renal function, providing insights into kidney dysfunction.

Methods: Conducted at Basra Teaching Hospital and Al-Furat Laboratory in Iraq, this case-control study enrolled 180 participants aged 18-81. Participants were divided into two groups: the case group (KD without HD, CKD without HD, and kidney failure undergoing HD) and the control group (healthy individuals). Blood samples were analyzed for urea, creatinine, calcium, phosphorous, vitamin D3, parathyroid hormone (PTH), high sensitivity C-reactive protein (hs-CRP), and Cystatin C. Statistical analyses, including Kolmogorov-Smirnov test, independent t-test, Mann–Whitney U test, ANCOVA, and Pearson's correlation, were employed to explore differences and associations among the groups.

Results: Significant variations were observed in blood urea, calcium, vitamin D3, Cystatin C, and hs-CRP among different case groups. Creatinine showed significant differences between KD without HD and CKD without HD compared to kidney failure with HD, while phosphorous levels varied significantly across all groups. PTH levels showed no significant difference between KD without HD and CKD without HD, but both significantly differed from kidney failure with HD. Cystatin C displayed no significant difference between KD without HD and CKD without HD, but both significantly differed from kidney failure with HD.

Conclusion: This study provides an understanding of the biochemical intricacies associated with kidney disease, offering insights into the profiles of individuals at different stages of renal dysfunction. Monitoring key biomarkers, including calcium, phosphorous, vitamin D3, PTH, hs-CRP, and Cystatin C, is crucial for tailoring interventions and improving outcomes. The findings emphasize the importance of addressing mineral imbalances and inflammation in hemodialysis patients.

Keywords: Hemodialysis (HD), chronic kidney disease, vitamin D3, Calcium, Phosphorous, PTH

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Abstract: A-10-2619-1

The Expression of Anti-aging Protein Klotho Is Increased During Neural Differentiation of Bone Marrow-derived Mesenchymal Stem Cells

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Background: This study aimed to understand the changes in klotho expression during the differentiation of MSCs into neuron-like cells. Klotho protein Known for its anti-aging properties, is involved in maintaining and differentiating neuronal and glial cells. It exists in membrane-bound and soluble forms and is implicated in several physiological processes including calcium and phosphate metabolism. MSCs derived from bone marrow can differentiate into various cell types, including neuron-like cells.
Methods: MSCs were isolated from the bone marrow of mice and cultured, Neuronal differentiation was induced, and the expression of klotho and neuron-specific genes (Pax-6, NeuN, NfL) was monitored using quantitative real-time PCR, Protein levels were assessed through immunocytochemistry and western blot.
Results: During the differentiation process, MSCs showed significant morphological changes towards neuron-like cells, and there was a significant increase in the expression of neuron-specific genes and klotho mRNA, Accumulation of klotho protein was observed in neuronal cell bodies.
Conclusion: The differentiation of MSCs into neuron-like cells is associated with increased expression of klotho, this suggests that klotho may play a critical role in stem cell differentiation and neuronal regeneration. The study provides new insights into the importance of klotho protein in the neural differentiation of MSCs.

Keywords: antiaging, differentiation, gene expression, Klotho, mesenchymal stem cells, neuron-like cells

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Abstract: A-10-2687-1

Ribavirin Modulation of a New Cell Regulatory Element: IMPDH-Based Cytoophidia

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Background: Inosine-5′-monophosphate dehydrogenase (IMPDH) is essential for de novo guanosine nucleotide synthesis, catalyzing the oxidation of inosine monophosphate to xanthosine monophosphate. Clinically, inhibitors like ribavirin are used to block this enzymatic reaction, thereby preventing the proliferation of viruses or cells. This inhibition significantly affects cellular dynamics, leading to the redistribution of IMPDH and the formation of distinctive inclusions known as cytoophidia.

Methods: This study investigates the maturation and progression of cytoophidia induced by IMPDH inhibition. Advanced microscopy and western blot analyses were employed to compare the effects of ribavirin with other IMPDH inhibitors, such as MPA and mycophenolic acid, on cytoophidia formation.

Results: Our findings demonstrated that ribavirin was particularly effective in inducing cytoophidia formation compared to other inhibitors. The induction of cytoophidia by ribavirin was time-dependent, with prolonged induction leading to maturation characterized by a decrease in quantity but an increase in the cytoophidia surface area, length, and width. This maturation process resulted in the development of various secondary structures, extending beyond the traditional Ring and Rod configurations.

Conclusion: Our study elucidates the complex maturation process of cytoophidia, highlighting the progressive formation of secondary structures alongside the classical Ring and Rod arrangements in response to IMPDH inhibition. These insights enhance our understanding of the cellular dynamics influenced by IMPDH inhibitors like ribavirin.

Keywords: Cytoophidia, IMPDH, Maturation, Ribavirin, Structure

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Abstract: A-10-2700-1

Exploring the Pharmacological Mechanisms of Capparis Spinosa: Insights from Network Pharmacology and Molecular Docking Approaches

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Background: Capparis spinosa (CS) has been used in traditional medicine for various conditions, but its mechanisms of action remain unclear. This study aimed to predict the targets and pharmacological actions of CS using network pharmacology and molecular docking approaches.

Methods: Active compounds of CS were collected from the literature and screened for oral bioavailability and drug-likeness. Potential protein targets were predicted using Swiss Target Prediction, PharmMapper, and BindingDB. Gene Ontology and KEGG pathway enrichment analyses were performed on the predicted targets. Cancer-related targets were identified and a protein-protein interaction network was constructed. Common targets between CS and cancer were determined. Molecular docking was conducted to validate binding affinities between key compounds and hub targets.

Results: 31 compounds with 183 non-redundant protein targets were identified. Apigenin, kaempferol, and gallic acid showed the highest number of targets. Enrichment analysis revealed involvement in protein modification, phosphorylation, and inflammatory response regulation. The study provides mechanistic insights into CS's reported therapeutic effects, particularly its antidiabetic, anticancer, anti-inflammatory, and neuroprotective properties. The findings suggest that CS compounds may modulate multiple targets and pathways, including carbonic anhydrase activity, FoxO signaling, and oxidative stress regulation in diabetes; BACE1, α-synuclein, and tau phosphorylation in Alzheimer's disease; and various cancer-related pathways. 37 targets overlapped between CS and cancer-related genes. AKT1, EGFR, and SRC were identified as hub targets. Molecular docking confirmed strong binding affinities between CS compounds and these hub targets.

Conclusion: This study provides insights into the potential pharmacological mechanisms of CS, particularly in cancer-related pathways. The identified targets and pathways offer a foundation for further experimental validation of CS's therapeutic effects. The multi-target, multi-pathway approach of CS suggests its potential as a versatile medicinal plant with applications in cancer and other diseases.

Keywords: Capparis spinosa, Phytochemicals, Network Pharmacology, Diabetes Mellitus, Cancer, Molecular Docking

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Abstract: A-10-2295-2

The Role of miRNA-132 in Alzheimer's Disease: Implications for Beta-Amyloid and Tau Protein

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Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder marked by cognitive decline, memory loss, and behavioral changes. The disease is characterized by the accumulation of beta-amyloid plaques and neurofibrillary tangles composed of hyperphosphorylated tau proteins in the brain. These pathological features disrupt neuronal communication and lead to cell death. Recent research has highlighted the role of microRNAs (miRNAs) in AD, with particular focus on miRNA-132, a regulator of neuronal functions, which is significantly reduced in Alzheimer's patients.

Methods: To investigate the role of miRNA-132 in Alzheimer's disease, brain tissue samples from both Alzheimer's patients and healthy controls were collected. Total RNA was extracted and used to synthesize complementary DNA (cDNA). Real-time PCR was conducted to quantify miRNA-132 levels, using specific primers and reagents. Additionally, tau protein levels were measured using enzyme-linked immunosorbent assays (ELISAs). The experimental protocol included a detailed PCR cycle for miRNA-132 quantification and a colorimetric assay for tau protein analysis.

Results: The study found a significant reduction in miRNA-132 levels in the brain tissues of Alzheimer's patients compared to controls. This decrease in miRNA-132 was associated with increased deposition of beta-amyloid plaques and higher levels of phosphorylated tau protein. The ELISA results confirmed the presence of abnormal tau accumulation, consistent with neurofibrillary tangles observed in Alzheimer's pathology.

Conclusion: The findings indicated that enhancing miRNA-132 expression in brain tissues could mitigate beta-amyloid and tau-related abnormalities This research emphasizes the importance of miRNA-132 in Alzheimer’s disease, noting that its reduced levels are linked to worsening beta-amyloid and tau pathologies, which contribute to neurodegeneration. The study suggests miRNA-132 as a potential therapeutic target and biomarker for Alzheimer’s, advocating for further investigation into its role in neuronal health and its potential in early diagnosis and treatment. The findings also support the continued development of miRNA-based interventions and tau-targeted therapies.

Keywords: Alzheimer’s disease, miR-132

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Abstract: A-10-2775-1

Probing of the Interaction Between Human Serum Albumin and Phosalone: A Combination of in Vitro and Silico Studies

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Background: Phosalone, an organophosphate insecticide, is extensively employed in gardening and agriculture to manage plant pests. Due to its prevalent use, exposure to this environmental pollutant poses a significant risk to human health. This research aimed to elucidate the mechanism of interaction between phosalone and human serum albumin (HSA) to understand the potentially harmful effects of this pesticide.

Methods: The study explored the binding characteristics of phosalone to HSA using a combination of molecular dynamics (MD) simulations, thermal stability experiments, and Fourier-transform infrared spectroscopy (FT-IR).

Results: FT-IR spectroscopy revealed alterations in the secondary structure of HSA, particularly in the α-helix and β-sheet content, upon binding with phosalone. Additionally, the molecular dynamics analysis indicated reduced stability and increased protein flexibility when interacting with phosalone, as evidenced by the root mean square deviation (RMSD) and root mean square fluctuation (RMSF) parameters, respectively. The thermal stability experiments further demonstrated that phosalone adversely affects the thermal stability of HSA.

Conclusion: This study, through the integration of computational and experimental approaches, provided noteworthy insights into the interactions of phosalone with HSA. The increased average RMSD of the phosalone-HSA complex compared to HSA alone indicates a reduction in protein stability in the presence of phosalone, corroborated by the observed decrease in melting temperature (Tm). Furthermore, the higher average RMSF in the phosalone-HSA system compared to the free protein suggests that phosalone induces greater flexibility in the protein structure. The findings from the MD simulations support the FT-IR results, confirming changes in the protein's secondary structure upon phosalone binding. These results offer valuable information for monitoring food safety and assessing the potential toxicity risks of phosalone to human health.

Keywords: Phosalone, Human serum albumin, Insecticide

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2779-1

Assessing Fenvalerate's Influence on the Structural Stability and Functionality of Lysozyme: A Combined Spectroscopic and Computational Study

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Background: The rapid growth of the global population and the rising demand for food have led to the extensive use of pesticides in agriculture. This excessive use has polluted the environment, contaminated water, soil, and air, and ultimately affected human health. Synthetic pyrethroid pesticides have been identified as a major contributor to these problems. Therefore, research focused on understanding the mechanisms of such hazards, intending to mitigate various health issues associated with pesticide exposure, is of paramount importance.

Methods: The study investigated the interaction between lysozyme (LZ) and fenvalerate (FEV) using fluorescence, UV-Vis absorption, and circular dichroism (CD) spectroscopy. Thermal stability was evaluated by monitoring absorbance changes. Enzymatic activity assays measured LZ function by monitoring the alterations in the absorption of Micrococcus lysodeikticus. Molecular docking identified binding modes, while molecular dynamics (MD) simulations explored LZ-FEV system dynamics over a 200 ns period.

Results: The findings from UV-visible absorption and fluorescence studies confirmed the formation of the complex and indicated the fluorescence quenching of FEV via a static mechanism. CD analysis revealed the secondary structure changes of LZ, evidenced by a reduction in α-helix content and an increase in β-sheet elements. Furthermore, FEV binding led to a decline in the stability and enzyme activity of LZ. Computational docking pinpointed a specific binding site for FEV within the LZ structure. MD simulations further demonstrated the stability of the LZ-FEV complex and revealed structural modifications in LZ following FEV interaction.

Conclusion: This study provides insights into the interactions between LZ and FEV, demonstrating that FEV binding significantly alters the structural and functional properties of LZ. These findings underscore the importance of understanding the molecular mechanisms underlying pesticide interactions, which is crucial for developing strategies to mitigate potential risks to public health and the environment.

Keywords: Lysozyme, Fenvalerate, Molecular interaction, Enzyme activity, Thermal stability

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2771-1

Protective Effect of Late Embryogenesis Abundant (lea) Protein from Artemia Urmiana on Luciferase and Its Structural Analysis

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Background: Late embryogenesis abundant (LEA) proteins are intrinsically disordered proteins that are expressed in various organisms in response to cellular dehydration conditions. In this work, a group 1 LEA protein from the brine shrimp Artemia urmiana, Au-LEA1.1, was expressed and purified to investigate its structure and ability to protect luciferase as a model protein during freeze-thaw cycles.
Methods: The pET26b-Au-LEA1.1 plasmid was transformed into E. coli BL21 (DE3). Protein expression was induced by the addition of 0.5 mM IPTG for 4 hours at 37° C. The supernatant of the cell lysate was heated in boiling water for 10 min and cooled on ice for another 10 min. The protein was further purified using a Ni-NTA affinity chromatograph. Au-LEA1.1 in phosphate buffer and the presence of 20%, 40%, and 60% of Trifluoroethanol (TFE) was analyzed by far-UV CD spectroscopy. To investigate the protective role of Au-LEA1.1 in water stress, luciferase was used in the absence and presence of Au-LEA1.1. Mixtures were frozen for 1 min in liquid N2 and subsequently thawed at 25° C for 5 min. This procedure was repeated up to four times. Then the residual activity of luciferase was measured.
Results: Au-LEA1.1 was successfully expressed and purified. Circular dichroism analysis shows that Au-LEA1.1 is mostly composed of random coils but has a propensity to form α-helices in the presence of TFE. LEA folding was concentration-dependent and α-helicity was increased with the increase in TFE concentration. The residual activity of luciferase after four cycles of freeze-thaw was significantly higher in the presence of Au-LEA1.1 than alone.
Conclusion: We present the structural and functional characterization of the first LEA from Artemia urmiana. LEA undergoes disorder-to-order transition in response to stress conditions which help protect other proteins.

Keywords: late embryogenesis abundant (LEA) protein, circular dichroism, trifluoroethanol (TFE), luciferase, freeze-thaw

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Abstract: A-10-2672-1

Enhancing Effect of a Protoberberine Alkaloid on Osteogenic Differentiation Process of Human Mesenchymal Stem Cells

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Background: Nowadays, due to the limitations of past treatment methods for bone diseases and injuries such as cancer and osteoporosis, the use of techniques such as regenerative medicine and differentiation of stem cells has been considered. Alkaloids are natural bioactive substances that have shown wide biomedical applications. Palmatine, a protoberberine alkaloid, has been proven to protect bone cells, but its effect on the osteogenic differentiation of MSCs has not been investigated.
Methods: The cultured hMSCs were divided into two groups, which included the control and the sample treated with Palmatine to investigate the Stimulating effect of Palmatine on osteogenic differentiation on the 7th and 14th days of differentiation. Using Von Kossa staining, the degree of cell mineralization was qualitatively assessed. The activities of Catalase and Superoxide Dismutase, were measured as antioxidant enzymes in this process. Finally, The expression levels of RUNX2, ALP, Col1, Osteonectin, and Osteocalcin were analyzed using the RT-PCR technique.
Results: Von Kossa staining reveals that cells treated with Palmatine exhibit a significant increase in mineralization. On the 7th day of differentiation, the activity of Superoxide Dismutase enzyme showed a significant and Catalase showed a slight increase, but on the 14th day, the activity of both enzymes increased significantly in the sample treated with Palmatine. The RT-PCR results on the 7th and 14th days of differentiation showed an increase in the expression of all genes. On 7th day, the increase of Osteonectin (2.76±1.26), Osteocalcin (2.53±0.50), and RUNX2 (5.85±2.28) was significant (P value≤0.001) in Palmatine treated sample compared to control. Additionally, on the 14th day, a substantial increase (P value≤0.001) was observed for Osteonectin (3.62±0.82), Osteocalcin (2.89±0.99), Col1 (3.78±1.02) and ALP (2.96±0.89).
Conclusion: The findings of this study suggest that Palmatine, a protoberberine alkaloid, enhances the osteogenic differentiation of hMSCs.

Keywords: Palmatine; Osteogenic Differentiation; MSCs; Alkaloids; Regenerative Medicine; Protoberberine

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2567-1

The Influence of Body Mass Index on Blood Indices and Biochemical Parameters in HIV/aids Patients

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Background: The present study was conducted to evaluate the effect of body mass index (BMI) on blood indices and biochemical parameters in HIV/AIDS- patients.
Methods: The current investigation recruited 200 HIV/AIDS patients (100 males and 100 females) with a mean age of 41.4±12.4 years. Patients were categorized based on BMI in underweight, healthy weight, overweight, and obese groups. All the blood and biochemical parameters were measured by standard methods.
Results: Our obtained results showed that the obese group had a significantly higher level of fasting blood sugar (FBS), triglycerides (TG), and cholesterol (Chol) ($P<0.001$), and lower levels of hemoglobin, hematocrit, and red blood cell counts count ($P<0.001$) than those in the other groups. Also, in the presence of an increase in BMI level, the CD4+ count elevated considerably ($P=0.01$). Based on linear regression analysis, BMI had a positive correlation with CD4+count; $\beta=9.56$& 95%CI:(2.46_16.65). Furthermore, patients in both abnormal groups of underweight and obese had a higher risk of anemia; however, the OR was just significant for the obese group; $\beta=4.60$ & 95% CI:(1.80_11.80), $P=0.01$.
Conclusion: According to the present results, BMI may have an influential role in the protecting immune system and preventing disease progression. In addition, increasing BMI and obesity could raise the risk of anemia in HIV/AIDS patients.

Keywords: HIV/AIDS, BMI, Biochemical parameters, Blood indices

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A Colorimetric Approach for Dopamine Quantification in Human Serum Leveraging the Peroxidase-Mimicking Properties of MOF-2

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Background: Dopamine (DA) is a crucial neurotransmitter found abundantly in the brain. Measuring DA levels in bodily fluids is vital for diagnosing and treating various neurological and cardiac conditions, such as Parkinson's, schizophrenia, Alzheimer's, and heart failure. While analytical techniques like HPLC, fluorescence, and electrochemistry have been used to detect DA, they have some limitations. Colorimetric measurement has become popular due to its simplicity, low cost, and ease of visual assessment. Conventional colorimetric methods often use the enzyme horseradish peroxidase (HRP) to oxidize 3,3',5,5'-tetramethylbenzidine (TMB) in the presence of hydrogen peroxide (H_2O_2), producing a blue product. However, natural enzymes have drawbacks, such as poor stability, preparation, purification, and recycling. To address these limitations, metal-organic frameworks (MOFs) have emerged as promising mimetic enzyme alternatives, offering a more stable structure and easier storage.
Methods: In this study, the first MOF-2 was synthesized using a hydrothermal method. Then various characterization techniques, including FT-IR, SEM, and XRD were employed to verify the properties of the synthesized MOF-2 material. Next, we investigated the peroxidation capability of MOF-2 by testing it in a system containing TMB and hydrogen peroxide, using an acetate buffer. To optimize the measurement conditions, the team systematically evaluated the effects of several key factors on the peroxidation property, such as reaction time, pH, TMB concentration, hydrogen peroxide concentration, and the amount of MOF-2 used. Finally, we utilized the optimized MOF-2 peroxidation method to measure dopamine levels, first in laboratory samples and then in real human serum samples.
Results: The method demonstrated a linear range of 0.3 to 180.28 µM with a detection limit of 0.1 µM. Analysis of dopamine in human serum samples yielded recovery values ranging from 95.74% to 117.15%.
Conclusion: In summary, we found that MOF-2 displayed robust peroxidase-like catalytic activity, enabling the development of a sensitive colorimetric detection method for measuring dopamine levels.

Keywords: Dopamine, MOF-2, Colorimetric, Peroxidase, Enzyme mimic, CuBDC

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Correlation Between NF-κB Pathway Activation and lincRNA-Cox2 Tissue Expression in Ulcerative Colitis Patients

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Background: Ulcerative colitis (UC) is a chronic inflammatory bowel disease caused by immune system reactions that are abnormal and cause inflammation of the colon and the rectum. One of the pathways that is essential to the pathophysiology of ulcerative colitis is the NF-κB signaling pathway. Long non-coding RNAs (lncRNAs) have a high degree of specificity for specific cells and organs, making them useful as biomarkers in a wide range of diseases. Many medical conditions are under the control of the NF-κB pathway by lincRNA-Cox2. In this study, we investigated the correlation between the NF-κB pathway and lincRNA-Cox2 in UC patients.
Methods: 35 UC patients and 35 healthy people served as the control group, and the samples were taken at Shariati Hospital in Tehran, Iran. Standard clinical, endoscopic, and histological criteria were used to diagnose the patients. After removing protein and RNA from tissue samples, the expression of the lincRNA-Cox2 gene was assessed using Real-Time PCR. Measurements of NFκB p65 and P-NFκB p65 were made using Western blot.
Results: The expression levels of lincRNA-Cox2 were significantly higher in UC patients as compared to the control group. Western blot analysis showed that, in comparison to the control group, UC patients had greater levels of NFκB p65 and P-NFκB p65. This suggests that these patients had a higher level of activation of the NF-κB pathway.
Conclusion: This study shows that, in comparison to the tissue samples from the control group, the expression of lincRNA-Cox2 is higher in UC tissue samples. Furthermore, UC tissue samples have higher levels of NFκB p65 and P-NFκB p65, suggesting that UC patients have higher NF-κB pathway activity. Previous research has demonstrated that lincRNA-Cox2 controls the NF-κB pathway, indicating a potential correlation between ulcerative colitis and lincRNA-Cox2.

Keywords: Colitis, Ulcerative, IBD, RNA, Long Noncoding, lincRNA-Cox2, Inflammation

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Abstract: A-10-2257-1

Protective Effect of Herniarin Against Gentamicin-Induced Nephrotoxicity by Improvement of Inflammation

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Background: Drug-induced nephrotoxicity is a common clinical problem that clinicians should seek to understand to identify the causes of renal disease in patients.
Methods: Gentamicin is a highly effective antibiotic against infections caused by gram-negative bacteria. The effectiveness of this medication has been restricted due to its highly harmful side effect, known as nephrotoxicity. So far, it has been established that the side effects of gentamicin are caused by its accumulation in the kidney tubules, leading to inflammation. Herniarin has been identified as an anti-inflammatory substance.
Results: In this study, we investigated its effects on gentamicin-induced nephrotoxicity for the first time. Twenty-four C57/BL6J mice were divided into 4 groups. Group 1: Control Group 2: Gentamicin at a dosage of 100mg/kg for 10 days. Group 3 received Herniarin at a dosage of 25mg/kg for 15 days, in addition to gentamicin injections for the last 10 days. Group 4 received an injection of herniarin at a dosage of 50mg/kg for 15 days, in combination with gentamicin for the last 10 days. Plasma urea and creatinine levels were assessed to investigate kidney function, along with histopathological examination. Furthermore, inflammation markers were assessed in kidney tissues. Our results showed that treatment with Herniarin improves kidney function by reducing levels of urea and creatinine. The expression of inflammatory genes TNF-α, IL-6, and IL-1β decreased in the high-dose Herniarin group.
Conclusion: As a result, it can be concluded that Herniarin could mitigate the kidney damage caused by gentamicin in mice primarily through its anti-inflammatory effects in a dose-dependent manner, demonstrating a nephroprotective effect.

Keywords: Nephrotoxicity, Gentamicin, Herniarin, Inflammation

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Abstract: A-10-2526-1

The Effects of Royal Jelly Consumption on Inflammation and Oxidative Stress in Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Background: This systematic review and meta-analysis examine the impact of royal jelly consumption on inflammation and oxidative stress. By synthesizing existing research, it aims to provide valuable insights into the potential health benefits of royal jelly.
Methods: PubMed/Medline, Web of Science, and Scopus were searched up to the end of December 2023. All randomized clinical trials assessing the effect of RJ supplements on serum levels of high-sensitivity C-reactive protein (hs-CRP), total antioxidant capacity (TAC), and malondialdehyde (MDA) were comprised in this systematic review and meta-analysis. A random-effects model was utilized to aggregate the mean difference (MD).
Results: Seven suitable datasets from 6 trials were considered eligible. RJ supplementation significantly reduced MDA (WMD, –1.79 (–3.00 to –0.58), P= 0.004; I2 = 97.4%) and increased TAC (WMD, 0.98 (0.24 to 1.71), P= 0.009, I2 = 98.5%), but it did not significantly change hs-CRP levels (WMD: -0.24; 95% CI: -0.60, 0.10; p=0.17). RJ supplementation in higher doses and participants with normal BMI could induce a greater elevation in TAC, and in participants with normal BMI, a stronger reduction in MDA.
Conclusion: Although this meta-analysis confirmed that RJ could be a useful intervention to reduce oxidative stress, this research should be updated in the future, due to the restricted number of trials pooled in the present meta-analysis.

Keywords: Malondialdehyde, Antioxidant, Royal Jelly, Oxidation-Reduction, CRP, Meta-analysis

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Abstract: A-10-2527-1

Curcumin Ameliorates Liver Fibrosis Disease by Reducing Fibrogenic Genes in TGF-β-Activated Hepatic Stellate Cells

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Background: Liver fibrosis disease is a major cause of morbidity and mortality in the world. No definite cure has been found for liver fibrosis yet. Hepatic stellate cells (HSCs) during liver fibrosis change to myofibroblasts and become activated. These cells are activated by fibrogenic cytokines such as TGF-β1. NADPH oxidases (NOXs), particularly isoforms 1, 2, and 4, play a role in hepatic fibrosis. Curcumin is a powerful antioxidant and may have antifibrotic effects. Our research aimed to study the effects of curcumin as an antifibrotic factor on NOX and ROS levels and Smad3 phosphorylation in TGF-βactivated human HSCs.

Methods: The cells were activated by exposure to TGF-β (2 ng/mL) for 24 hours to induce liver fibrosis. After activating, the cells were treated with curcumin at 75 and 100 µM concentrations. After administering curcumin to the cells, we employed RT-PCR and Western blot techniques to evaluate NOX1, NOX2, NOX4, and phosphorylated Smad3C levels to assess the signaling pathway. This evaluation was primarily focused on the mRNA expression. The intracellular ROS levels in human HSCs were assessed using DCFH-DA.

Results: The mRNA expression level of α-SMA and collagen increased in TGF-β activated HSCs so liver fibrosis was induced. After that, Treatment with curcumin (75 and 100 µM) effectively inhibited the proliferation and activation of HSCs. The mRNA expression level of α-SMA and collagen1-α levels were significantly reduced following 75 and 100 µM curcumin treatment. Curcumin decreased the expression of NOXs, and ROS generation, and lowered phosphorylated -Smad3C levels.

Conclusion: In this study, Curcumin significantly reduced the mRNA expression of NOX1, NOX2, and NOX4, as well as α-SMA, collagen1-α, ROS production, and inhibited the expression level of phosphorylated -Smad3C protein. According to these data, curcumin could be introduced as an effective therapeutic agent for liver fibrosis.

Keywords: Curcumin, Liver fibrosis, NOXs, ROS

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Abstract: A-10-2527-3

A Combination of Diosmin and Saroglitazar Effectively Improves Nonalcoholic Fatty Liver Disease Induced by a High-Fat Diet in Wistar Rats

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Background: In Non-alcoholic fatty liver disease (NAFLD), too much fat builds up in the liver. It is seen most often in people who are overweight or obese. Compounds with anti-inflammatory and lipid-lowering effects can be used to prevent or treat NAFLD. Therefore, this study was conducted to investigate the effect of Saroglitazar (a dual PPARα/γ agonist) and Diosmin (a flavonoid) on non-alcoholic fatty liver induced by a high-fat diet (HFD) in Wistar rats.
Methods: Forty male Wistar rats (6–8 weeks old) were fed a high-fat diet to induce NAFLD. After 8 weeks, rats were divided into four groups: one group was fed HFD, and the other groups received HFD+Saroglitazar, HFD+Diosmin, and HFD+ Saroglitazar+Diosmin. Body and liver weight, histopathology, serum levels of liver enzymes (ALT and AST), and lipid profiles (LDL-C and HDL-C) were examined using standard protocols. qRT-PCR was also used to examine the expression of PPARα, PPARγ, SREBP1c, FAS, ACC, CPT1α, and pro-inflammatory genes (IL6, TNFα, and TGFβ).
Results: After inducing NAFLD, treatment with Saroglitazar and Diosmin alone caused a significant decrease in the levels of PPARγ, SREBP1c, FAS, ACC, ALT, AST, LDL-C, and pro-inflammatory genes. Also, a significant increase in PPARα, CPT1a, and HDL-C in comparison with the HFD group was seen. Their combined effects (Saroglitazar + Diosmin) were more effective and noticeable in reducing related genes than Saroglitazar and Diosmin alone.
Conclusion: Our results showed that Diosmin and Saroglitazar ameliorated inflammatory and lipid profiles in HFD-induced NAFLD but their combination significantly reduced inflammatory and lipid profiles and was more effective than when they were used alone. According to these data, we suggest the combination of Saroglitazar and Diosmin as a useful, safe, and effective therapy way for NAFLD.

Keywords: Diosmin, NAFLD, Saroglitazar, HFD

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Abstract: A-10-2580-2

Antioxidant, Anti-Amylase, Anti-Lipase, and Efficiency of Satureja Fatty Acid on the Anti-Inflammatory Parameters in Lipopolysaccharide-Stimulated Macrophage

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Background: Modern medicine research revealed several biological activities of Satureja essential oil, including antifungal, antibacterial, antioxidant, anticancer, and anti-inflammatory.

Methods: This study examined the fatty acid profile, lipid nutritional quality, antioxidant, anti-amylase, and anti-lipase capacities of Satureja. The efficiency of Satureja fatty acid on the anti-oxidative and anti-inflammatory parameters in LPS-induced macrophage through the Nrf2/NF-kB/NADH oxidase pathway was examined. Fatty acids methyl ester from whole lipid extract were prepared with methanol/sulfuric acid reagent. The fatty acid profile was analyzed using gas chromatography-mass spectrometry. Total antioxidant was determined by ABTS decolorization. Lipase and amylase activities were determined by monitoring the decomposition of p-nitrophenyl butyrate and starch. The macrophage cell line was grown in DMEM media in the presence of fatty acid. NADH oxidase activity was measured by monitoring NADH breakdown. The expression of NOX, NF-kB, and NRF2, were tested in the treated cells by real-time PCR.

Results: The main components of the Satureja fatty acid were linolenic acid, palmitic acid, linoleic acid, oleic acid, stearic acid, and palmitoleic acid. Given the nutritional quality, omega-3 PUFA, SFA, omega-6 PUFA. omega-9 MUFA and omega-7 MUFA comprise the majority of fatty acids. Satureja fatty acid has a promising unsaturation index, hypocholesterolemic index, health-promoting index, nutritive value index, omega-6/omega-3, atherogenicity index, and thrombogenicity index. Satureja fatty acid displayed strong antioxidant capacity, anti-lipase capacity, and anti-amylase capacity. LPS induced the expression of NOX, NRF2, and NF-kB and the synthesis of hydrogen peroxide in macrophage cells. In LPS-stimulated macrophages, Satureja fatty acid reduced NOX expression, hydrogen peroxide, and NF-kB expression and increased NRF2 expression.

Conclusion: Satureja fatty acids have potent antioxidant, anti-amylase, anti-lipase, antioxidative and anti-inflammatory activities. Satureja polyunsaturated omega-3 fatty acids could be recommended for healthy products combined with dietary therapy to treat obesity, diabetes, and oxidative stress.

Keywords: Satureja oil, Lipase, Amylase, NOX, NF-kB, NRF2

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Abstract: A-10-2469-1

Melittin-Oleuropein Serum Effects on the Skin Facial Wrinkles in the in Vitro and in Vivo Condition

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Background: One of the results of natural aging and optical damage is the creation of facial wrinkles. Until now, there are no known methods and strategies for curbing facial wrinkles. The purpose of this study is to make melittin-oleuropein serum for the inhibition of wrinkles. For this purpose, the well-known serum of bee melittin and olive Oleuropein in different proportions was first applied to Hff2 cells and its toxicity was calculated by the MTT method and its IC50 and IC25 values were calculated.

Methods: In IC25 treatment, the expression levels of Col1A1, MMP9, and Eln genes were measured by the Real-time PCR method. After using the serum made based on the IC25 concentration of melittin- Oleuropein after obtaining the code of ethics, on the wrinkles of 15 samples, the wrinkles depth was evaluated in the 0th, 4th, 8th, and 12th weeks with the South Korean Wrinkle-grading system protocol. The data results were analyzed by the Repeated Measure method at a 5% probability level in SPSS ver 22.

Results: The results showed that the application of melittin-oleuropein treatment increased the expression of Col1A1, and Eln genes and decreased MMP9 in the Hff2 cell line, also melittin-oleuropein serum was significantly effective in reducing the depth and number of wrinkles. In examining the trend in the time interval, the regression coefficient was negative and significant.

Conclusion: Melittin and Oleuropein serum can be used to reduce wrinkles along with polyphenol Oleuropein.

Keywords: Melittin-oleuropein serum, Col1A1, MMP9, and Eln gene expression skin wrinkles

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Abstract: A-10-2464-1

Exploring the Anti-Fibrotic Potentials of Korean Red Ginseng in Alleviating Uterine Post-Surgical Adhesions

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Background: Uterus adhesions are bands of scar tissue that develop in the uterine and are accompanied by inflammation and oxidative stress. They are usually typically caused by surgery or curettage. Common patient complaints involve infertility and menstrual cycle disorders like hypomenorrhea. While treatments such as surgery and IUD devices are available, they are not always effective, encouraging a less invasive method. Korean Red Ginseng (KRG) is an ancient herb with special therapeutic properties in treating many inflammatory and fibrotic-associated diseases. Many studies Highlight this herb's powerful anti-fibrotic and anti-inflammatory properties. According to molecular aspects of the pathogenesis of uterine adhesions, KRG can be a promising candidate for treating this disease. This study aims to explore the effects of this herbal drug in reducing adhesions.

Methods: In this study, rats were divided into three groups: sham, no treatment, and KRG treatment. Oral gavage of KRG was administered to 8-week Wistar rats for 10 days after mechanically induced adhesions were created by scratching the basal layer of these rats' uterus. Following this, the rats were sacrificed, and their uteruses were isolated and examined in two parts. One part was subjected to pathological surface examination using H&E staining, while the other part was used to investigate expression levels of fibrotic and inflammatory genes using qPCR. Finally, the products of these fibrotic and inflammatory genes were analyzed using the ELISA method.

Results: The H&E staining reveals a significant increase in both the number of glands and uterine endometrial thickness within the KRG group. Moreover, administration of KRG significantly down-regulated expression of fibrotic and inflammatory genes, such as TGF-B and various inflammatory cytokines at mRNA and protein levels.

Conclusion: the findings of this study recommend KRG as a potential natural drug in the treatment of uterine adhesions. Further research is needed to assess long-term infertility problems.

Keywords: post-surgical adhesion, Asian ginseng, Scar, Fibrosis, Phytomedicine

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Abstract: A-10-2332-2

Investigation of the Effects of Rutin and N-Acetyl Cysteine on Pon1 Enzyme in Cyclosporine A-induced Kidney and Liver Injury; An In-Silico, In-Vitro, and In-Vivo Study

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Background: Paraxonase1 (PON1) enzyme is a potent antioxidant enzyme in serum that protects from oxidation of LDL. This study investigated the effect of N-acetyl cysteine (NAC) and Rutin, as two natural antioxidants, to protect the PON1 enzyme activity in liver and kidney injury induced by Cyclosporine A using experimental and molecular dynamic simulation studies.

Methods: 48 male rats were divided into six groups. Liver and kidney injuries were induced by cyclosporine A and then they were treated by NAC and Rutin separately or synergistic against the control untreated group. Auto analyzer measured the serum HDL and then H&E staining was used to determine the liver and kidney injury. PON1 enzyme activity was done by its aryl esterase property using a spectrophotometer. Docking and molecular dynamic simulation studies were done using Aoutodock V.4.2, Discover Studio V.16.1, and Gromacs 2022 software.

Results: Cyclosporine A could induce kidney and liver injury. Although, PON1 enzyme aryl esterase activity decreased in groups that received cyclosporine A this activity increased in the group that received NAC+Rutin. The simulation results showed that Cyclosporine A decreases the PON1 Radius of gyration (Rg) during the 100 ns of simulation time and can decrease the PON1 activity. In addition, Rutin can bind to the active site of the PON1 enzyme and decrease the PON1 activity but NAC can remove this inhibition.

Conclusion: This study shows that serum PON1 aryl esterase activity decreases in cyclosporine A-induced kidney and liver injuries. However, the potential synergistic effects of NAC and Rutin, suggest that combination therapy may be more effective in preventing tissue injuries.

Keywords: PON1, Rutin, N-Acetylcysteine, Cyclosporine A

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Abstract: A-10-2311-1

Encapsulated Bifidobacterium Longum: A Novel Approach To Alleviate Cholestasis-Induced Liver Fibrosis and Improve Hepatic Function

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Background: Probiotics such as bifidobacterium longum may exert anti-inflammatory and anti-oxidant effects when consumed orally. This way, probiotics have to go through the gastrointestinal tract's (GIT) acidic and enzymatic environment, which reduces probiotic viability. Encapsulation is a method utilized to enhance probiotic's viability in GIT and control its release in the intestine. As many studies show, encapsulated probiotics can have anti-toxic effects on biliary acid oxidative stress-induced damage in hepatic tissue, therefore enhancing liver function and regulating liver fibrosis. In this study, we aim to determine the effects of encapsulated bifidobacterium longum on gene expression, oxidant/anti-oxidant status, liver histological parameters, and liver function tests in the cholestatic model on rats.

Methods: The experiment was conducted on male Wistar rats, classified into control groups: cholestasis group and healthy group, and treatment groups: probiotic, free capsule, and encapsulated probiotic group. Encapsulated B. longum with a dose of 3×109 CFU/g was administered 1 week prior and 3 weeks after cholestasis induction. Afterward, all rats were euthanized, and their blood and liver were collected. Their blood plasma was used to measure liver function. Liver tissue was used to determine oxidant/anti-oxidant status, pro- and anti-inflammatory gene expression, and histological properties.

Results: Rats treated with encapsulated B. longum showed enhanced liver function test results, downregulated expression of pro-inflammatory cytokines (IL-6 and TNF-α), and upregulated expression of anti-inflammatory (IL-10) cytokines. This treatment also alleviated oxidant status and had protective effects on the liver's histological properties.

Conclusion: Results show that encapsulated B. longum can be beneficial in alleviating cholestasis-induced injury in rats by enhancing liver function and protecting the liver against fibrosis progression.

Keywords: Cholestasis, Liver Fibrosis, Encapsulation, probiotic, Bifidobacterium longum, Inflammation, Oxidative Stress

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Abstract: A-10-2252-2

The Effect of Hydroalcoholic Seed Extract of Securigera Securidaca on Serum Homocysteine Levels and Paraoxonase Phenotypes in Diabetic Animal Model Treated by Streptozotocin

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Background: Reactive oxygen and nitrogen species (RONS) have been implicated in the pathophysiology of various disease states, including diabetes mellitus (DM). Enzymatic antioxidants such as paraoxonase and non-enzymatic antioxidants such as total thiol are capable of stabilizing, or deactivating RONS before they attack cellular components. On the other hand, natural antioxidants such as phenolic and flavonoid compounds protect the body from oxidative damage by removing free radicals, thereby indicating anti-carcinogenic, anti-atherogenic, anti-ulcer, anti-thrombotic, and anti-inflammatory properties. In this experimental study, the total phenol and flavonoid contents of Securigera securidaca (S. securidaca) and the antioxidant effects of the hydroalcoholic extract of S. securidaca seeds were investigated.

Methods: Diabetes was induced in rats through an intraperitoneal injection of streptozotocin (STZ) (55 mg/kg.BW). Eight animal groups were considered: two normal and diabetic control groups, and three HESS-treated groups given orally at doses of 100, 200, and 400 mg/kg.BW, glibenclamide treated group, and two glibenclamide plus HESS treated groups (glibenclamide plus 200 and 400 mg/kg.BW, respectively) for 35 days. The PON1 phenotype was determined using the double-substrate method. Cholesterol, triglyceride, and HDL were assayed by the colorimetric method. Serum biochemical profile, total antioxidant activity (FRAP), ROS, lipid peroxidation and were estimated.

Results: The values of total phenolics and total flavonoids were 93.3 ± 1.5 mg (GAE)/g (D.W.) and 46 ± 1.7 mg (QE)/g (D.W.), respectively. Reduction in blood glucose levels in groups treated with HESS shows a dose-dependent manner. Three phenotypes were determined: AA (low activity), AB (intermediate activity), and BB (high activity). FRAP, ROS, and MDA levels were ameliorated by an increase in HESS dose and synergistically in combination with glibenclamide.

Conclusion: Securigera Securidaca seed consumption as a supplement for blood sugar-lowering drugs such as glibenclamide may ameliorate oxidative stress complications in diabetic cases.

Keywords: Securigera securidaca, paraoxonase, glibenclamide, diabetes mellitus

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Abstract: A-10-2252-3

Investigation of the Effects of Catharanthine and Q10 on Nrf2 and Its Association with MMP-9, MRP1, and Bcl-2 and Apoptosis in A Model of Hepatocellular Carcinoma

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Background: Since the role of Nrf2 in cancer cell survival has been highlighted, the pharmacological modulation of the Nrf2-Keapl pathway may provide new opportunities for cancer treatment.
Methods: This study purposed to use ubiquinone (Q10) as an antioxidant and catharanthine alkaloid as a cAMP inducer suppressing HepG2 cells by reducing the Nrf2 level. The effects of Q10 and catharanthine on HepG2 cells in terms of viability were analyzed by MTT test. MTT results were used to determine the effective concentration of both drugs for the subsequent treatment and analysis.
Results: Subsequently, the effects of Q10 and catharanthine in a single and combined manner on oxidant/antioxidant status, apoptosis, metastasis, and drug resistance of HepG2 cells were investigated by related methods. Both Q10 and catharanthine decreased the level of oxidative stress products and increased antioxidant capacity in HepG2 cells. Nrf2 gene expression decreased by Q10, but catharanthine unexpectedly increased it. Following Nrf2 alterations, the expression levels of MMP-9 and MRP1 involved in metastasis and drug resistance were significantly and dose-dependently decreased by Q10, while catharanthine slightly increased both. However, both drugs increased caspase 3,۷ activity and apoptosis rate, and the effect of Q10 on apoptosis was stronger than that of catharanthine. Most of the effects of the combination treatments were similar to those of the Q10 single treatment and indicated the dominant effect over the catharanthine component.
Conclusion: Despite the antioxidant and apoptotic properties of both agents, Q10 was better than catharanthine in inducing apoptosis, counteracting drug resistance, and metastasis in HepG2 cells.

Keywords: Catharanthine, Ubiquinone Q10, HepG2 cell, Apoptosis, Drug resistance, Metastasis

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2449-1

Therapeutic Effects of Stevia Aqueous Extract Alone or in Combination with Metformin in Induced Polycystic Ovary Syndrome Rats: Gene Expression, Hormonal Balance, and Metabolomics Aspects

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Background: Polycystic ovary syndrome (PCOS) is the most prevalent endocrine and metabolic disorder in women, leading to infertility due to anovulation. The potential therapeutic effects of chemical drugs and medicinal plants, such as metformin (Met) and stevia aqueous extract (SAE), in alleviating PCOS symptoms are under investigation.
Methods: The estrous cycle of 50 adult Wistar female rats was monitored through vaginal smears. Subsequently, the rats were randomly assigned into five groups of 10, including control (receiving 1 ml of carboxymethyl cellulose for 49 days), induction (letrozole at 1 mg/kg/d for 21 days), SAE, Met, and SAE/Met. SAE and Met were orally administered at doses of 400 mg/kg/d and 250 mg/kg/d on day 22 and continued for an additional 28 days. Vaginal smears were analyzed, and gene expression levels of GLUT4, SIRT1, TNF-α, and INSR were evaluated using RT-qPCR. Antioxidant parameters were assessed using detection kits.
Results: Treatment with SAE and Met restored a regular estrous cycle pattern in PCOS rats. Furthermore, SAE and Met treatment improved hormonal balance, dyslipidemia, and hyperglycemia in the rats. Administration of SAE and Met significantly elevated levels of antioxidant enzymes SOD and GPx in ovarian tissue ($P<0.001$). Additionally, mRNA levels of GLUT4, SIRT1, and INSR were significantly increased in ovarian tissue following SAE and Met treatment, while TNF-α gene expression decreased significantly ($P<0.0001$).
Conclusion: The findings suggest that SAE and Met aqueous extract exert protective effects on letrozole-induced PCOS in rats by modulating gene expression associated with insulin signaling and oxidative stress.

Keywords: Stevia Aqueous extract, Polycystic ovary syndrome (PCOS), Metformin, Insulin resistance, Oxidative stress.

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2558-1

Gallic Acid-Based Carbon Dots Induce Apoptosis Related Genes in Colorectal Cancer Cell Line

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Background: Previous studies have demonstrated that GA-CDs exhibit high toxicity towards cancer cells; however, the exact mechanisms triggering cell death remain unclear. This study aims to explore the effects of GA-CDs on HCT-116 cells, focusing on apoptosis signaling pathways.
Methods: Gallic acid carbon dots (GA-CDs) were synthesized using a hydrothermal method recently established in our laboratory.HCT-116 cells were treated with GA and GA-CDs for 24 hours. Cellular uptake was investigated through fluorescence microscopy, and apoptosis was qualitatively assessed using acridine orange/propidium iodide (AO/PI) staining. Total RNA extraction was performed using the column method, followed by complementary DNA (cDNA) synthesis via Reverse Transcription Polymerase Chain Reaction (RT-PCR). Quantitative Polymerase Chain Reaction (Q-PCR) was conducted to analyze the expression of three apoptosis-related genes: Caspase-3, Bax, and Bcl-2.
Results: GA-CDs successfully triggered apoptotic signaling in HCT-116 cells. Fluorescence microscopy confirmed cellular uptake of GA-CDs, and AO/PI staining revealed an increase in apoptotic cell numbers. Q-PCR analysis revealed overexpression of Caspase-3 and Bax genes in cells treated with GA-CDs compared to those treated with GA and the control group. However, no significant changes were observed in the Bax/Bcl-2 ratio across treatments.
Conclusion: This study demonstrates the ability of GA-CDs to induce apoptosis in HCT-116 colorectal cancer cells, further supporting their potential as novel anticancer agents. These findings warrant further investigation into the molecular mechanisms underlying GA-CD-induced apoptosis and their potential clinical applications.

Keywords: Gallic acid, Carbon dots, Colorectal cancer, HCT-116 cell line, Apoptosis

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Abstract: A-10-2558-2

Gallic Acid-Based Carbon Dots Induce Apoptosis Related Genes in Colorectal Cancer

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3. Solid Tumor Research Center, Cellular and Molecular Research Medicine Institute, Urmia University of Medical Sciences, Urmia, Iran.

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Conclusion: This study demonstrates the ability of GA-CDs to induce apoptosis in HCT-116 colorectal cancer cells, further supporting their potential as novel anticancer agents. These findings warrant further investigation into the molecular mechanisms underlying GA-CD-induced apoptosis and their potential clinical applications.

Keywords: Gallic acid, Carbon dots, Colorectal cancer, HCT-116 cell line, Apoptosis

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2655-1

Effects of Topical Application of Royal Jelly on Second-Degree Burn Wound Healing in Male Rats

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Background: Burn injury remain a major medical problem throughout the world. This injury is accompanied by inflammatory and wound-healing responses. Since royal jelly (RJ) has anti-inflammatory and wound-healing activity, therefore, this study aimed to evaluate the repairing effects of RJ on skin burn - damage.

Methods: In an experimental study, 40 male Wistar rats (8 weeks old) were engaged. The animals were divided into five equal groups. Group 1 was considered healthy control. Group 2 (positive control) was treated topically with Silver Sulfadiazine Cream, group 3 received Eucerin as negative control, and groups 4, and 5 were treated with RJ (10 and 30%). Sampling was performed after observing the second-degree burns on the first, seventh, and fourteenth days. Then after 28 days, rats were sacrificed and their skin tissues were used for morphological and morphometric assessments.

Results: The results of this study showed that the amount and arrangement of collagen type 1 protein was higher in the RJ treatment groups versus the control group. Reconstruction and thickening of the epithelium in RJ-treated groups confirmed the therapeutic effects of RJ. In addition, RJ increased angiogenesis compared to the control group. The wound's surface area was reduced in the RJ treatment groups compared to the control group. In addition, fibroblast cell proliferation was increased in the groups receiving RJ versus control.

Conclusion: It could be concluded that RJ induces wound healing effects and might be considered as a potential treatment option to improve burn wound healing.

Keywords: Burns, Inflammation, Royal jelly, Wound healing.

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Abstract: A-10-2165-1

The Beneficial Effects of Vitamin D on Oxidative Stress in Ethanol-Dependent Rats

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Background: Ethanol abuse significantly impacts brain health by inducing oxidative stress, which generates reactive oxygen species (ROS) that lead to cellular damage and neuroinflammation. On the other hand, studies have shown that Vitamin D may play a protective role against brain damage by enhancing the brain's antioxidant defenses. Therefore, this study aimed to investigate the effect of different doses of vitamin D on the brain in rats with ethanol-induced brain injury.

Methods: 42 male albino Wistar rats were randomly divided into six groups: control, vehicle, Ethanol (1.25 g/kg), and three groups that received Ethanol + vitamin D (250, 500, and 1000 IU/kg respectively, administered intraperitoneally). After that, the levels of total antioxidant capacity (TAC), malondialdehyde (MDA), nitric oxide (NO), total oxidative status (TOS), and the activity of catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GPx) were determined in the brain tissue homogenate of the rats.

Results: The levels of MDA and TOS in each Ethanol + vitamin D group were significantly lower; additionally, the level of NO significantly decreased in the ethanol + 500 and 1000 IU/kg vitamin D groups compared to the ethanol control group ($P \leq 0.05$). Moreover, the levels of TAC and the activity of CAT and GPx in the ethanol + 500 IU/kg vitamin D group, as well as SOD activity in the Ethanol + 500 and 1000 IU/kg groups, were significantly higher than in the Ethanol control group ($P \leq 0.05$).

Conclusion: The outcomes of this study indicated that vitamin D, especially at a dose of 500 IU/kg was effective in reducing oxidative damage in the rat brain. Overall, our results suggest that vitamin D is potentially helpful in ethanol-induced brain injury.

Keywords: vitamin D, oxidative stress, ethanol, brain injury

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2645-2

The Effect of Spirulina Consumption on Liver Function Enzymes and Inflammation Parameters in Adults: A Grade-Assessed Systematic Review of Randomized Clinical Trials

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Background: Common liver disease treatments have some side effects and require harmless treatments, such as spirulina. This systematic review of randomized clinical trials (RCTs) is presented for the first time to reveal the spirulina's impact on liver functional enzymes (AST, ALT, and ALP) and inflammation factors (IL-6, TNF-α, and hs-CRP). **Methods:** This study carried out systematic searches until April 5, 2024, to distinguish related RCTs. We employed contracted procedures for publication bias, heterogeneity, sensitivity analysis, and meta-regression. We applied the GRADE criteria and the Cochrane assessment procedure to measure the risk of bias and the certainty of study outcomes, respectively.

Results: Spirulina consumption lowers ALT (WMD: -2.44 U/L, 95%CI: -4.14 to -0.66) and AST (WMD: -2.05 U/L, 95%CI: -3.63 to -0.48) levels but does not significantly change ALP levels. Also, spirulina intake at 8 ≥ weeks, dose < 5 g/day, and age < 50 years is effective in decreasing these. Also, spirulina reduced inflammatory factors like IL-6 (WMD: -0.68 pg/ml, 95%CI: -1.31 to -0.06) and TNF-α (WMD: -0.34 pg/ml, 95%CI: -0.6 to -0.08) levels. Indeed, spirulina has no significant effect on overall hs-CRP levels. While subgroup analysis has shown spirulina intake > 8 weeks, dose ≥ 5 g/day, and age < 50, it has continued to decline inflammation factors. Indeed, in hs-CRP, we observe publication bias (Egger = 0.03) and no relationship between spirulina dose and duration with outcomes. The quality of evidence for AST, ALT, IL-6, and TNF-α is high, while ALP and hs-CRP have moderate and low quality, respectively.

Conclusion: This study confirmed that spirulina intake improves liver function and reduces inflammation in different situations. So, spirulina can be an effective and helpful supplement or adjutant with other medical supplements to reduce inflammation and improve liver function.

Keywords: Meta-analysis, Spirulina, Liver enzymes, Inflammation

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Abstract: A-10-2184-1

Protective Effects of Graded Iranian Honey Against Cold-Induced Gastric Ulcers in Rats

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Background: Honey, rich in diverse bioactive compounds, possesses significant therapeutic potential beyond its nutritional value. With a history of traditional use spanning centuries, this study aimed to evaluate the protective effects of various Iranian honey samples against cold water immersion stress-induced gastric ulcers in rats.
Methods: This experimental study involved 40 male Wistar rats (250-280g) randomly assigned to eight groups (n=5). A control group was compared to a group subjected to cold water immersion stress (CWIS). Three groups received strong honey varieties (Eucalyptus, Annaba, and Jangale) in conjunction with CWIS, while three other groups were administered weak honey types (Chand Giah, Sumaq, and Gaz) alongside CWIS. For fourteen days, rats received oral honey solutions (20% w/v) at a dose of 1ml/kg twice daily, with the control group receiving saline. After a 24-hour fasting period, a three-hour CWIS was induced to establish an ulcer model. Macroscopic stomach examinations, gastric ulcer index (GUI), gastric juice volume, and histopathological assessments were conducted. Additionally, MDA, total antioxidant capacity (TAC), serum TNF-α, and IL-6 levels were measured.
Results: Results demonstrated that Eucalyptus, Annaba, and Jangale honey exhibited superior total phenolic content (TPC), antioxidant capacity (FRAP, DPPH), and protein levels compared to Chand Giah, Sumaq, and Gaz, categorizing them as strong and weak honey, respectively. The ulcer group displayed a significant 64% increase in MDA and concurrent decreases of 26%, 14.39%, and 26% in FRAP, DPPH, and thiol compared to controls. Furthermore, TNF-α and IL-6 levels were elevated by 98.5% and 111.6%, respectively, in the ulcer group. GUI was notably reduced by 50% in groups treated with strong honey compared to those receiving weak honey formulations.
Conclusion: Honeys rich in antioxidants, phenolic compounds, and proteins (strong) demonstrated superior efficacy in protecting rats against stress-induced ulcers compared to those with lower concentrations of these bioactive components (weak).

Keywords: Cold water immersion stress, Rat, Strong honey, Stress ulcer, Weak honey

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2431-2

Correlation of Vitamin E Serum Level with Oxidation of the Low-Density Lipoprotein in Patients with Diabetes with and Without Coronary Artery Disease

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Background: Oxidative modification of low-density lipoprotein (LDL) is closely related to increased risk of coronary artery disease (CAD) in diabetic patients. On the other hand, vitamin E, as the main fat-soluble antioxidant in LDL particles, increases the resistance of LDL against oxidation by preventing lipid peroxidation of unsaturated fatty acids and modification of proteins in LDL by ROS. Also, by reducing the expression of CD38 receptors, it reduces the absorption of Ox-LDL particles by macrophages. The purpose of this study was to investigate the protective effect of vitamin E in preventing the oxidation of LDL in patients with diabetes with and without coronary artery occlusion.
Methods: This study was designed as a cross-sectional survey of 82 patients with diabetes divided into two groups including T2DM alone (as group I) and both T2DM and CAD (as group II). Blood samples of all subjects were taken after 12-h fasting. Serum samples were saved after centrifugation (20 min; 3000 rpm) at –80 °C. The serum value of Ox-LDL was measured by the Enzyme-linked immunosorbent method. The level of serum vitamin E was measured by the high-performance liquid chromatography method.
Results: The mean values of ox-LDL in group II were significantly higher compared with group I (1498.17±159.82 vs 1276.56±271.31: P value = 0.000). The mean values of vitamin E were significantly lower in group II compared with group I (2.65±0.84 vs 4.61±2.01: P value = 0.000). There was a negative correlation between Ox-LDL and vitamin E in the entire study population (P value = 0.000 and R = − 0.382).
Conclusion: The results of this study support the belief that deficiency of the antioxidant factors may be an important etiological factor that may predispose patients with diabetes to CAD. Increasing antioxidants may be a potential therapeutic target in the prevention and management of CAD in diabetic patients.

Keywords: Diabetes Mellitus, Coronary Artery Disease, vitamin E, Ox-LDL

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2695-1

Enhancement of the Antiproliferative and Antimetastatic Effect of Chlorogenic Acid by Cyclodextrin-Graphene Oxide Conjugates

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Background: Glioblastoma is the most common primary brain cancer. Research is exploring new agents with better efficacy and fewer side effects. Chlorogenic acid (CGA), found in plants like coffee and blueberries, shows potential against this aggressive cancer. Cyclodextrin, a cyclic oligosaccharide with a hydrophilic external surface and a hydrophobic internal cavity, has been explored to improve the solubility and cellular uptake of hydrophobic drugs. Cyclodextrin-graphene oxide conjugates improve drug delivery, stability, and bioavailability of CGA. Combining cyclodextrin-graphene oxide nanoparticles with CGA (CGA-NPs) represents a promising strategy for glioblastoma treatment.

Methods: We assessed the physicochemical properties of NPs and CGA-NPs. The cytotoxicity of NPs, CGA, and CGA-NPs was evaluated using the MTT assay. We studied their effects on apoptosis and cell cycle arrest of U87 cells via flow cytometry, as well as measuring apoptosis-related gene expression, ROS levels, and cell migration ability.

Results: CGA-NPs demonstrated significant antiproliferative and apoptotic effects on glioma cells, with ROS generation likely involved. CGA-NPs caused G2/M arrest and substantially reduced U87 cell migration and invasion. MMP-2 activity and gene expression were notably inhibited in the presence of CGA-NPs, and the Bax/Bcl2 expression ratio was significantly decreased.

Conclusion: CGA-NPs show promising anticancer effects in U87 cells, indicating potential for future glioblastoma therapies.

Keywords: Cancer, Glioblastoma, Chlorogenic acid, Cyclodextrin-Graphene oxide.

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2170-1

Spirulina Platensis Ameliorates Cognitive Decline and Neuroinflammation in D-galactose-induced Aging Model Rats

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Background: Age-related cognitive decline (ARCD) and neurodegenerative diseases pose a significant and growing burden on global healthcare. Current therapies require drugs with better efficacy and safety. Recently, herbal supplements like Spirulina platensis (SP) have been shown neuroprotective effects. SP a blue-green algae rich in antioxidants and anti-inflammatory compounds, has emerged as a potential therapeutic candidate for neurodegenerative diseases. This study aimed to assess the effects of Spirulina platensis on neurobehavioral and biochemical parameters in a D-galactose-induced aging model in rats.

Methods: In this experimental study 30 Male Wistar rats were divided into three groups: control, D-galactose-induced aging (Dg), and Dg with Spirulina platensis treatment (Dg+SP). For aging induction in Dg+SP and Dg groups, the Dg (300 mg/kg) was subcutaneously injected for six weeks. In the Dg+SP group, all animals were fed with a diet containing SP 5% during the six weeks. After the sixth week, Cognitive function was assessed using the passive-avoidance test. Hippocampus oxidative stress markers (MDA, ROS) and SOD activity were measured biochemically. Protein expression of inflammatory markers (TNF-α, IL-1β, NF-κB) was evaluated by ELISA kits. Finally, the data were presented as mean ± standard error of the mean (SEM) and analyzed with Prism 8.0 software. Statistical analyses were conducted through one-way ANOVA. Differences were considered significant at p 0.05.

Results: Dg-treated rats exhibited memory impairment, increased oxidative stress, and inflammation in the hippocampus compared to controls, while SP treatment significantly improved memory performance and reversed Dg effects. ELISA analysis revealed that SP downregulated TNF-α, IL-1β, and NF-κB expression, suggesting a protective effect on the brain.

Conclusion: SP administration improved memory function and alleviated Dg-induced oxidative stress and neuroinflammation. These findings suggest SP may be a promising strategy to combat age-related cognitive decline. However, Further research is warranted to confirm these results and explore the underlying mechanisms.

Keywords: Spirulina platensis, Cognitive decline, Aging, Oxidative stress, Neuroinflammation, Gut-brain axis

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2717-1

Resveratrol Mitigates Colorectal Cancer Progression by Targeting the JNK Signaling Pathway to Reduce Oxidative DNA Damage

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Background: Recent evidence has proved that resveratrol, a natural polyphenol, has great anti-cancer and anti-proliferative effects in cancer cells. In this study, we aimed to examine the protective effects of resveratrol in rats with 1,2-dimethylhydrazine (DMH)-induced colorectal cancer and investigate the potential underlying molecular mechanisms.

Methods: Male Wistar rats were classified into different groups, including Group 1 without any intervention, group 2 as resveratrol-received rats (8 mg/kg), Group 3 as DMH-received rats, and Group 4, as DMH and resveratrol-received rats. DNA damage, DNA repair, the expression levels and activities of antioxidants, and JNK signaling were evaluated in colon tissues.

Results: We found that DNA damage and DNA repair were significantly suppressed and induced, respectively, in DMH + resveratrol groups. The expression levels and activities of antioxidants were increased in DMH + resveratrol groups. Lipid and protein peroxidation were significantly suppressed in DMH + resveratrol groups. In addition, resveratrol also modulated JNK signaling in DMH + resveratrol groups.

Conclusion: Our finding demonstrated that resveratrol effectively reversed DMH-mediated oxidative stress and DNA damage by targeting the JNK signaling pathway.

Keywords: Colorectal Cancer, Resveratrol, JNK signaling, DNA damage

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2729-1

The Association Between Maternal Selenium Levels and the Risk of Neural Tube Defects: A Systematic Review and Meta-Analysis

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Background: Neural tube defects (NTDs) are serious congenital anomalies of the central nervous system that develop early in pregnancy. Emerging evidence suggests that imbalances in essential trace elements, such as selenium (Se), may influence fetal development and increase the risk of NTDs. This systematic review and meta-analysis examine the relationship between maternal selenium status and the risk of NTDs.

Methods: This systematic review and meta-analysis adhered to PRISMA guidelines. Databases including PubMed, Scopus, and Web of Science, along with Google Scholar search engine, were searched using the keywords "neural tube defects" AND "selenium." Observational studies comparing selenium levels in pregnant women with NTD-affected fetuses to healthy controls were included. Reviews, interventional and animal studies, conference papers, and case reports were excluded. Two authors independently screened and extracted data, with discrepancies resolved by a third author. Study quality was assessed using the Newcastle-Ottawa Scale, and heterogeneity was evaluated using I^2 statistics. A random-effects model was employed to calculate weighted mean differences (WMD) and pooled odds ratios (ORs). Analyses were conducted with Stata version 14.2.

Results: From an initial 198 studies, 50 duplicates and 140 irrelevant studies were excluded, leaving 8 studies (3 cross-sectional and 5 case-control) with 2,243 women, of whom 985 (43.91%) had infants with NTDs. The meta-analysis revealed significantly lower selenium levels in NTD cases [WMD = -19.63; 95% CI: -22.45, -9.81; I^2 = 91.9; N = 4]. The difference in placental selenium levels was not significant [WMD = -56.7; 95% CI: -149.57, 36.23; I^2 = 98.3; N = 3]. Lower selenium levels were associated with increased odds of NTDs [Pooled OR = 0.30; 95% CI: 0.22, 0.39; I^2 = 0; N = 3].

Conclusion: According to these results, monitoring Se levels during pregnancy is recommended, especially among populations at risk of nutritional deficiency.

Keywords: Neural tube defects, Selenium, Pregnancy, Placenta, fetus

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Abstract: A-10-2747-1

Co-Administration of NLRP3 Inhibitor and Naringin Reduces Inflammation and Oxidative Stress in Cuprizone-Induced Demyelination Model

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Background: Considering the interaction between inflammation and oxidative stress in demyelination and its potential role in neurodegenerative diseases, this study investigated the effects of MCC950 as an inflammasome inhibitor and naringin, a flavonoid compound, on the levels of inflammation and oxidative stress in cuprizone (CPZ)-induced demyelination model.

Methods: To induce demyelination, cuprizone (0.2% w/w) was incorporated into the standard diet of mice for 42 days. Following this period, the male C57BL/6 mice that received cuprizone were divided into two groups: control group (CPZ+Saline) and naringin + MCC950 treated group (CPZ+Nar+MCC950) for 14 days. The expression levels of genes associated with oligodendrocytes, antioxidants, and inflammation (MBP, Nrf2, HO-1, IL1β, and IL18) were analyzed through RT-qPCR.

Results: Our results indicated that the co-administration of naringin and MCC950 elevated the expression levels of antioxidant genes Nrf2 and HO-1 ($P<0.05$), decreased the expression of IL1β and IL18 ($P<0.0001$), and increased the expression of the oligodendrocyte gene MBP ($P<0.001$) compared to the CPZ+Saline group.

Conclusion: These findings suggest that the co-administration of naringin and MCC950 could serve as a pharmacological intervention to improve myelin repair by enhancing antioxidant capacity, and reducing inflammation in the CPZ-induced demyelination model.

Keywords: Naringin, Cuprizone, Oxidative stress, Inflammation, MCC950

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2755-1

The Protective Potency of Vitamin E Supplementation on Working Memory, Oxidative Stress and Age-Related Gene Expression in Aged Mice

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Background: Aging is an inherent biological process that involves the gradual buildup of detrimental changes in cells. This accumulation of damage to cells results in impaired cellular function and disrupts the balance within tissues. Oxidative stress contributes to aging by causing damage to cells, tissues, and organs. So, this study aimed to evaluate the effect of vitamin E as an antioxidant on oxidative stress, cognitive function, and age-related gene expression in aged mice.

Methods: Twenty-eight male NMRI, 48-week-old mice, were used in 4 groups of vitamin E daily gavage: the control group (distilled water), and three treatment groups who received 100, 200, and 400 mg/kg, for 4 weeks. In the end, y-maze tests, brain and heart histology, tissue antioxidant enzyme (SOD and GPx activities, and MDA amount), and gene expression were evaluated.

Results: The results showed significant improvements in cognitive function, specifically in working memory and spatial learning, in the groups that received vitamin E (100 mg/kg, 200 mg/kg, or 400 mg/kg) compared to the control group. The markers of oxidative stress and antioxidant enzyme activities also demonstrated improvements, with higher doses of vitamin E showing greater effects. The analysis of gene expression revealed increased expression of SIRT1, Nrf2, and Calstabin2, particularly at higher doses of vitamin E.

Conclusion: The study concludes that vitamin E supplementation can reduce oxidative stress, enhance cognitive function, and affect genetic markers of aging in mice, which may have therapeutic benefits in addressing age-related cognitive decline and oxidative damage.

Keywords: Aging, Vitamin E, Oxidative stress, Mice

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Abstract: A-10-2496-1

Kaempferol Attenuates Amyloid-Beta Toxicity in dPC12 Cells by Enhancing UPR and Autophagy

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Background: To date, a definitive cure for Alzheimer's Disease (AD) remains elusive. One of the important factors responsible for the onset and progression of the disease is oligomer and fibrillary Aβ plaque primarily composed of Aβ peptides. Hence, a possible approach to overcome the ailment could be reducing Aβ oligomerization and fibril formation. Using compounds potentially inhibiting Aβ aggregation is considered a good approach to treat and prevent AD. Natural products containing polyphenolic compounds, such as Crocus Sativus, berries, etc. are known to have neuroprotective activities. Kaempferol is a polyphenolic compound that was found in the Crocus Sativus petals.

Methods: We induced the AD model in the differentiated PC12 cell line. Kaempferol, a polyphenol compound, was applied as a treatment in both a preventive and therapeutic manner. Flow cytometry was used to assess apoptotic rate and cell cycle distribution. In addition, we used Western blot to evaluate some signaling protein levels, and RT-PCR to determine the XBP-1s at the mRNA level.

Results: Aβ1-42 oligomer form led to apoptosis in dPC12 cells. Kaempferol in both a therapeutic and preventive manner led to a significant reduction in apoptosis rate compared to the AD model. In addition, Kaempferol significantly reduced the Sub-G1 and significantly increased the G0/G1 phases. Kaempferol remarkably decreased the p-eIF2α/T-eIF2α expression and remarkably upregulated the XBP1s expression. Furthermore, it increased autophagy markers level, Beclin-1, and LC3 in the treated cells.

Conclusion: Our results indicated that Kaempferol could reduce apoptotic rate in preventive and therapeutic modalities, compared to AD. By assessing UPR and autophagy, we suggested that these impacts could occur through the clearance of unfolded/ misfolded proteins by inducing autophagy and attenuating the cargo load on the endoplasmic reticulum. Kaempferol can be introduced as a potential candidate for the prevention and treatment of AD for further studies.

Keywords: amyloid-beta, UPR, Autophagy, Kaempferol

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Abstract: A-10-2349-2

Exogenous Glutathione Ameliorates Gentamicin-Induced Nephrotoxicity by Reducing Oxidative Stress and Apoptosis

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Background: Gentamicin (GM) is clinically used to treat infections caused by gram-negative bacteria. However, the undesirable effects of GM on kidney function restrict its clinical use. Glutathione (GSH) is a tripeptide compromising from glutamate, cysteine, and glycine and has strong antioxidant activity. In the present study, we examined the nephroprotective effects of GSH against GM-mediated nephrotoxicity in Wistar rats.

Methods: Adult male rats were divided into four groups (n = 8). The control group was treated with intraperitoneal normal saline. GSH group was intraperitoneally administered with GSH. Intraperitoneal GM (100 mg/kg) was administered to rats in the GM group to induce nephrotoxicity. GM + GSH group was treated with GM (100 mg/kg) and GSH (100 mg/kg). GM and/or GSH were administered to the animals for 12 consecutive days. After treatment, the right kidney was frozen for biochemical analysis. The left kidney was stored in neutral buffered formalin (10%) for immunohistochemical analysis. Malondialdehyde (MDA) concentrations and glutathione peroxidase (GPX) activity were determined spectrophotometrically in the kidney tissues. Renal caspase-3 expression was examined using immunohistochemistry.

Results: The GM group exhibited considerably elevated MDA concentration and caspase-3 expression compared with those in the control group. In contrast, GPX activity was significantly lower in nephrotoxic animals than in the control group. Interestingly, GSH significantly decreased MDA concentration and caspase-3 expression compared to nephrotoxic animals. Conversely, GSH treatment significantly promoted GPX activity in the GM + GSH group compared with that in the GM group.

Conclusion: GSH administration attenuated GM-induced nephrotoxicity in rats by regulating oxidative stress and apoptosis.

Keywords: Gentamicin, Nephrotoxicity, Exogenous glutathione, Oxidative stress, Apoptosis

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Abstract: A-10-2824-1

The Role of Linarin in Increasing the Sensitivity To 5-Fluorouracil in Colorectal Cancer Cells 77by Targeting the PI3K/AKT/FOXO3a Pathway

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Background: Colorectal cancer (CRC) remains a formidable health burden challenge worldwide, with drug resistance complicating treatment. Combination therapies with natural compounds that can potentiate the anti-cancer effects of chemotherapeutics agents and overcome resistance mechanisms represent a promising therapeutic strategy. This study explores the potential of linarin, a plant-derived flavonoid, to enhance 5-fluorouracil (5-Fu) efficacy in CRC cells.

Methods: Using SW480 cells, we investigated the combined effects of linarin and 5-Fu on cell viability, apoptosis, and migration. Molecular mechanisms were probed via qPCR and Western blotting, focusing on the PI3K/AKT/FOXO3a pathway. We established 5-Fu-resistant cells to evaluate resistance reversal. In vivo studies utilized a DMH-induced rat model. Pharmacokinetic interactions were assessed in rats.

Results: Our findings revealed synergistic cytotoxicity between linarin and 5-Fu, with enhanced apoptosis and reduced migration. Mechanistically, the combination modulated the PI3K/AKT/FOXO3a pathway more effectively than either agent alone. Both linarin and 5-Fu independently inhibit the phosphorylation of Akt, leading to the activation of the pro-apoptotic transcription factor FOXO3a and the subsequent upregulation of Bax while downregulating Bcl-2. Linarin partially reversed 5-Fu resistance in SW480-5FuR cells. In vivo, the combination significantly reduced tumor burden without apparent toxicity. Pharmacokinetic studies showed mutual influences, potentially contributing to enhanced efficacy.

Conclusion: These findings highlight linarin's potential as an adjuvant to 5-Fu, offering a novel approach to improving CRC treatment outcomes. The unique synergistic mechanism via PI3K/AKT/FOXO3a modulation offers insights warranting further clinical investigation.

Keywords: Colorectal cancer, linarin, 5-fluorouracil, PI3K/AKT/FOXO3a pathway, Drug resistance

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Abstract: A-10-2842-1

Effects of Naringenin on Inflammation and Oxidative Stress in Patients with Diabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Background: Naringenin, a flavonoid abundant in citrus fruits, has garnered attention for its potential therapeutic effects on inflammation and oxidative stress, particularly in diabetic patients. This systematic review and meta-analysis aimed to evaluate the efficacy of naringenin in reducing inflammatory markers and oxidative stress in individuals with diabetes.

Methods: A comprehensive literature search was conducted across multiple databases, including PubMed, Scopus, and Cochrane Library, for randomized controlled trials (RCTs) published until August 2023. Studies were included if they assessed the effects of naringenin supplementation on inflammation and oxidative stress markers in patients with diabetes patients. Data extraction was performed independently by two reviewers, and the quality of the studies was assessed using the Cochrane risk-of-bias tool. Meta-analysis was conducted using random-effects models to calculate standardized mean differences (SMD) and 95% confidence intervals (CIs).

Results: A total of 10 RCTs involving 600 diabetic patients were included in the analysis. Naringenin supplementation significantly reduced levels of inflammatory markers, including C-reactive protein (CRP) and interleukin-6 (IL-6), with SMDs of -0.75 (95% CI: -1.10 to -0.40, $p < 0.001$) and -0.65 (95% CI: -0.95 to -0.35, $p < 0.001$), respectively. Additionally, naringenin was associated with a significant decrease in oxidative stress markers, including malondialdehyde (MDA), with an SMD of -0.82 (95% CI: -1.20 to -0.44, $p < 0.001$).

Conclusion: Naringenin appears to be an effective agent in reducing inflammation and oxidative stress in patients with diabetes. These findings support the potential of naringenin as a complementary therapeutic option for managing diabetes-related complications. Further large-scale studies are warranted to confirm these results and elucidate the underlying mechanisms.

Keywords: Naringenin, inflammation, oxidative stress, diabetes, systematic review, meta-analysis

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Abstract: A-10-2723-1

Ameliorating the Toxicity Induced By L-Arginine Through Iris Germanica Methanolic Extract in An Experimental Model of Acute Pancreatitis

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Background: L-arginine, a popular supplement among athletes, has been observed to potentially induce pancreatic toxicity and acute pancreatitis when consumed in high doses. This study investigated the antioxidant and anti-inflammatory effects of Iris germanica (I. germanica) methanolic extract on pancreatic tissues in male rats with L-arginine-induced Toxicity. The quantification of total polyphenols, flavonoids, and antioxidant activity in the extract of I. germanica was conducted through a colorimetric assay, with the individual components being analyzed using HPLC.

Methods: The male rats were divided into five groups: normal control, L-arginine only, L-arginine + melatonin (positive control), L-arginine + I. germanica extract (100 mg/kg), and L-arginine + I. germanica extract (400 mg/kg). Various parameters were measured to evaluate the extract's effects, including serum amylase and lipase activity, oxidant/antioxidant parameters (SOD activity, TAC, lipid peroxidation), and tissue MPO and NO levels. A histopathological examination was also conducted.

Results: Results showed that the L-arginine group had significantly increased serum lipase and amylase levels compared to the normal control group. However, treatment with I. germanica extract (at doses of 100 and 400 mg/kg) and melatonin significantly reduced serum lipase levels at all time points (24 hours, 72 hours, and 14 days) and serum amylase levels at 24 hours. Additionally, I. germanica extracts dose-dependently increased TAC levels and decreased MPO and malondialdehyde levels. No significant differences were observed in TNF-α, IL-6, and IL-10 levels among the groups. Histopathological analysis revealed that I. germanica extracts reduced cell necrosis and interstitial edema in the pancreas compared to the L-arginine group.

Conclusion: I. germanica methanolic extract exhibited antioxidant and anti-inflammatory effects in L-arginine-induced acute pancreatitis in male rats. This suggests its potential as a therapeutic option for acute pancreatitis.

Keywords: Acute pancreatitis, Iris germanica, Methanolic extract, Antioxidant, Anti-inflammatory

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Abstract: A-10-2454-2

Melatonin Has a Neuroprotective Effect on Cerebral Ischemia/reperfusion Injury Via Anti-Inflammation and Antioxidant properties

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Background: Stroke is a leading cause of death and disability worldwide, with over 80% of strokes classified as ischemic, which occur due to blockages in cerebral arteries. The primary objective of this research was to evaluate the neuroprotective effects of melatonin on a rat model of cerebral ischemia/reperfusion injury (CIRI).
Methods: Cerebral ischemia/reperfusion injury was induced in rats through the occlusion of the middle cerebral artery. To assess the neuroprotective impact of melatonin, intra-peritoneal injections of melatonin at a dose of 40 mg/kg body weight were administered 30 minutes before and after the induction of CIRI. The study measured several markers of oxidative stress, including Nitrite (NO2-), Ferric Ion Reducing Antioxidant Power (FRAP), and Malondialdehyde (MDA), in hippocampal tissues and serum. Additionally, neural damage in the CA1 and CA3 regions of the hippocampus was evaluated using hematoxylin and eosin (H&E) staining to determine the extent of neuronal preservation and damage.
Results: The administration of melatonin resulted in a notable increase in the pyramidal cell layers of the CA1 region of the hippocampus following stroke. This suggests enhanced neuronal survival and reduced ischemic damage. Furthermore, melatonin treatment led to a significant decrease in the levels of NO2- and MDA, both of which are markers of oxidative stress. Concurrently, there was a considerable increase in FRAP levels in both hippocampal tissues and serum, indicating an overall enhancement in antioxidant capacity.
Conclusion: The findings of this study suggest that melatonin exhibits significant neuroprotective properties in the context of cerebral ischemia/reperfusion injury through its ability to reduce oxidative stress and inflammation.

Keywords: Stroke, melatonin, oxidative stress, inflammation

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Abstract: A-10-2694-1

The Effect of Berberine from Berberis Vulgaris on Treating Type 1 Diabetes in Streptozotocin-Induced Diabetic Rat Models

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Background: In traditional medicine, B. vulgaris is used to treat diabetes. Berberis vulgaris contains a variety of valuable isoquinoline alkaloids such as berberine. Berberine has many clinical effects on the human body, the most important of which is the effect of treating and improving diabetes.
Methods: Type one diabetes was induced in 16 rats using 65 mg/kg of streptozotocin. Rats in two groups of eight were treated orally with 500 and 1000 mg of berberine for 60 days. The HPLC-UV method was used to measure the half-life of the berberine. In addition, the best time for berberine's impact on reducing blood sugar was determined using an in vivo approach. The rat blood was collected at the end of 60 days to investigate the effect of berberine on the blood biochemical factor. Pathological analyses were done using hematoxylin-eosin (H&E) staining. Additionally, the effects of berberine on improving the endocrine and exocrine parts of the pancreas were evaluated.
Results: The concentration of berberine in rat blood was measured from zero to 90 minutes, and the half-life of berberine was 60 minutes after gavage. FBS levels in healthy and diabetic rats were 94 and around 600 mg/dL, respectively. Berberine reduced FBS by 50%, to an average level of about 300 mg/dL in the treated groups. Also, other measured biochemical factors showed significant positive changes. The destruction of the islets of Langerhans, along with the severe degeneration, atrophy, and vacuolation of the pancreas, showed improvement.
Conclusion: Berberine is an effective herbal medicine for reducing blood sugar (hyperglycemia) and improving pancreatic function in type 1 diabetes. Therefore, berberine has therapeutic potential for treating this disease.

Keywords: Type one diabetes, Berberine, Berberis vulgaris

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Abstract: A-10-2225-1

Positive Association of Serum CCN5/WISP2 Levels with the Risk of Developing Gestational Diabetes Mellitus: A Case–control Study

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Background: CCN5/WISP2 is prominently manifested in adipose tissue and has been linked to the pathogenesis of obesity, diabetes, and insulin resistance. However, discrepancies exist in previous studies, and little is known about its association with gestational diabetes mellitus (GDM). The current investigation is designed to examine the correlation of WISP2 with risk factors in GDM patients in comparison to healthy pregnant women for the first time.
Methods: This case–control study measured serum levels of CCN5, TNF-α, IL-6, adiponectin, and fasting insulin using ELISA kits in 88 GDM patients and 88 pregnant women.
Results: The GDM group had remarkably higher serum levels of CCN5 (379.41 ± 83.078 ng/ml) compared to controls (212.02 ± 77.935 ng/ml). Similarly, it was observed that patients diagnosed with GDM exhibited elevated levels of pro-inflammatory cytokines such as IL-6 and TNF-α; while conversely, adiponectin levels were found to be significantly lower than those observed in the control group ($P<0.0001$). In women with GDM, a positive and significant correlation was observed between CCN5 and BMI, FBG, insulin, HOMA-IR, as well as IL-6 and TNF-α levels. In the adjusted model, the risk of GDM was significantly increased with elevated serum CCN5 level.
Conclusion: Our research indicates a noteworthy and affirmative correlation between the levels of CCN5 in the serum and the risk of developing GDM, along with its associated risk factors such as BMI, insulin resistance index, FBG, and inflammatory cytokines (TNF-α and IL-6). These findings suggest that CCN5 could potentially play a role in the etiology of GDM.

Keywords: CCN5/WISP2, Gestational diabetes mellitus, Inflammation, Pregnancy, Women

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Abstract: A-10-2183-1

Modulation of Metabolite Interconversion Enzyme Gene Expression in Sperm and Sertoli Cells of Non-Obstructive Azoospermia: Insights from Microarray Data and In-Silico Analysis

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Background: Numerous factors intricately regulate the metabolism of Sertoli cells and sperm, with sex steroid hormones emerging as a pivotal player. These hormones not only maintain energy homeostasis but also wield considerable influence over the metabolic equilibrium of the human body. Given the critical role of energy status in reproductive function, understanding its regulation is paramount, as the reproductive axis demonstrates responsiveness to metabolic cues.

Methods: To delve into this intricate interplay, advanced methodologies such as microarray and bioinformatics were employed. These techniques shed light on the activity of metabolite interconversion enzymes within the context of 200 genes expressed in sperm and Sertoli cells.

Results: In sperm, heightened expression of monooxygenase DBH like 1 (MOXD1) and cytochrome P450 family 46 subfamily A member 1 (CYP46A1) was observed, juxtaposed with decreased expression of arginine decarboxylase (ADC) and cytochrome b5 type B (C0YB5B). Conversely, Sertoli cells from individuals with non-obstructive azoospermia (NOA) exhibited upregulation in RPIA, PIK3C3, LYPLA2, and HDHD2 expression, while a slew of genes—including L2HGDH, GALNTL2, OXCT1, GSTT2, HSD17B7, PDPR, SESN1, ESCO2, SYNJ2, EBPL, DHFR, SORD, and CES1—showed downregulation. To unravel the functional and molecular networks underlying these changes, STRING and Cytoscape online assessments were employed. They revealed intricate connections among proteins and helped identify master genes. Notably, G1/S-specific transcription, pyruvate and citric acid metabolism, and alkylation damage caused by DNA dioxygenases emerged as primary molecular functions of the up/down-regulated genes in sperm. In Sertoli cells, folate metabolism and the p53 signaling pathway took precedence.

Conclusion: Validation of these findings through weighted gene co-expression network analysis and single-cell data corroborated the observed changes in gene expression patterns. Collectively, these results unveil a novel mechanistic insight into NOA and unveil potential therapeutic targets for patients grappling with this condition.

Keywords: Sertoli cells, sperm, dioxygenases, p53, signaling pathway, co-expression

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Abstract: **A-10-2267-1**

HDL Functionality Assessments and Its Relevance to the Cardiovascular Endpoint

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Background: HDL functionality instead of plasma concentrations has focused, on specific cellular cholesterol efflux capacity (CEC). A cholesterol-efflux capacity (CEC) measure has been reported to be inversely related to the incidence of cardiovascular events. The efficiency of high-density-lipoprotein (HDL) to CEC contributes to the reverse cholesterol transport (RCT) pathway as one of HDL's proposed functions. It depends on the ability of HDL to uptake cholesterol. In this project, we developed a new assessment and investigated cholesterol uptake capacity (CUC) in subjects from the MASHAD (Mashhad-Stroke and Heart-Atherosclerotic Disorders) cohort study.
Methods: The study population, 35-65 years old, included 194 individuals who developed CVD diagnosed by a specialist cardiologist and 309 subjects without CVD over 10 years of follow-up. We used a modified method in our study. There are three principal steps in this method: (1) preparation of the plate containing the antibody; (2) preparing the serum mixture; and (3) cholesterol uptake capacity measurement.
Results: The mean level of HDL was significantly lower in the CVD group compared to the control (p=0.002) and also, there were differences in serum CUC level but, it was not significant between the groups. According to our result, there was a significant association between HDL and serum CUC with the risk of progressive CVD. Multivariate logistic regression analysis showed that there was a significantly negative association between CUC and risk of CVD after adjustment for confounding parameters (OR=0.87, 95%CI=0.95–0.77, P=0.03). Regarding evaluating lipid profiles, we found significant differences in serum total cholesterol and LDL. Furthermore, the CUC value was important in determining the CVD risk stratification derived from data mining analysis. The CUC assay was highly reproducible with values for inter- and intra-assay variation of 12.07 and 6.55, respectively.
Conclusion: Reduced HDL functionality seems to predict CVD events in population samples from north-eastern Iran.

Keywords: cholesterol uptake capacity (CUC), HDL function, cardiovascular disease (CVD), cohort study

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Abstract: A-10-2299-1

Inflammatory and Hematology Parameters and ANGPTL3 Polymorphism in Cardiovascular Disease Risk Assessment

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Background: Recent findings have confirmed that chronic inflammatory disorders are associated with an increased risk of cardiovascular disease (CVD). Moreover, numerous GWAS studies have elucidated the role of a loss-of-function variant of the angiopoietin-like 3 gene (ANGPTL3) with different inflammatory cell types in promoting vascular oxidative stress. The aim of this study is to investigate the association of ANGPTL3 genetic variants and inflammatory and oxidant parameters in assessing the risk of cardiovascular diseases.

Methods: The participants were 1002 individuals in the Mashhad-Stroke and Heart-Atherosclerotic-Disorders (MASHAD) cohort study, Mashhad, Iran. Participants were divided into two groups: cardiovascular patients who were confirmed by cardiologists after 6 years of follow-up (n=153) and healthy ones (n=849). Inflammatory and hematology parameters including Anti-hsp27, Hs-CRP, PAB, WBCs, RDW, and NLR were calculated for each subject. DNA was extracted and genotyping of rs10789117, rs1748195, and 11207997 variants of the ANGPTL3 gene was performed using the Tetra-ARMS PCR assay.

Results: According to the results, there was a significant relationship between rs10789117 polymorphism and hs-CRP and WBCs parameters in individuals carrying AC and CC genotypes, with respectively. Also, this relationship between CC genotype, rs1748195 polymorphism, and hs-CRP was observed. For the rs11207997 C>T, CT genotypes were significantly associated with hs-CRP and WBCs in both CVD and no-CVD groups (P=0.042 and P=0.033, respectively). The rs10789117 variant was significantly related to the hs-CRP and WBCs parameters in the dominant models (AC and CC refer to AA). The important point is that this relationship remained significant even after adjusting with age, sex, dyslipidemia, PAL, and BMI (P-value<0.05). There was no significant relationship in PAB and Anti-hsp27.

Conclusion: The data of this study suggests that investigating inflammatory parameters such as hs-CRP and hematology parameters can be helpful in CVD risk assessment studies.

Keywords: Cardiovascular disease (CVD), ANGPTL3, Tetra-ARMS PCR, Inflammatory parameters, Hematology parameters

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2388-3

Exploring the Down-regulation of Chemerin, Visfatin, Nefestin and Resistin in the Inflammatory Response in Women with Recurrent Implantation Failure

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Background: Adipokines may serve as a crucial link between reproduction and energy metabolism, potentially contributing to recurrent implantation failure (RIF). However, existing research on adipokines has predominantly focused on blood samples, resulting in a significant gap in our understanding of their expression in the endometrium and endometrial decidualization. As a result, this study aimed to investigate the expression of Chemerin, Resistin, Visfatin, and Nefestin in the endometrium of women experiencing RIF compared to fertile women.
Methods: In the present study, 50 women with RIF and 50 fertile women were recruited. The endometrial expression of Chemerin, Resistin, Visfatin, and Nefestin was measured using real-time PCR. Serum levels of hs-CRP, LH, FSH, PRL, progesterone (P4), and estrogen (E2) were measured using the ELISA method.
Results: The recent study found that levels of Chemerin, Resistin, Visfatin, and Nefestin in the endometrium were lower in women with Recurrent Implantation Failure (RIF) compared to fertile women. In RIF women, there was a significant positive correlation between Chemerin and Visfatin, as well as between Chemerin and Resistin ($r=0.363$, $r=0.385$, p-value<0.05). On the other hand, in fertile women, there was a significant positive correlation between Nefestin and Resistin, as well as between Nefestin and Visfatin ($r=0.368$, $r=0.309$, p-value<0.05). The multinomial logistic regression analysis indicated that in women with obesity, low levels of hs-CRP and downregulation of Visfatin were associated with a reduced risk of RIF, with odds ratios of 3.3 and 5.2, respectively, compared to women with normal BMI.
Conclusion: Based on our research, it is suggested that adipokines, including chemerin, visfatin, Nefestin, and resistin, are involved in endometrial decidualization. These adipokines are vital for regulating processes in the uterus that are crucial for embryo implantation. Low expression of these adipokines in the endometrium may lead to immune responses, structural changes, and inflammatory responses.

Keywords: Chemerin, Visfatin, Nefestin, Resistin, recurrent implantation failure, inflammation

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2195-1

Exploring the Relationship between miR-16-5p and PDK4 in Fatty Liver Disease: Evidence from Clinical and Microarray Studies

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Background: Fatty liver disease (FLD) is a major public health issue. The expression of miR-16-5p varies in different cancers, but its role in FLD is not well-defined, with inconsistent reports. Pyruvate dehydrogenase kinase 4 (PDK4) is crucial for glucose metabolism, influencing the pyruvate dehydrogenase complex. PDK4 may be connected to hepatic steatosis in FLD by affecting pathways like gluconeogenesis and fatty acid metabolism. This study aims to examine the miR-16-5p/PDK4 relationship in FLD patients versus controls.

Methods: The GSE135251 and GSE244605 microarray datasets were downloaded from the GEO database. Gene expression differences between FLD patients and controls were analyzed using "limma" and "Dseq2" in R software. A miRNA-mRNA ceRNA network was established based on miRTarBase and TarBase interactions. Serum samples and white blood cells were collected from 40 FLD patients and 23 healthy individuals. qRT-PCR was employed to assess miR-16-5p and PDK4 gene expression.

Results: In the analysis of the data downloaded from the GEO database, 39 miRNAs and 4565 mRNAs with different expression were obtained. Also, the expression of mir-16-5p was significantly increased in FLD patients compared to the control group (logFC=3.2 & P-value=0.00044), and the expression of PDK4 was significantly decreased in FLD patients compared to the control group (logFC= -1.62 & P-value=0.000084). By analyzing qRT-PCR data, the expression level of miR-16-5p gene in patients with FLD was insignificantly increased compared to the control group (P-value>0.05). Also, the level of PDK4 gene expression in the patient group was significantly decreased compared to the control group (P-value<0.05).

Conclusion: From the results of this study, it can be concluded that the reduction of PDK4 gene expression can be related to the pathogenesis of fatty liver disease and can play an important role in the development of this disease.

Keywords: FLD, PDK4, miR-16-5p, NASH, NAFLD, MAFLD

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Abstract: A-10-2358-1

The Vitronectin (VTN) Gene Expression Levels Increased through the Suppression of hsa-miR-34a-5p in Patients With Vessel Restenosis

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Background: Vascular stenosis and restenosis are the most important causes of death in patients with coronary artery disease (CAD). The vessel in-stent restenosis (ISR) is due to inflammatory events that typically occur with platelet activation, neointima formation, VSMC migration, and proliferation at the vascular stent site. Monocytes play a major role in neointimal hyperplasia. The study aimed to focus on the Vitronectin gene expression levels and hsa-miR-34a-5p in PBMCs isolated from patients with vessel stenosis and healthy controls.
Methods: A total of 60 people who underwent coronary angiography, including patients with stent-no restenosis (SNR), in-stent restenosis (ISR), and healthy participants participated in this study. The age and sex parameters were matched between the patients and controls. The hematologic and biochemical factors including the lipid profile, FBS, CK-MB, WBC, and para-clinical indicators containing BP, DBP, and PR were measured in the participants. Furthermore, the Vitronectin gene expression levels were estimated using the RT-qPCR technique. The hsa-miR-34a-5p expression levels were measured by stem-loop technique. The data was analyzed with SPSS software.
Results: The data analysis in subjects who had significant TG and VLDL values showed that the PBMC Vitronectin gene expression level in ISR patients was significantly higher compared to the control group (p=0.02). However, the Vitronectin gene expression level in SNR was not significantly different from the control group (p=0.63). Moreover, the data showed that the hsa-miR-34a-5p expression level was significantly decreased in PBMC of ISR patients (p=0.02), but there was no significant change in SNR compared to the control group (p=0.31). There was inversely significant correlation between Vitronectin and hsa-miR-34a-5p gene expression levels (r = -0.44, p = 0.04).
Conclusion: The results showed that the increase of Vitronectin, as an inducer of molecular adhesion-involved signaling pathways, might be due to the suppression of hsa-miR-34a-5p expression level in ISR patients.

Keywords: Vascular Stenosis, Restenosis, has-miR-34a-5p, Vitronectin

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Abstract: A-10-2285-2

Novel Cardiometabolic Biomarkers Based on HDL Functionality

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Background: Developing reproducible, clinically-available, and cost-effective laboratory assays to evaluate HDL functions and improve cardiovascular disease (CVD) risk assessment has recently emerged as a challenge. The atherogenic ratios LDL-C/HDL-C, non-HDL-C/HDL-C, and log (TG/HDL-C) can provide a balance between proatherogenic and antiatherogenic lipoproteins; however, HDL-C may not always represent HDL function. The present study was conducted to help predict the risk of coronary artery disease (CAD) by investigating new cardiometabolic risk factors based on substituting paraoxonase 1 (PON1) as a critical enzyme in the functionality of HDL for that of HDL-C.

Methods: The present study recruited 274 subjects undergoing diagnostic coronary angiography, 92 without significant CAD (non-CAD), and 182 with a severe CAD. ROC curves were constructed by plotting true positivity (sensitivity) on the y-axis and false positivity (1–specificity) on the x-axis.

Results: The diagnostic accuracy of the new biomarkers in non-CAD versus multi-vessel disease was obtained in descending order of AUC as 0.72 (P<0.001) for log (TG/PON1), 0.70 (P<0.001) for non-HDL-C/PON1, and 0.67 (P<0.001) for LDL-C/PON1. After performing a multivariate adjustment for age, gender, BMI, statin therapy, and diabetes mellitus, the increased odds of CAD remained significant for the new cardiometabolic ratios as independent variables [adjusted OR=1.47 (1.15-1.88), p=0.002 for LDL-C/PON1; adjusted OR=2.15 (1.41-3.5), p=0.009 for non-HDL-C/PON1; adjusted OR=5.03 (2.14-13.02), p=0.004 for log (TG/PON1)]. CAD was diagnosed with an optimal discriminating cutoff of 1.84 for LDL-C/PON1, 2.8 for non-HDL-C/PON1, and 0.48 for log (TG/PON1).

Conclusion: To improve CAD's risk assessment, the PON1 activity was proposed as an alternative to HDL-C in the commonly used atherogenic lipid ratios. Substituting the PON1 activity for the HDL-C concentration can provide an index of the HDL activity. The present study sought to exploit the lipoprotein-related risk factors of CAD from a more effective perspective.

Keywords: PON1, HDL, Biomarkers, Coronary artery disease, Lipoproteins

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Abstract: A-10-2269-1

Determining the Cut Off of Amino Acids and Acylcarnitine in the Screening of Metabolic Diseases of Newborns in Mazandaran Province by Tandem Mass Spectrometry

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Background: Hereditary metabolic diseases are mainly caused by genetic defects in the production or function of one of the proteins in the body. Hereditary metabolic disorders include fatty acid oxidation disorders, amino acid metabolism disorders, urea cycle disorders, and organic acidemias, which have been determined as the goal of the newborn screening program for hereditary metabolic diseases and are determined using Tandem mass spectrometry technology (LC- MS/MS) are detectable. Most of these diseases are manifested at young ages, and almost in most of these diseases, the central nervous system is involved in primary or secondary form.

Methods: In this study, twenty thousand (20,000) screening samples were used in the form of dried blood spot (DBS) on Whatman paper from newborn babies between 3-5 days after birth. The analysis method was that the DBS samples were punched inside the 96-well plate and then 100 microliters of the standard solution was added to the samples and injected into the LC MS/MS machine.

Results: The recorded data were analyzed by Stata 16 software. Then descriptive statistics of quantitative variables including mean ± standard deviation, median, range, interquartile range and normality were obtained. Normality was evaluated using the Kolmogorov-Smirnov test. Then, the calculation of the upper and lower pathological cut-offs of the laboratory was carried out.

Conclusion: The instructions issued by the Ministry of Health to start the analysis of the screening tests that the kit used does not provide the values of the reference range and the cut-off range is to use the universal cut-off. Therefore, it is necessary to determine the normal values and native cut-off range according to the genetic history, population structure, diet and age, which leads to the actualization of the reference range and the disease, as well as the reduction of false positive and negative cases.

Keywords: cut off, Hereditary metabolic diseases, newborn screening program, LC-MS/MS

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Abstract: A-10-2516-1

Impact of Modifiable Risk Factors on Prediction of 10-Year Cardiovascular Disease Utilizing Framingham Risk Score in Southwest Iran

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Background: This cohort study was conducted to examine the association between modifiable risk factors, including hypertension, smoking, physical activity, diabetes, cholesterol, and high-density lipoprotein with Framingham risk score in the prediction of 10-year-risk of cardiovascular diseases (CVD) between men and women in an Arab community of Southwest Iran, Hoveyzeh.

Methods: A total of 8,526 people aged 35–70 participated in this cohort study. Framingham was used to estimate the 10-year risk of CVD. Also, the linear regression models were used to assess the relationship between modifiable risk factors and the 10-year risk of CVD. Finally, the area under the receiver operating characteristic curve (AUC) was used to measure the ability of modifiable risk factors to predict the 10-year risk of CVD.

Results: Our results of linear regression models showed that hypertension, smoking, PA, diabetes, cholesterol, and HDL were independently associated with the CVD risk in men and women. Also, AUC analysis showed that hypertension and diabetes have the largest AUC in men 0.841; 0.778 and in women 0.776; 0.715, respectively. However, physical activity had the highest AUC just in women 0.717.

Conclusion: Hypertension and diabetes in both gender and physical activity in women are the most important determinant for the prediction of CVD risk in Hoveyzeh. Our cohort study may be useful for adopting strategies to reduce CVD progression through lifestyle changes.

Keywords: Cardiovascular disease, Framingham, Hoveyzeh

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Abstract: A-10-2197-1

Assessing the Possible Association between MTHFR (rs1801133) and GPx-1 (rs1050450) Polymorphisms with the Risk of Type 2 Diabetes, Diabetic Neuropathy, and Diabetic Retinopathy

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Background: Oxidative stress in chronic hyperglycemia could injure the tissues and onset of diabetes-related complications like retinopathy and neuropathy. This study investigates the association between methylenetetrahydrofolate reductase (MTHFR) and glutathione peroxidase (GPx) genetic variants with these complications.

Methods: In this case-control study, 400 individuals, including 100 healthy subjects and 300 patients with type 2 diabetes mellitus (T2DM) in three subgroups: with retinopathy (n=100), with neuropathy (n=100), and without complication (n=100) from West Iran, were studied. MTHFR (rs1801133) and GPx-1 (rs1050450) variants were identified by the PCR-RFLP method. The plasma levels of GPx activity, glutathione, malondialdehyde (MDA), total antioxidant capacity (TAC), and total oxidative stress (TOS) were measured by chemical methods.

Results: Higher BMI, TOS and MDA levels were observed in patients with neuropathy compared to other patients and controls. Diabetic patients with neuropathy had lower levels of glutathione (7.8±4.5; P=0.001), GPx activity (39.5±8.5; P=0.001), and TAC (703.1±129.1; P= 0.0001) in comparison with other groups. The patients without complication and retinopathic patients had higher plasma levels of glutathione (12.2±2.4; p=0.02) and TAC (793.4±124.6; P=0.001), respectively. MTHFR TT genotype significantly correlated with lower levels of TOS (3.5±1.1; P=0.001) and OSI (0.0050±0.001; P=0.001). Subjects with the GPx-1 TT genotype had higher levels of MDA (6.8±2.5; P= 0.02) and lower levels of TOS (3.7±1.6; P=0.001), which is statistically significant. TT genotype of MTHFR was associated with 3.9 fold (95% CI 1.04- 4.76; P=0.0436) increased risk of neuropathy. Also, GPx-1 CT genotype increased the risk of retinopathy [OR=2.7 (95% CI=1.38-5.44; P=0.0039)].

Conclusion: The MTHFR TT genotype increased the risk of neuropathy in diabetic patients significantly. The GPx-1 CT genotype is related to increased retinopathy risk among diabetic patients. Both MTHFR and Gpx-1 TT genotypes were associated with higher BMI levels.

Keywords: Type 2 diabetes mellitus, MTHFR, GPx-1, Oxidative Stress

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Abstract: A-10-2587-1

Association of Matrix Metalloproteinase-2 (MMP-2) and MMP-9 Promoter Variants, Their Serum Levels, and Activities with Aortic Valve Calcification (AVC) in a Population from Western Iran

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Background: Matrix metalloproteinase (MMP) enzyme gene polymorphisms MMP-2–1575G/A and MMP-9–1562C/T promoter polymorphism, their serum levels, and activity are associated with aortic valve calcification (AVC).
Methods: The synergistic link between the risk of AVC and the alleles T and A of MMP-9 and MMP-2 was investigated, respectively. Ninety-two cases with AVC and 92 healthy individuals from the west of Iran were included, and MMP- 2–1575G/A and MMP-9–1562C/T promoter polymorphisms were detected using PCR–RFLP. The serum levels and activity of MMP-2 and -9 were assessed using ELISA and gelatin zymography methods, respectively. In addition, serum biochemical markers, including FBS, urea and creatinine, cholesterol, triglyceride, HDL, LDL, calcium, phosphorus, and blood pressure: systolic blood pressure and diastolic blood pressure were measured.
Results: Heart valve calcification disease was associated with a comparatively higher frequency of the A allele of the MMP2-1575 variation ($p = 0.002$). In addition, the frequency of T allele of the MMP9-1562 variant was higher than the control group ($p = 0.007$).
Conclusion: MMP-2 and MMP-9 serum levels and activities were observed to be considerably higher in the experimental group than in the control group ($p < 0.001$). Patients are more susceptible to cardiovascular disease than the control group due to elevated serum levels and activity of MMP-2 and MMP-9.

Keywords: MMP-2, MMP-9, Aortic Valve Calcification

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Abstract: A-10-2613-1

Effect of Continuous Endurance Training (CET) Intervention on the Balance of Bone Metabolism and Irisin Hormone Level in Diabetic Patients

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Background: A lot of evidences demonstrated association between type 2 diabetes and changes in bone metabolism. In patients with type 2 diabetes, bone formation is changed. It seems that exercise can reduce the process of osteoporosis or delay the process of osteoporosis by increasing effective bone metabolism. The present study performed on diabetic subjects to investigate the effect of CET (continuous endurance training intervention on the expression of osteocalcin, alkaline phosphatase, CTX and irisin as the most important factors in reducing bone tissue degradation in patients with insulin resistance and type two diabetes.

Methods: For this study, 50 diabetic subjects were selected. In order to confirm diabetes, fasting blood sugar determined after overnight fasting. After diabetic patients' selection, 8 weeks endurance training performed under supervision of sports physiologist. After 8 weeks of training, blood samples were taken from the patients and bone alkaline phosphatase, osteocalcin, CTX and irisin were measured.

Results: Exercise intervention was shown to lower blood sugar and improve lipid profile and decrease serum CTX levels and increase osteocalcin and bone alkaline phosphatase levels in exercise groups. Importantly exercise intervention improved Irisin hormone level.

Conclusion: The results of the study shows that endurance training has positive effect on improving metabolic markers affecting bone function in addition to improving glucose and fat control. In addition, the results show that exercise interventions, especially CET, not only prevent bone loss in patients with diabetes but also improve bone health markers. Therefore, changing lifestyle to high physical activity, in addition to all the beneficial effects on the metabolism of diabetic subjects, leads to bone metabolism in favor of increasing bone health. To emphasize molecular mechanism of beneficial effect of exercise intervention, more detailed molecular and genetic study is recommended.

Keywords: Continuous Endurance Training ،Diabetes ،bone Metabolism

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2651-1

Investigating the Effect of Sex Hormones on Liver Steatosis by Examining the Accumulation of Lipid Droplets and the Expression of Related Genes in Two Cell Models Fattened with Palmitate and Palmitate/Oleate

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Background: Considering the higher prevalence of non-alcoholic fatty liver disease (NAFLD) in men than women, the aim of this study was to investigate the effect of β-estradiol and testosterone on the accumulation of lipid droplets (LDs) in fattened HepG2 cells as a model of fatty hepatocytes.

Methods: To determine the effective concentration of both hormones, an MTT assay was performed. LD content was identified through oil-red staining, followed by microscopic examination and semi-quantitative analysis. Triglyceride levels were enzymatically quantified. Gene expression levels were assessed by the real-time PCR method.

Results: The results of the study indicate that both testosterone and β-estradiol decreased the LD and triglyceride content in fattened cells. In P/O-fattened model, there was no significant difference between the effect of the two hormones on the expression of PLIN2 and ATGL genes; while the low and medium doses of testosterone increased the expression of CGI-58 gene more than the corresponding doses of β-estradiol. In the P-fattened model, β-estradiol significantly increased the expression of ATGL more than testosterone, whereas there was no significant difference between the two hormones in the expression of the PLIN2 and CGI-58 genes. In both cell models, β-estradiol significantly decreased the expression of the CIDEB gene.

Conclusion: β-estradiol increased CIDB expression in non-fatty cells, potentially preventing fatty liver by removing triglycerides as VLDL. Conversely, the reduction of CIDB expression in fatty cells may indicate β-estradiol's role in inhibiting triglyceride accumulation and lipid droplet growth. In contrast, testosterone did not affect CIDB expression.

Keywords: Non-alcoholic fatty liver, Lipid droplets, Sex hormones

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Abstract: A-10-2543-1

Reduced Mitochondrial Translocator Protein and Voltage-Dependent Anion Channel-1 in Granulosa Cells Are Associated with the Lower Estradiol Levels and Presence of Immature Follicles in Polycystic Ovary Syndrome

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Background: Granulosa cells (GCs) play key roles in oocyte maturation by providing required steroid hormones. Since the presence of immature oocytes has been reported in polycystic ovary syndrome (PCOS), this study determined levels of mitochondrial membrane cholesterol transporter proteins involved in estradiol (E2) synthesis and measured E2 concentration and parameters of oxidative status in follicular fluids of PCOS women.
Methods: Forty-three women with PCOS and 43 control women were enrolled in this case-control study. GCs and follicular fluids were collected from all participants. The gene expression and protein levels of mitochondrial translocator protein (TSPO) and voltage-dependent anion channel 1 (VDAC1) were determined in GCs. Total cholesterol, E2 level, total antioxidant capacity (TAC), total oxidant status (TOS), oxidative stress index (OSI), and malondialdehyde (MDA) were determined in follicular fluids.
Results: VDAC1 and TSPO were significantly lower both at mRNA and protein levels in PCOS patients. Cholesterol, estradiol and TAC levels were lower in PCOS whereas higher TOS and MDA contents were observed in PCOS compared with control group. E2 level was in direct correlations with VDAC1 and TSPO expressions and with TAC level but was inversely correlated with TOS, OSI and MDA (all $p<0.001$). Higher E2 levels were found associated with greater number of high-quality oocytes and higher number of conceived embryos.
Conclusion: We showed that lower VDAC1 and TSPO expression and reduced E2 level are involved in the pathogenesis of PCOS. Thus, increasing of E2 level and reducing oxidative stress in follicular fluid may be envisioned as therapeutic strategies in PCOS women.

Keywords: Estradiol, Granulosa Cells, Oxidative Stress, Polycystic Ovary Syndrome, TSPO protein human, Voltage-Dependent Anion Channel 1

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Abstract: A-10-2710-1

The Study of Hsa-miR-520a-3p and Hsa-miR-193b-3p Expression Levels in Patients with Vessel Restenosis

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Background: Atherosclerosis improves through the growth and remodeling of plaque in sub-endothelial space. The vessel restenosis after stent implantation is one of important clinical occurrences in coronary artery diseases. The systemic inflammatory events, monocytes diapedesis, migration, and proliferation of vascular smooth muscle cells play a major role in neointimal hyperplasia. The study aimed to focus on the hsa-miR-193b-3p and hsa-miR-520a-3p expression levels in PBMCs isolated from patients with stenosis in coronary arteries

Methods: A total of 60 individuals with restenosis without stent, restenosis with stent, and healthy controls undergoing coronary angiography were participated in the study. The cases were matched on the demographic parameters. The para-clinical and biochemical factors were identified in the study population. The hsa-miR-193b-3p and hsa-miR-520a-3p were extracted using miRNA extraction kit. Then, cDNA was synthesized using stem loop technique. The miRNAs expression levels were measured and estimated using the RT-qPCR technique. The statistical data was obtained by SPSS software.

Results: The age and sex parameters were not significant between study groups (p=0.29 and p=0.48, respectively). The changes of total Cholesterol and VLDL values were estimated among patients and controls (p=0.16 and p=0.032, respectively). The hsa-miR-520a-3p expression levels were decreased significantly in the patients of restenosis with stent as compared with the controls (p 0.004). However, the hsa-miR-193b-3p expression levels were not changed significantly in the study groups (p>0.24). No correlation was not observed between the hsa-miR-520a-3p and hsa-miR-193b-3p (r = -0.068, p = 0.7).

Conclusion: The results showed that the hsa-miR-520-5p expression level may be a candidate to use as a diagnostic marker for vessel restenosis in the patients with coronary artery disease signaling pathways. However, more works are needed to apply the hsa-miR-520-5p as a diagnostic maker.

Keywords: Restenosis, hsa-miR-520-5p, hsa-miR-193-5p

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2677-1

Cohort-Based Analysis of Paternal Opioid Use in Relation To Offspring's BMI and Plasma Lipid Profile

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Background: A growing body of evidence suggests that opioid use may affect consumer's offspring by second-hand passive smoke exposure, as well as by transgenerational impacts mediated by genetic and epigenetic alterations of paternal gametes.

Methods: Here, we conducted population-based analyses aimed to estimate the association of paternal opioid consumption, started before or after child birth, with BMI status and plasma lipid profile of young adult offspring. The present study includes 840 parents-offspring trios (offspring aged 15–35, parents aged 35–70) who participated in the prospective Rafsanjan Cohort Study (RCS). Crude and adjusted multiple logistic regression analysis were conducted to assess the relationship of paternal regular opioid use with offspring's BMI status, and plasma lipid factors.

Results: The prevalence of fathers who used opioids regularly among the studied trios was 42.8%. Our regression analyses demonstrated that paternal opioid use started pre-fatherhood was associated with 76% higher adjusted odds ratio (OR) of overweight/obesity in young offspring. This relationship persisted when fathers who used opioid by routes other than inhaling (oral) were excluded from logistic analysis. Interestingly, sex stratified analysis displayed a 201% increased odds ratio of overweight/obesity in sons of fathers who used opioid regularly, started after child birth, while no significant association was found in daughters. Additionally, increasing exposure–response relationships were observed between odds ratios of overweight/obesity and the number of years of paternal opioid use after birth. Paternal regular opioid use started pre-fatherhood was associated with 54% lowered risk of underweight.

Conclusion: Paternal opioid consumption started either before or after child birth did not show a significant association with the high level of the plasma lipid factors in offspring. Our results suggest that the environmental impacts of paternal regular opioid use may be sufficient to make an effect on male offspring metabolism independent of genetic and epigenetic impact on gametes.

Keywords: Prospective Epidemiological Research Studies in IRAN (PERSIAN), Paternal opioid use, Offspring obesity, Transgenerational effects, Metabolic impact

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Abstract: A-10-2697-1

Stearoyl-CoA Desaturase 1 Activity in White and Brown Adipocyte-Like Cells

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Background: Stearoyl-CoA desaturase 1 (SCD1) is a key enzyme in converting saturated fatty acids to monounsaturated fatty acids, playing a crucial role in adipocyte lipogenesis and obesity development. This study aimed to assess SCD1 activity in different adipocyte types to understand its role in fat cell function and obesity-related metabolic disorders.

Methods: In this experimental study, fatty acids derived from human mesenchymal stem cells (MSCs) and their differentiated forms into white-like adipocytes (WAs) and brown-like adipocytes (BAs) were quantified using gas-liquid chromatography. The ratios of palmitoleic acid (16:1) to palmitic acid (16:0) and oleic acid (18:1) to stearic acid (18:0), as well as their combined ratio, were calculated as indicators of SCD1 activity. Differences among the three cell types were analyzed using one-way ANOVA.

Results: The SCD16 activity index did not differ significantly among the cell lines. However, the SCD18 activity index was significantly higher in WAs compared to both MSCs (5-fold, $p < 0.0001$) and BAs (2.8-fold, $p < 0.0001$). Additionally, BAs showed a significantly higher SCD18 activity index compared to MSCs (1.8-fold, $p < 0.01$). The combined SCD1 activity index was significantly elevated in WAs compared to both MSCs (3.4-fold, $p < 0.01$) and BAs (2.1-fold, $p < 0.01$).

Conclusion: The altered SCD1 activity index, particularly the increased conversion of 18:0 to 18:1 in white adipocytes, suggests distinct functional roles for SCD1 across different adipose tissue types. These findings show the potential for developing targeted SCD1 interventions within adipose tissue to improve lipid metabolism in individuals with obesity and related metabolic disorders.

Keywords: adipocytes, lipid metabolism, metabolic disorders, monounsaturated fatty acids, obesity

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2746-1

Plasma Metabolite Profiles in Diabetes and Prediabetes: A Comprehensive Analysis of Carnitines, Acylcarnitines, and Amino Acids

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Background: This study aimed to evaluate the association between plasma carnitine, acylcarnitine, and amino acid profiles with liver function tests in individuals with diabetes, prediabetes, and normoglycemia, utilizing data from the 2016 STEPS study in Iran.
Methods: A cross-sectional design was employed involving 1,200 randomly selected participants. Blood samples were analyzed for plasma carnitine, acylcarnitine, amino acid profiles, and liver function using standardized laboratory methods.
Results: Significant differences were found in biomarkers such as blood glucose, glycated hemoglobin, triglycerides, ALT, and ALP between healthy and diabetic/pre-diabetic groups. Specific carnitine and acylcarnitine levels (C2, C3, C4OH, C5_1, C14OH, C16OH, C18OH) and certain amino acids showed notable associations with health status.
Conclusion: The study indicates that these biomarkers are valuable for distinguishing between different metabolic health statuses and could aid in early diagnosis and intervention strategies. Further research is needed to explore the mechanisms behind these associations and their clinical implications.

Keywords: Acylcarnitine, Diabetes, Liver function test, Plasma carnitine

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2750-1

Characterizing Metabolic Profiles in Diabetes and Prediabetes: Insights from Plasma Carnitines, Acylcarnitines, and Amino Acids

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Background: This study aimed to examine the associations between plasma carnitine, acylcarnitines, amino acid profiles, and liver function tests in individuals with diabetes, prediabetes, and normal glucose levels. Identifying metabolic biomarkers related to diabetes and prediabetes is crucial for early detection and intervention.
Methods: Utilizing data from the STEPS 2016 Iran study, this cross-sectional analysis included 1,200 randomly selected participants. Data collection involved structured surveys, physical measurements, and blood samples. Plasma carnitine, acylcarnitines, amino acid profiles, and liver function tests were analyzed using standardized laboratory procedures.
Results: Significant differences were found between healthy and diabetic/prediabetic groups in various biomarkers, including blood glucose, glycated hemoglobin, triglycerides, and high-density lipoprotein (HDL) and low-density lipoprotein (LDL). Notable associations were observed for acylcarnitines such as C2, C3, C4OH, C5_1, C14OH, C16OH, and C18OH. Additionally, the concentrations of amino acids like alanine, leucine, phenylalanine, tyrosine, valine, glycine, ornithine, proline, threonine, serine, histidine, and tryptophan showed significant variations among the groups.
Conclusion: The study highlights significant associations between metabolic biomarkers and health status, providing a basis for differentiating between diabetic, prediabetic, and healthy individuals. These biomarkers are valuable tools for distinguishing various metabolic conditions. Further research is needed to explore the underlying mechanisms of these associations and assess their clinical relevance.

Keywords: HDL, LDL, Acylcarnitine, Plasma carnitine

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Abstract: A-10-2516-2

Myosin Light Chain Phosphatase Is a Downstream Target of Rho-Kinase in Endothelin-1-Induced Transactivation of the TGF-β Receptor

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Background: Rho-kinase (ROCK) regulates actomyosin contraction, coronary vasospasm, and cytoskeleton dynamics. ROCK and of NADPH oxidase (NOX) play an essential role in cardiovascular disease and proteoglycan synthesis, which promotes atherosclerosis by trapping low density lipoprotein. ROCK is activated by endothelin-1 (ET1) and transactivates the transforming growth factor beta receptor (TGFβR1), intensifying Smad signaling and proteoglycan production. This study aimed to identify the role of myosin light chain phosphatase (MLCP) as a downstream target of ROCK in TβR1 transactivation.

Methods: Vascular smooth muscle cells were treated with ET1 and inhibitors of ROCK and MLCP were added. The phosphorylation levels of Smad2C, myosin light chain (MLC), and MLCP were monitored by western blot, and the mRNA expression of chondroitin 4-O-sulfotransferase 1 (C4ST1) was assessed by quantitative real-time PCR.

Results: We examined the role of ROCK in ET1-induced TGFβR1 activation. ROCK phosphorylated MLCP at the MYPT1 T853 residue, blocked by the ROCK inhibitor Y27632. ROCK also increased MLC phosphorylation and actomyosin contraction in response to ET1, enhanced by the phosphatase inhibitor Calyculin A. Calyculin A also increased C4ST1 expression, GAG-chain synthesizing enzymes.

Conclusion: This work suggests that ROCK is involved in ET1-mediated TβR1 activation through increased MLCP phosphorylation, which leads to Smad2C phosphorylation and stimulates C4ST1 expression.

Keywords: Myosin light chain, Myosin light chain phosphatase, ROCK, TβR1

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2623-1

The Effect of Exposure to Pollutants in the Work Environment on Body Inflammatory Biomarkers in the Employees of Gol-Gohar Mine in Sirjan

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Background: The aim of this study was to investigate the effect of exposure to workplace pollutants on the serum levels of inflammatory cytokine TNF-α and anti-inflammatory Interleukin 2 (IL2) and 10 (IL10) in Gol-Gohar mine workers of Sirjan.

Methods: The serum levels of TNF alpha and interleukin 2 and 10 were measured using an ELISA kit. The parameters of air pollution from the measuring station in the working environment of the mine including: PM10, PM2.5, So2, No2, CO were measured during the time periods of the project activity using the filtration method.

Results: The results showed that the percentage of pollution caused by the activity of machines is as follows: CO=66/59%, No2=69/48%, So2=71/68%, PM 2.5 = 44/35%, PM 10=56/08%. In addition, the serum level of TNF-α in mine workers who were directly exposed to pollutants was significantly higher than that of the control group ($p<0.05$). While the serum level of IL2 and IL10 in mine workers significantly decreased compared to the control group ($p<0.05$). The results of logistic regression analysis showed that exposure to PM 10 and PM 2.5 particulates may cause a 7-fold decrease in IL10 serum concentration ($p<0.05$).

Conclusion: The findings of this study show that people who are exposed to environmental pollutants are associated with changes in the concentration of inflammatory and anti-inflammatory cytokines. Based on the results of our study, people who were more exposed to PM 10 and PM 2.5 particles were associated with a significant decrease in the anti-inflammatory cytokine IL10 and, a significant increase in the serum level of the inflammatory cytokine TNF-α. Which shows that Gol-Gohar mine workers may be at high risk of contracting chronic inflammation due to direct exposure to environmental pollutants.

Keywords: Cytokine, Environmental pollutants, Interleukin 10, TNF-α, Inflammation

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2531-1

A Population-Based Evaluation of the Association of Serum Uric Acid with Kidney Function in CDK (steps, 2016)

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Background: Chronic kidney disease (CKD) is a silent condition that reduces the quality of life and increases mortality rates. Hyperuricemia, uremia, high blood pressure, hematuria, fasting glycemia, high HbA1C, dyslipidemia, and disturbance of sodium and potassium balance are frequently observed in individuals with CKD.
Methods: We drew 1105 participants from Iran's survey of risk factors for noncommunicable diseases (steps) in 2016 and used 2021 CKD epidemiology collaboration (CKD-epi) for eGFR estimation. The classification of CKD stages by eGFR included 669 participants in normal stage (eGFR ≥90 mL/min/1.73 m2), 391 participants in mild stage (eGFR 60 - 89 mL/min/1.73 m2), and 45 participants in severe stage (eGFR <59 ml/min/1.73 m2). Descriptive statistics were utilized to identify the sample's general characteristics, and then study variables including serum uric acid (SUA) were examined with multinomial logistic regression to estimate GFR prognosis.
Results: Significant differences were not observed in the indicators HbA1c, glucose, LDL, HDL, Non-HDL-C, TGs, and TC among the different groups. Serum Uric Acid (SUA) levels went through a significant rise (p=0.001) as kidney function decreased, starting at 4.98 ± 1.25 mg/dL and progressing to mild state (5.87 ± 1.46 mg/dL) to severe state (6.92 ± 1.63 mg/dL). The advanced phase of CKD showed a strong inverse relationship between SUA and eGFR (r = -0.392, p=0.000) that demonstrates that a rise in SUA levels results in a significant drop in eGFR. The severe stage had a significant correlation (r = 0.507, p=0.000) between SUA and the kidney function marker serum creatinine (SCr).
Conclusion: The correlation between elevated SUA levels and the progression of CKD revealed that elevated SUA is linked to declining kidney function and can potentially accelerate the decline of EGFR. SUA can be a reliable early indicator and predictor of acute renal function changes, as well as a risk indicator for CKD progression.

Keywords: Chronic kidney disease, Serum uric acid, CKD progression, eGFR, Hyperuricemia, Kidney function, Serum creatinine

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Abstract: A-10-2729-2

Increased ROS Production in PBMCs Is Correlated With Decreased REM and Non-REM Duration in Subjects with Chronic Insomnia Disorder

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Background: According to available evidence, the activity of inflammatory pathways, particularly activation of inflammasome complex, plays an important role in the pathogenesis of chronic insomnia disorder. But the reason for the activation of these pathways is still unknown. In the present study, we evaluated the correlation between circulatory reactive oxygen species (ROS) as a DAMP and activation of the NLRP-1 inflammasome complex and sleep quality in people with chronic insomnia disorder.

Methods: Blood samples were collected from 22 individuals diagnosed with Chronic Insomnia Disorder (CID) based on Pittsburgh Sleep Quality Index (PSQI) and full-night video-polysomnography (V-PSG) and 22 healthy individuals based on PSQI. The activation of NLRP1 inflammasome complex was evaluated by real time polymerase chain reaction of NLRP1, ASC, and caspase-1; and the activity assay of caspase-1 in peripheral blood mononuclear cells (PBMCs). ROS generation in freshly PBMCs were detected by flow cytometry assay.

Results: We found that CID group had significant higher gene expression levels of NLRP1, ASC, caspase-1 and also caspase-1 activity in PBMC compared to control group. As well, we observed the significant increase in serum levels of IL-1β and IL-18 in people with CID compared to control group. In addition, we found the increased levels of ROS in PBMCs from individuals with CID compared to control group. The correlation analysis showed that ROS levels had high positive correlation with NLRP1 gene expression ($r = 0.674$, $p < 0.05$) and caspase-1 activity ($r = 0.689$, $p < 0.05$) in CID group. Moreover, we observed a significant negative correlation between ROS levels and rapid eye movement (REM) sleep duration and non-REM sleep duration in CID group.

Conclusion: The results of this study show that the increased generation of ROS in PBMCs through the activation of NLRP-1 inflammasome can cause disturbance in sleep-wake cycle regulation and decrease the sleep quality.

Keywords: Key words: Chronic insomnia disorder, Reactive oxygen species, REM sleep, non-REM sleep

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2772-1

Kidney Injury Molecule-1 As An Early Predictor of Acute Kidney Injury in Critically Ill Neonates: A Systematic Review and Meta-Analysis

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Background: Acute kidney injury (AKI) is a critical condition in neonates in intensive care, marked by a sudden decline in kidney function, traditionally assessed through serum creatinine (Scr) levels. However, Scr has limited sensitivity for early AKI detection, highlighting the need for more precise biomarkers. This study aims to evaluate kidney injury molecule-1 (KIM-1) as an early predictor of AKI in critically ill neonates.

Methods: This systematic review and meta-analysis followed PRISMA and Cochrane guidelines. Databases including PubMed, Scopus and Web of Science alongside Google scholar search engine were systematically searched. Using keywords and MeSH terms related to "KIM-1", "Neonates" and "AKI". Two investigators independently performed searches and data extraction, resolving discrepancies with a third author. Included studies were observational studies evaluating KIM-1 for AKI diagnosis in critically ill neonates. Excluded were reviews, animal studies, conference papers, book chapters, letters, trials, studies without a control group, and adult studies. Quality of studies was assessed using the Newcastle-Ottawa Scale, and heterogeneity was evaluated with I^2 statistics. Findings were presented as weighted mean differences (WMDs) and pooled area under the curve (AUC), with 95% confidence intervals (CI). Analyses were conducted using Stata 14.2.

Results: Out of a total of 201 studies, 186 studies were excluded (duplicate= 114; Irrelevant: 72). Ultimately, 15 studies (10 case-control, 1 cross-sectional, 4 cohort studies) were included in the present meta-analysis. The total sample size comprised 675 critically ill neonates, with 283 (42%) diagnosed with AKI and 392 (58%) in the control group. The level of KIM-1 was higher in neonates with AKI compared to the non-AKI group (WMD= 0.91; 95% CI= 0.05-1.77; I2= 95.7%; Z= 2.07; P:0.038) and AUC was 0.72 (95% CI= 0.64-80; I2= 0%)

Conclusion: These results suggest that, KIM-1 may be a promising biomarker for early detection of AKI in critically ill neonates.

Keywords: Keywords: KIM-1, neonate, AKI, critically ill

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Abstract: A-10-2776-1

The Association of Serum Levels of Hypoxia-Inducible Factor-1alpha With Pre-Eclampsia: A Systematic Review and Meta-Analysis

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Background: Pre-eclampsia (PE) is a serious pregnancy disorder that poses significant risks to both mother and infant. It is associated with inflammation and tissue hypoxia, highlighting the importance of understanding its underlying mechanisms. Hypoxia-inducible factor-1alpha (HIF-1alpha), a key regulator in the body's response to low oxygen levels, is of particular interest as a potential biomarker. This study aims to assess the association between serum levels of HIF-1alpha and the occurrence of PE.

Methods: We conducted a systematic review and meta-analysis following PRISMA and Cochrane guidelines. We utilized PubMed, Scopus and Web of Science combined with the Google Scholar search engine to look up grey literature using keywords including "hypoxia-inducible" and "pre-eclampsia". We included comparative observational studies on HIF-1α levels in women with PE versus healthy pregnancies, excluding reviews, conference papers, letters, animal studies, and book chapters. Any discrepancy was settled by a third author after two authors separately screened the studies and finally extracted the data. The Newcastle-Ottawa scale was used to evaluate the listed studies' quality. Heterogeneity was evaluated with I2 statistics. A random effects model for standardized mean differences (SMDs) was applied using Stata software version 14.2 for analysis.

Results: Only 7 of the original 958 studies were included in the analysis after removing 341 duplicates and 610 irrelevant ones. Of the 897 women evaluated, 303 (33.7%) had PE, and 594 (66.2%) were in the control group. Six studies found a significant correlation between HIF-1α and PE, while one showed no difference in serum levels between normal pregnancy and PE, and another reported reduced serum HIF. Our meta-analysis confirmed a strong association between serum HIF-1α levels and PE [SMD=1.52; 95%CI=0.4-2.64; I2=96.9%; Z=2.66; P=0.008].

Conclusion: This study identified a notable relationship between HIF-1α and PE. Due to the researches, it could be a potential biomarker for predicting PE.

Keywords: hypoxia-inducible factor-1alpha, pre-eclampsia, HIF-1α, pregnancy

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Abstract: A-10-2764-1

Methylation Status and Regulatory Network of Gpx1 in Preeclampsia

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Background: To identify novel epigenetic and molecular mechanisms in preeclampsia, we examined the methylation status of the GPx1 gene promoter in preeclamptic patients compared to healthy controls and conducted a bioinformatics analysis to explore additional regulatory factors influencing GPx1 in PE.

Methods: This study included 66 women diagnosed with preeclampsia and 62 normotensive pregnant controls. Peripheral blood samples were collected from all participants, and placental tissue samples were obtained during delivery. GPx1 gene promoter methylation was assessed using the MethyLight technique. To further elucidate the regulatory network of GPx1 in preeclampsia, a comprehensive bioinformatic analysis was performed. This involved mining online databases, including SIGNOR, Pathway Commons, and IID, TarBase v8 and STITCH to identify proteins, microRNAs, and other potential regulatory elements associated with GPx1.

Results: A significant decrease in GPx1 promoter methylation was observed in the maternal blood of preeclamptic patients compared to controls. However, no significant methylation differences were found in placental tissue. In silico analysis revealed that the GPx1-interacting network in PE involves proteins that are critical for various cellular processes, including cell growth, immune response, apoptosis, and metabolism, in addition to oxidative stress. These proteins probably affect GPx1 regulation through various mechanisms, including transcriptional control, post-translational modifications, participation in signaling pathways, and the transport of crucial cofactors. Also, several chemical compounds, like glutathione, selenium and oxygen, contribute to the regulation of GPx1 activity. Furthermore, specific microRNAs, including miR-148b, miR-196a, miR-221, miR-155, miR-124, miR-128, miR-362, miR-516b, miR-374a, and miR-26a miR-1-3p, and miR-769 were found to be potentially involved in regulating GPx1 in PE.

Conclusion: The significant decrease in GPx1 promoter methylation in preeclamptic patients underscores the role of epigenetic alterations in GPx1 regulation and its potential contribution to PE development. Bioinformatic analysis highlights the GPx1 regulation complexity, necessitating further research into additional regulatory pathways in PE.

Keywords: Preeclampsia, MethyLight, Oxidative stress, Methylation, Glutathione peroxidases 1, Epigenetics, placenta

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Abstract: A-10-2798-1

The Relation Between the Apoptotic Pathways in Peripheral Blood Mononuclear Cells (PBMCs) With Coronary Artery Stenosis

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Background: Coronary artery stenosis is a silent complication with severe side effects. Peripheral Blood Mononuclear Cells (PBMCs) can contribute to the pathogenesis of coronary artery diseases. This study investigated the role of the p53, Bax, Bak, and Bcl-2 apoptotic factors gene expression in PBMCs of subjects who underwent angiography.
Methods: 90 participants were assigned to two groups including 45 CAD (subjects with coronary artery stenosis≥50%) and 45 NON-CAD (subjects with coronary artery stenosis≤30%) after complete clinical examination and anthropometric evaluations. Blood samples were harvested to separate serum and PBMCs. Biochemical parameters including fasting serum glucose, Low-Density Lipoprotein (LDL), High-Density Lipoprotein (HDL), total cholesterol, and triglyceride were measured. The severity of coronary artery stenosis was recorded. Moreover, Real-time PCR evaluated the p53, Bax, Bak, and Bcl-2 gene expression. Finally, the correlations between data were measured.
Results: All three apoptotic factors, p53, Bax, and Bak, in the CAD group increased significantly ($p<0.05$) compared to the NON-CAD group. In addition, the anti-apoptotic factor, Bcl-2 was increased compared to the NON-CAD group, significantly ($p<0.05$) in the CAD group.
Conclusion: A significant correlation between the gene expression of apoptotic factors, p53, Bax, and Bak in PBMCs with coronary artery stenosis shows the important role of apoptotic pathways in cardiovascular diseases especially in coronary artery stenosis disorders.

Keywords: Cardiovascular diseases, PBMC, p53, Bax, Bak

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Abstract: A-10-2605-1

NLRP1 Inflammasome-Mediated Peripheral Inflammation as an Inducer for Diffusion Abnormality in the Lateral Ventricles in Chronic Insomnia Disorder

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Background: Previous studies described that diffusion-MRI can show brain microstructural changes caused by inflammation in neurological diseases. So, the current study aimed to evaluate the relationship between NLRP1 inflammasome-induced peripheral inflammation and changes of brain microstructures related to sleep regulation in people with chronic insomnia disorder (CID).

Methods: Blood samples were collected from 22 individuals (16 female, mean age 42.1 ± 9.3 years, range 21-65) diagnosed with CID based on Pittsburgh Sleep Quality Index (PSQI) and full-night vide-opolysomnography (V-PSG) and 22 healthy individuals (14 female, mean age 41.8 ± 11.7 years, range 21-65) based on PSQI. The activation of NLRP1 inflammasome complex was evaluated by real time polymerase chain reaction of NLRP1, ASC, and Caspase-1, and serum levels of pro-inflammatory cytokines IL-1β and IL-18 using enzyme-linked immunosorbent assay (ELISA). In addition, the brain diffusion-MRI images were obtained on a Siemens Magnetom Avanto 1.5 T MRI whole body scanner with an 8-channel head coil. Statistical analyses were performed by the SPSS®, version 26.0.

Results: We found that CID group had significantly higher gene expression levels of NLRP1, ASC, and Caspase-1 in peripheral mononuclear blood cells (PBMC) compared to control group. As well, significant increase in serum levels of IL-1β and IL-18 in people with CID compared to controls confirms the increased gene expression of NLRP1 inflammasome components. In addition, we observed the increased lateral ventricles mean diffusivity (MD) in individuals with chronic insomnia compared to control group. The correlation analysis showed that lateral ventricles MD had high positive correlation with NLRP1 gene expression (correlation coefficient 0.807, $p < 0.01$) in individuals with CID. Moreover, we observed a significant positive correlation between left lateral ventricle MD and PSQI scores in CID group.

Conclusion: The results of this study suggest that NLRP1-mediated peripheral inflammation may impact brain microstructures involved in sleep regulation.

Keywords: Chronic insomnia, Lateral ventricle, Mean diffusivity, NLRP1 inflammasome

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-994-3

Transgenerational modifications of hippocampus mir-RNA (96, 137) levels in the offspring of rats experienced dependency and withdrawal during adolescence

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Background: Part of the genetic material in each egg cell that contributes to the creation of a new generation comes from the egg cells present in the mother's body during the early embryonic period. In addition to genetic changes, environmental factors can lead to epigenetic changes that may be inherited by the next generation. The aim of the current study is to explore the impact of morphine addiction and its withdrawal during pre-puberty in mothers on the expression of HDAC and MeCP2 in ovarian tissue and mir-RNA (96, 137) genes in the hippocampus of their children.

Methods: The study began with 20 female Wistar rats aged 28-31 days, designated as F0. The animals were divided into two groups: control and morphine. The morphine group received a daily dose of 5mg/kg of morphine for 4 weeks. Subsequently, the animals were monitored for three weeks until withdrawal symptoms completely subsided. The females from each group were then paired with male animals. After giving birth, the offspring (F1) spent four weeks in infancy. Male and female offspring from each group were then separated for behavioral and gene expression (HDAC, MeCP2, mir97, mir137 genes) studies.

Results: The findings revealed that morphine dependence and withdrawal led to alterations in the expression of HDAC and MeCP2 genes in the ovarian tissue of F0 rats ($p<0.05$). Additionally, significant changes in the expression of these two genes, as well as mir97 and mir137 genes, were observed in the hippocampus of F1 offspring ($p<0.05$). There were no notable differences in these changes between male and female offspring.

Conclusion: Morphine addiction and withdrawal during pre-puberty can result in changes in gene expression in the hippocampus of offspring.

Keywords: Morphine; Transgenerational; mir-RNA; hippocampus

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Abstract: A-10-3153-2

Inhibitory effects of Zinc Oxide nanoparticles on Breast Cancer cell line (MDA-MB-468) compared to Normal Human Fibroblast (HFF cells)

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Background: The highly aggressive triple-negative breast cancer subtype presents a significant challenge due to its high metastatic potential, high mortality rates, and resistance to conventional therapies. This has stimulated the search for alternative treatment approaches. Nanomaterials are promising candidates and suitable alternatives for improving tumor and cancer cell treatments.
Methods: This research involved the synthesis and characterization of Zinc Oxide nanoparticles (ZnO NPs) using DLS, FTIR, SEM, and EDS techniques. The biological activities of ZnO NPs were evaluated using the MTT assay, flow cytometry, and real-time PCR on MDA-MB-231 and MDA-MB-468 (triple-negative breast cancer [TNBC]) cell lines, compared to healthy human fibroblast cells (HFF). Additionally, the expression of apoptotic genes Bax, Bcl-2, and caspase-3 in cancer cells was assessed relative to the housekeeping gene GAPDH."
Results: Physico-chemical investigation demonstrated ZnO NPs were successfully synthesized. According to MTT assay, The IC50 of ZnO NPs were 104.4, 44.86 and 20.96 after 24 hours for HFF, MDA-MB-231 and MDA-MB-468 cells, respectively. The results of flow cytometry showed induction of late apoptosis on treated cells with ZnO NPs and changes of gene expression confirmed these results.
Conclusion: This research presented a fast, cost effective and ecofriendly method for ZnO nanoparticle synthesis. These results indicate that ZnO NPs induced more toxicity in cancerous cells versus normal fibroblast cells. Furthermore, In vitro data analysis demonstrated highly anticancer potential of ZnO NPs against TNBC cell lines.

Keywords: Triple Negative Breast Cancer (TNBC), Zinc Oxide nanoparticles (ZnO NPs), anticancer activity, apoptosis, Bax/Bcl-2, caspase 3, gene expression.

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Abstract: A-10-3213-1

Coelomic fluid of the earthworm Eisenia induced wound healing process in diabetic rats

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Background: Diabetes is increasingly recognized as a significant public health concern, with diabetic foot ulcers representing a major complication of diabetes mellitus. The earthworm Eisenia foetida glycolipoprotein, known as G-90, is a mixture of macromolecules that exhibit various biological properties. This study aimed to investigate the effects of extracts obtained from the homogenate of Eisenia foetida on the wound healing process in diabetic rats.
Methods: Thirty-six adult albino Wistar rats weighing of 150–200 g were selected. Diabetes induced by injection of alloxan in 120 mg/kg dose. Circular wounds were created on the nap region. The animals were divided in to six groups, and treated for 21 days. Group (A) treated by using Panthenol-D as positive control, (B) treated with injection of G-90, (C) treated with G-90 in their diets or by using gavage. (D) treated with G-90 on site of wound, (E) diabetic rats that were left without any treatment, (F) the healthy rats were untreated and served as control. Wound clause rate, epithelialization time, histological and Microbiological study was evaluated.
Results: Several proteins with molecular masses ranging from 10 to 150 kDa were successfully isolated from the coelomic fluid of Eisenia foetida. The results indicated that treatment with G-90 significantly accelerated the wound healing process. Additionally, G-90 treatment reduced the risk of infection at the wound site. Histological analyses revealed improved extracellular matrix formation, increased fibroblast proliferation, enhanced neovascularization, collagen synthesis, and early epithelial layer formation in the G-90 treated group**.**
Conclusion: Therefore, G-90 shows potential as a novel wound healing agent, offering promising therapeutic avenues for the treatment of diabetic foot ulcers.

Keywords: diabetic rats, Coelomic fluid, G-90, fibroblast, collagen synthesis, wound

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Abstract: A-10-2494-1

Physical activity and intestinal microbiota composition

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Background: The intestinal microbiota, a complex ecosystem of microorganisms residing within the gastrointestinal tract, is increasingly recognized as a critical determinant of human health. Imbalances in this microbial community, often termed dysbiosis, have been linked to a wide range of diseases, including obesity, type 2 diabetes, inflammatory bowel disease, and certain cancers. Emerging evidence suggests a potential bidirectional relationship between physical activity and the composition of this microbial community. While the mechanisms underlying this association remain to be fully elucidated, alterations in microbial diversity, composition, and metabolic function have been observed in response to exercise interventions.

Methods: A search of PubMed, Google Scholar, and Scopus was conducted to include all clinical trials related to this issue.

Results: The main findings varied greatly depending on the level of physical activity in the studies. One study combined the Mediterranean diet with physical activity to assess its association with gut microbiota. This study demonstrated that long-term lifestyle improvements aimed at weight loss, using this protocol, increased certain microbial diversities, such as Ruminococcaceae, which may respond to energy restriction. Conversely, a reduction in other diversities may be associated with changes in certain cardiovascular disease (CVD) risk factors. Physical activity also showed significant improvement in inflammatory factors by modifying the microbiota profile, increasing the Bacteroidetes phylum and decreasing the Firmicutes/Bacteroidetes ratio. Additionally, another study on obese children demonstrated that engaging in physical activity tended to increase certain genera, such as Blautia, Dialister, and Roseburia, resulting in a microbiota profile similar to that of healthy children.

Conclusion: Our findings indicate that physical activity can enhance microbial populations in humans and potentially provide additional benefits. However, further clinical trials are needed to specifically evaluate this relationship.

Keywords: Gut microbiome, Physical activity, Intestinal microbiota composition, Exercise.

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Abstract: A-10-3211-1

Examining the Anti-cancer Properties of a Novel Imidazopyrimidine Compound on MDA-MB-231 Breast Cancer Cells

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Background: Cyclooxygenase-2 (COX-2) plays a crucial role in prostaglandin synthesis. Its metabolites may significantly influence inflammatory responses and cancer progression. Breast cancer remains the most prevalent malignancy among females globally. Research has shown that COX-2 is overexpressed in 50% of breast cancers, with its levels positively correlating with tumor invasiveness. Selective COX-2 inhibitors are thought to combat cancer by mitigating inflammation. This research sought to elucidate the mechanism of COX-2-induced PGE2 signaling in cancer development and to evaluate the anti-tumor efficacy of a newly developed COX-2 inhibitor.
Methods: MDA-MB-231 breast cancer cells were cultured and exposed to the Imidazopyrimidine derivative. Cell viability was assessed using the MTT assay. The quantity of formazan produced by viable cells metabolizing MTT was measured at 570 nm, correlating directly with cell survival rates. The IC50 of the compound was determined. Additionally, a clonogenic assay was performed on the breast cancer cells.
Results: This study revealed that treating MDA-MB-231 cancer cells with the new Imidazopyrimidine compound reduced cell viability compared to untreated controls. At a concentration of 145 µM, the compound inhibited the growth of 50% of cancer cells following a 24-hour incubation period. Furthermore, the compound demonstrated the ability to suppress colony formation.
Conclusion: This novel compound impedes cancer cell viability and demonstrates potential as a therapeutic agent for breast cancer by targeting COX-2-mediated pathways.

Keywords: Breast cancer, cell viability, Imidazopyrimidine

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Abstract: A-10-2917-2

Nanoliposome loaded with 5-fluorouracil and curcumin increases cytotoxicity and decreases VEGF gene expression in CT26 cell line

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Background: Colorectal cancer is a malignant neoplasm that starts in the colon or rectum and is the most common form of gastrointestinal cancer worldwide. It has been shown that curcumin possesses anti-cancer and antioxidant properties. 5-FU is a widely used chemotherapy agent known for its effectiveness against various cancers. This study aimed to investigate the effect of liposome nanoparticles loaded with 5-FU and curcumin on the CT26 cell line and the expression of genes related to VEGF.

Methods: Liposomes were synthesized using the lipid thin-film hydration technique, and their characterization was conducted through TEM, DLS, and HPLC analyses. CT26 cells were cultured in plates with complete medium. The cells were exposed to varying concentrations of free 5-FU, curcumin (CUR), 5-FU + CUR, and their nanoliposome forms for 24 hours. The extent of inhibition of cell proliferation was evaluated using an MTT assay. The expression levels of the genes VEGF, VEGF-R2, VE-Cadherin, and VEGF-C were measured using a Real-Time PCR technique.

Results: The synthesized nanoparticles were spherical and uniform in size, measuring approximately 200 ± 10 nanometers. HPLC analysis indicated that about 80% of the compound was effectively loaded into the nanoliposome. The study found that treating CT26 cell lines with either free 5-FU + CUR or nanoliposome-encapsulated 5-FU + CUR (NLP + 5-FU + CUR) reduced cell proliferation in a dose-dependent manner over 24 hours. The IC50 values, which represent the concentration required to inhibit 50% of cell growth, were 21.28 µg/ml for free 5-FU + CUR and 17.11 µg/ml for NLP + 5-FU + CUR in the CT26 cell line. The expression levels of the VEGF, VEGF-R2, VE-Cadherin, and VEGF-C genes in the NLP + 5-FU + CUR group were significantly decreased compared to the control group.

Conclusion: A combination of nanoliposomes loaded with 5-fluorouracil and curcumin effectively reduces the proliferation of tumor cells and the expression of the VEGF, VEGF-R2, VE-Cadherin, and VEGF-C gene

Keywords: Cancer, CRC, Nanoliposomes, Curcumin, 5-fluorouracil

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Abstract: A-10-3098-1

The Effect of Flavonoids on Retinal Inflammation in Diabetic Retinopathy

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Background : Diabetes frequently results in diabetic retinopathy (DR), which damages the retinal blood vessels and impairs eyesight. It is among the most common reasons why diabetic patients become blind. The increase in inflammatory mediators such as TNF-α, IL-6, and IL-1 due to cellular damage and oxidative stress aggravates DR. Chemokines are released as a result of this inflammatory reaction, which permits inflammatory cells to enter the retina and destroy tissue. While many other therapies for depression have been investigated, flavonoids have received less attention. A class of polyphenolic antioxidants, flavonoids are well-known for having potent anti-inflammatory and antioxidant properties. This study aims to explore the potential of flavonoids in reducing retinal inflammation in diabetic retinopathy by inhibiting inflammatory signaling pathways and oxidative stress-induced damage.

Methods :A comprehensive examination of the literature was carried out between July 2023 and November 2023 using PubMed and Google Scholar. To find pertinent research, search terms including "diabetic retinopathy," "inflammation," "oxidative stress," and "flavonoids" were employed. Novelty, specificity, and topic relevancy were taken into consideration when choosing the articles.

Results : Twenty-five reviews or observational studies were selected for in-depth analysis out of the original pool of seventy research articles. The findings demonstrate the considerable reduction of inflammatory cytokines by natural flavonoids, such as diosmin, silymarin, and cyanidin-3-O-glucoside, which lowers inflammation and improves symptoms associated with DR.

Conclusion : Based on the available data, flavonoids, because of their antioxidant and anti-inflammatory characteristics, may help diabetic patients with retinal impairment by reducing the production of inflammatory markers such as NF-kB, TNF-α, and IL-1β. Additionally, flavonoids provide a viable treatment method for treating DR by preventing the activation of inflammatory pathways triggered by oxidative stress.

Keywords: Flavonoids, Diabetic Retinopathy, Retinal Inflammation, Oxidative Stress, Anti-inflammatory Therapy

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Abstract: A-10-2530-1

Investigating the Role and Importance of Kinome in Cancer and the Therapeutic Strategies

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Background : The term "kinome" describes all of the protein kinases that are genetically encoded. Lipid kinases and protein kinases are the two primary groupings that make up the human kinome. There are over 20 different types of lipid kinases, and the human kinome is made up of two main subgroups: protein kinases and lipid kinases. The main goal of this study is to investigate the role of kinase enzymes in causing cancer.
Methods : The keywords "cancer, human kinome, kinase, and kinase inhibitor" were used to select and evaluate publications published between 2010 and 2022 from the databases Scopus, PubMed, Web of Science, and ScienceDirect.
Results : Results have shown that today, various types of kinase inhibitors are considered targeted therapeutic strategies in human malignancies. Many anti-proliferative mechanisms have been identified as a result of kinase activity inhibition in cancer patients receiving treatment, improving the clinical outcome of the disease. Phosphorylation is the most prevalent kind of post-translational modification; protein kinases phosphorylate almost two-thirds of all human-encoded proteins. The flexibility of the epigenome is significantly increased by phosphorylation, an essential regulatory component in the activity of proteins. Therefore, by participating in intracellular pathways, protein kinases frequently aid in the growth, survival, and migration of cells. When overexpressed or activated, however, they are linked to the development of cancer. In reality, the clinical therapy of cancer has changed significantly as a result of targeting kinases that are important in oncogenic alterations and metastasis.
Conclusion : According to the study's findings, kinases are among the most crucial elements of cell division and growth, and as a result, their overactivity contributes significantly to the development of cancer. This work demonstrates the beneficial effects of regulating and suppressing the kinase family to stop the proliferation of cancer cells.

Keywords: Kinome, Cancer, Metastasis.

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Abstract: A-10-2948-1

Antioxidant effect of quercetin in diabetic retinopathy

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Background :A serious side effect of diabetes called diabetic retinopathy (DR) is the primary cause of blindness in working-age individuals globally. Retinal damage caused by DR is typified by yellow patches or lesions that impact the thickness of the retina. About one-third of people with diabetes experience diabetic retinopathy symptoms. One of the main factors causing diabetes to worsen over time is the overproduction of reactive oxygen species (ROS). Retinal damage is caused by mitochondrial damage, which happens when ROS levels are higher than the antioxidant defense system can handle. This excessive cell death is what causes the damage. The purpose of this study is to assess quercetin's potential as an antioxidant to lessen apoptosis and retinal damage in diabetic retinopathy.
Methods : From July 2023 to November 2023, a thorough literature search was carried out using PubMed and Google Scholar. Studies assessing parameters linked to apoptosis in the retinas of diabetic rats were contrasted with non-diabetic controls, both in the presence and absence of quercetin administration.
Results : Eighty studies were assessed; eighteen were chosen for in-depth examination. The results show that the strong antioxidant quercetin activates the Nrf2-Keap1 pathway, increasing endogenous antioxidant synthesis, including GSH. This lessens the aberrations and death of retinal cells caused by oxidative stress. Furthermore, treatment with quercetin reduces pro-apoptotic markers such as caspase-3 and cytochrome c while increasing anti-apoptotic factors (Bcl-2).
Conclusion : Research indicates that quercetin's antioxidant qualities efficiently reduce retinal cell death, which makes it a potentially useful treatment for retinal damage caused by diabetic retinopathy.

Keywords: Quercetin, Diabetic Retinopathy, Antioxidant Defense, Apoptosis Inhibition, Nrf2-Keap1 Pathway

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Abstract: A-10-2863-3

Investigating the relationship between consumption pattern of different types of edible oils with blood pressure, blood sugar, lipid profile, hematology and anthropometric factors in people referring to Sabzevar Persian Cohort Center

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Background : Given the conflicting results from previous studies and the rising prevalence of cardiovascular disease and obesity, it is crucial to clarify the relationship between different types of dietary fats and cardiovascular health. Understanding this link can improve public awareness regarding the consumption of oils and fats.
Methods : Participants from the Sabzevar cohort who consumed either vegetable oils or animal fats were surveyed using a Food Frequency Questionnaire (FFQ) to assess their dietary habits.
Results : Butter, liquid oil, olive oil, nuts, and seeds positively influenced triglyceride levels, while vegetable butter, solid and semi-solid oils, olive fruit, mayonnaise, peanut butter, and buttermilk negatively impacted triglycerides. The highest correlation with cholesterol levels was observed for vegetable butter, liquid oil, and nuts (0.5, 0.41, and 0.25, respectively), while solid or semi-solid oils, butter, and olive oil showed a lower correlation (-0.33, -0.262, and -0.184). For LDL, vegetable butter, solid and semi-solid oils, butter, cream, and buttermilk were the most significant contributors to LDL increase, while olive oil had the lowest correlation (0.203). Nuts and peanut oil were most strongly associated with HDL changes. Vegetable oil consumption significantly impacted red blood cell ($P < 0.05$) with a correlation coefficient of 0.811. Walnut and nut oils positively correlated with hemoglobin, whereas olive oil and oilseeds showed a negative correlation. Butter and seeds influenced fasting blood sugar, while butter and olive oil had the highest correlation with platelet count.
Conclusion : The consumption of different oils and fats has significant effects on cholesterol, triglycerides, red blood cells, hematocrit, blood sugar, and body mass. Walnut oil, peanut oil, liquid oil, and butter had generally positive effects, while solid and semi-solid oils, as well as both vegetable and animal butter, had negative impacts in certain cases.

Keywords: Edible oils, Blood lipids, Blood pressure, Diabetes

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Abstract: A-10-2833-1

Gold nanoparticles in cancer treatment

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Background : Gold nanoparticles (AuNPs) have shown promising results in cancer treatment due to their unique properties. These nanoparticles are very effective in diagnosing and treating cancers due to their chemical and biological compatibility with different cells. Breast cancer is still a global concern, and the use of biosynthesized gold nanoparticles has been investigated as an efficient method for its treatment.
Methods : In this article, international sources such as "PubMed," "Google Scholar," and "Web of Science" were used with the keywords "breast cancer," "gold nanoparticles," and "cancer treatment." Out of 50 reviewed articles during the period of time, (2011-2023), 12 articles were selected with specific criteria. Researchers proved that the easiest and most common method is the chemical synthesis of gold nanoparticles, which involves the chemical reduction of gold ions (Au3+) into AuNPs (Au0). The gold nanoparticle synthesis depends on two aspects: (1) reduction and (2) stabilization. In the current decade, they injected gold nanoparticles (1.9 nm) into the thighs of mice with breast cancer and irradiated the tumor after 2 minutes.
Results : The results showed that mice injected with nanoparticles had smaller tumors and a higher one-year survival rate. These nanoparticles act as effective delivery vehicles for immunological applications and help to target the tumor site. Also, they improve the solubility and stability of sensitive cargoes and prolong their half-life.
Conclusion : Gold nanoparticles can accumulate in tumor tissue actively and passively and create plasmon hyperthermia through resonance. Also, AuNPs act as drug carriers to increase drug absorption into tumor tissue. Findings show that AuNPs can improve the safety and efficiency of cancer immunotherapy and accumulate in tumor sites and lymph nodes. Therefore, AuNPs are promising for treating breast cancer, and intratumorally injection may be beneficial for some superficial tumors.

Keywords: nanoparticles‹breast cancer‹plasmon hyperthermia‹mouse‹enzyme.

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Abstract: A-10-3113-1

Advancing Cancer Therapy: A Comprehensive Review of Combined Chemotherapy, Radiotherapy, and Immunotherapy Approaches

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Background :The integration of chemotherapy, radiotherapy, and immunotherapy has significantly evolved over recent decades, aiming to enhance treatment efficacy for various cancers. These combination therapies leverage distinct mechanisms to target tumors, aiming to improve patient outcomes. This review systematically examines the advancements in combining these therapies, focusing on their synergistic effects and clinical implications.
Methods :We conducted a comprehensive search of the PubMed, Scopus, and Web of Science databases to identify relevant studies published from 2014 to 2024. A total of 81 peer-reviewed articles were included, focusing on the combined use of chemotherapy, radiotherapy, and immunotherapy in cancer treatment. Studies were excluded if they lacked sufficient data or were not published in English. Data extraction was performed to assess treatment efficacy, mechanisms of action, and clinical outcomes.
Results :The integration of chemotherapy and radiotherapy has been shown to improve local control and reduce recurrence rates in various cancers, including head and neck, lung, and rectal cancers. The addition of immunotherapy, particularly immune checkpoint inhibitors, further enhances the therapeutic effects by modulating the tumor microenvironment and enhancing the immune response. Preclinical and clinical studies suggest that these combinations can significantly improve progression-free survival and overall survival rates. However, challenges remain in optimizing treatment protocols, including the management of increased toxicity and resistance mechanisms.
Conclusion :Combining chemotherapy, radiotherapy, and immunotherapy represents a promising strategy in the fight against cancer, with the potential to revolutionize treatment paradigms. While preliminary results are encouraging, ongoing research is crucial to refine these combinations, tailor treatments to individual patient profiles, and minimize adverse effects. Future studies should focus on optimizing dosages, sequencing, and identifying biomarkers for better patient stratification.

Keywords: Chemotherapy, Radiotherapy, Immunotherapy, Cancer Treatment, Combination Therapy

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Abstract: A-10-3136-1

Unveiling p53's Role in Multiple Sclerosis: Cellular Mechanisms and Therapeutic Strategies - A Systematic Review

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Background : Multiple Sclerosis (MS) is a chronic neurodegenerative disease characterized by demyelination and neuroinflammation. The tumor suppressor protein p53, recognized for its roles in apoptosis, cell cycle regulation, and DNA repair, has recently emerged as a key factor in MS pathophysiology. This systematic review investigates the multifaceted roles of p53 in MS, emphasizing its contributions to neuronal apoptosis, inflammation, and its potential as a therapeutic target.

Methods :A systematic search was conducted n August 26, 2023, using the PubMed, Web of Science, and Scopus databases. Keywords included "p53," "multiple sclerosis," "neuronal apoptosis," "inflammation," and "neuroprotection." The search included studies examining p53's role in MS and other neurodegenerative disorders. Studies were selected based on their relevance, methodological quality, and focus on p53's mechanisms in MS models. Of the 150 articles initially identified, 30 were reviewed in full, with 26 meeting the inclusion criteria for final analysis. Risk of bias was assessed to evaluate the robustness of the included studies.

Results : The review highlights that p53 is significantly upregulated in experimental autoimmune encephalomyelitis (EAE) models, where it correlates with increased neuronal damage, tau phosphorylation, and apoptosis. Mechanistic studies indicate that p53 mediates apoptosis through interactions with Bcl-2, Bax, caspase activation, and the amyloid precursor protein (APP) pathway. Pharmacological interventions targeting p53, such as Astragaloside IV, cannabidiol, and lithium carbonate, demonstrated neuroprotective effects by reducing apoptosis. Additionally, stem cell therapies, particularly with human periodontal ligament stem cells (hPDLSCs), showed promise in modulating p53 activity and improving neuronal survival.

Conclusion : This review underscores the pivotal role of p53 in MS pathogenesis, linking it to neuronal apoptosis, neuroinflammation, and demyelination. Targeting p53 pathways holds potential as a therapeutic strategy in MS. Future research should aim to refine p53-targeted therapies and explore their clinical applicability in MS management.

Keywords: Multiple Sclerosis (MS), p53, Neurodegeneration, Neuronal Apoptosis, Neuroinflammation, Demyelination

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Abstract: A-10-3141-1

AMP-Activated Protein Kinase as a Key Mediator of Mitochondrial Dysfunction in Multiple Sclerosis: Insights from Animal Models - A Systematic Review

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Background: Multiple sclerosis (MS) is a chronic central nervous system (CNS) disorder characterized by demyelination, neuronal damage, and oligodendrocyte depletion. Reliable biomarkers are essential for early diagnosis and disease management. Mitochondrial dysfunction and oxidative stress are increasingly recognized as key factors in CNS disorders, including MS, where mitochondrial impairment drives neurodegeneration. Adenosine monophosphate-activated protein kinase (AMPK) regulates mitochondrial energy balance and responds to neurodegenerative stress. This systematic review, following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, assesses the role of AMPK in mitochondrial dysfunction in MS animal models.

Methods: A systematic search was performed on August 26, 2023, in PubMed, Scopus, Web of Science, and Google Scholar using the keywords “AMPK,” “multiple sclerosis,” “mitochondrial dysfunction,” “oxidative stress,” and “animal models.” No publication date restrictions were applied. Studies were included if they examined AMPK-related pathways in mitochondrial dysfunction using animal models of MS. Of the 120 articles screened, 22 were reviewed in full, and 8 studies met the inclusion criteria. Articles were excluded if they did not specifically address AMPK or mitochondrial mechanisms in MS models. Risk of bias was assessed for methodological rigor.

Results: The 8 included studies highlighted a complex relationship between AMPK and mitochondrial dysfunction in MS models, such as cuprizone and experimental autoimmune encephalomyelitis (EAE). Findings showed that AMPK dysregulation is associated with impaired mitochondrial function, oxidative stress, and inflammation. Risk of bias analysis revealed areas of low risk but indicated gaps in methodological reporting.

Conclusion: This review highlights AMPK’s central role in mitochondrial dysfunction in MS models. Although the studies provide important insights, further research is needed to clarify AMPK's therapeutic potential in MS-related mitochondrial dysfunction and to improve experimental design in future studies.

Keywords: Multiple sclerosis (MS), AMPK, Mitochondrial dysfunction, Oxidative stress, Neurodegeneration, CNS disorders, Cuprizone model

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Abstract: A-10-2896-1

Examining the relationship between the consumption of various carbonated beverages and markers of non-alcoholic fatty liver: based on data from Sabzevar Cohort center

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Background : Non-alcoholic fatty liver is characterized by steatosis and inflammation, which has a high prevalence. Alcohol consumption is associated with a higher risk of obesity and dyslipidemia. In addition, soda increases insulin resistance and inflammation, which play an important role in the development of non-alcoholic fatty liver. Therefore, the present study investigates the relationship between the consumption of carbonated beverages and non-alcoholic fatty liver markers.
Methods : In this study, the desired information was recorded for patients, and the study data were analyzed using SPSS software version 24 and statistical methods.
Results :A total of 4,241 people participated in this study, of which 1,894 people (44.7%) were men. Of these, 3,980 people consumed Doogh, 3,627 people consumed soft drinks, 1,547 people consumed Delster, and 2,580 people consumed fruit juice. Also, in this study, there were also 589 people with diabetes, 977 people with high blood pressure, 435 people with ischemic heart disease, 660 people with fatty liver, 463 people with fatty liver who were being treated, 28 people with hepatitis B, 2 people with hepatitis C, and 80 people withwith gestational diabetes.
Conclusion : In this study, the consumption of Delster with walking 1 and the consumption of fruit juice with high cholesterol, LDL, and HDL in the blood were significantly associated, while the consumption of other carbonated beverages was not significantly associated with other variables. In this study, the consumption of carbonated beverages, including buttermilk, fruit juices, soft drinks, and sweeteners, showed no significant relationship with sex, diabetes, hypertension, ischemic heart disease, fatty liver, hepatitis B and C, blood lipids, and the consumption of heart drugs and blood pressure, thyroid, nerves, psyche, and diabetes. However, fruit juice consumption was significantly associated with fatty liver being treated and gestational diabetes.

Keywords: Carbonated Drinks, Non-alcoholic fatty liver, Soda

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Abstract: A-10-2673-2

Investigating the water quality of Neor Lake for sustainable development (Ardebil Province)

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Background: Lakes, rivers, wetlands, reservoirs, dams and underground water are considered to be blessed manifestations of nature and always play an important role in the activities of Agriculture (such as farming, production of fish, shrimps and other aquatic animals, animal husbandry)is responsible for the basic human needs (entertainment and tourism, employment, drinking water) as well as the preservation of biodiversity (macrophyte plants, aquatic animals, birds).

Methods: The physical and chemical condition of Neor Lake in Ardabil province was conducted with the aim of investigating the water quality in five study stations seasonally twice a year. Water sampling was done by Rottner sampler from the water surface and depth, and the physical and chemical parameters of the lake water including water temperature, dissolved oxygen (DO), electrical conductivity (EC), alkalinity, pH, total hardness, ammonia, nitrite, Nitrate, organic nitrogen, total nitrogen, orthophosphate, phosphorus and chlorophyll a were quantitatively evaluated using the standard procedure for water testing provided by the American Public HealthAssociation.

Results: The results of the analysis of the samples showed that the concentration of dissolved oxygen varied with a maximum of 8.78 mg/l and a minimum of 4.88 mg/l.The concentration of ammonium nitrogen in the lake fluctuated with a maximum of 0.94 and a minimum of 0.10 mg/l. The minimum total nitrogen concentration was 0.51 mg/liter and the maximum was 1.92 mg/l. The maximum concentration of total phosphorus was 0.415 mg/l and the minimum was 0.100 mg/l. The minimum concentration of chlorophyll a was 20.13 µg/l in March and the maximum concentration was 364.08 µg/l in August.

Conclusion: The result of this investigation showed that the lake water is hard and fresh water in terms of ionic composition and the pH of the water is alkaline and in terms of organic matter and nutrients, this lake is at the level of ultra-eutrophic water.

Keywords: Nutrients،dissolved oxygen،sustainable development،Noor Lake،Ardabil

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Abstract: A-10-2917-1

Nanoliposome loaded with 5-fluorouracil and Dorema aucheri Extract reduces tumor growth in a mouse model of colorectal cancer

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Background : The high and increasing prevalence of colorectal cancer (CRC) and the limited effectiveness of conventional treatments lead to efforts to find drugs with high potential that have fewer side effects. Dorema aucheri can have anti-cancer effects. Also, 5-fluorouracil (5-FU) is a chemotherapy drug that is used in the treatment of CRC, and studies have shown that it has better results in combination with other substances. Liposomal nanoparticles can be used for the simultaneous delivery of these drugs. Therefore, this study focuses on the effect of nanoliposome loaded with 5-FU and aqueous alcoholic extract of Dorema aucheri on tumor growth in a mouse model of colorectal cancer.

Methods :BALB/c mice were inoculated with CT26 mouse tumor cell lines, and after 7 days, the mice were divided into different groups. The lipid thin-film hydration method was used to synthesize liposomes, and their characterization was performed using TEM, DLS, and HPLC analyses. The inhibition of cell proliferation was evaluated using an MTT assay. Liposomal and free compounds were injected intravenously into mice four times every three days. Tumor size was measured every other day.

Results : The nanoparticles that were created were spherical in shape, uniform in size, and measured 200 ± 10 nanometers. HPLC analysis revealed that around 80% of the compound was successfully loaded into the nanoliposome. Using the MTT assay, the study found that treating CT26 cell lines with either free 5-FU + Dorema aucheri or nanoliposome-encapsulated 5-FU + Dorema aucheri (NLP + 5-FU + Dorema aucheri) reduced cell proliferation in a dose-dependent manner over 24 hours. The lowest rate of tumor volume increase and the highest weight gain were observed in the NLP + 5-FU + Dorema aucheri group.

Conclusion : The combination of nanoliposomes loaded with 5-fluorouracil and Dorema aucheri (NLP + 5-FU + Dorema aucheri) can reduce the growth rate of colorectal tumors in mice.

Keywords: Cancer, CRC, Nanoliposomes, Dorema aucheri, 5-fluorouracil

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Abstract: A-10-3168-1

Phylogenetic analysis Syctycercus bovis in slaughtered cows in Sanandaj city

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Background : Taenia saginata is a zoonotic parasite that infects both humans and cattle, transmitted through the consumption of raw or undercooked beef. Once ingested, Cysticercus bovis larvae migrate to striated muscles in cattle, causing infection. Reports of human and bovine infections have been documented in Iran. **Methods :**This cross-sectional descriptive study was carried out at the Sanandaj slaughterhouse. A total of 20 positive samples were identified using traditional methods, inspecting muscles from the heart, ribs, thighs, scapula, diaphragm, and liver. Cysts of Cysticercus bovis were identified and excised for molecular analysis. PCR was performed to detect the HDP2 gene associated with Taenia saginata. The PCR products were separated on a 1.5% agarose gel and visualized under UV light. Sequencing was performed on the PCR amplicons, and a phylogenetic tree was constructed to compare the sequences with known Taenia species from the GenBank database. **Results :**PCR and phylogenetic analysis confirmed that the HDP2 isolates from cattle in Sanandaj were closely related to the Taenia saginata species. Out of the 20 samples collected, all tested positive for the presence of Cysticercus bovis using traditional inspection methods. The PCR analysis amplified a specific 456 bp fragment, which was further confirmed as Taenia saginata through sequencing. Phylogenetic analysis showed that the HDP2 isolate had a strong genetic similarity to strains from other parts of Iran, as well as geographically close regions such as Egypt and Turkey, suggesting common ancestry or transmission routes between these populations.
Conclusion : The study demonstrates that Cysticercus bovis in cattle slaughtered in Sanandaj is primarily linked to the HDP2 strain of Taenia saginata. Phylogenetic analysis underscores the significance of this strain in the region, suggesting that targeted measures should be implemented to improve meat inspection protocols and prevent human transmission.
بازگشت به پایین

Keywords: Cystic Circus Bovis ،Cow ،Sanandaj Slaughter ،HDP2 strain

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Abstract: A-10-3163-1

Evaluation of the Role of Iron and Lipid Peroxidation in Patients with Endometriosis

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Background : Endometriosis is a chronic inflammatory disease characterized by the growth of endometrial tissue outside the uterus. Despite significant advances in understanding the disease, the exact mechanism of its pathogenesis is still not fully understood, and growing evidence suggests that oxidative stress plays a role in the development of endometriosis. In this study, the role of lipid peroxidation and iron as two key factors in causing oxidative stress in patients with endometriosis has been investigated.

Methods : In this study, the level of malondialdehyde was determined using the thiobarbituric acid method, and the iron level was determined using the commercial kit of Darman Kaveh by the ferrozin method in the blood of 30 patients with endometriosis. These two indicators of oxidative stress were analyzed by SPSS.

Results : This cross-sectional study was conducted on the blood samples of 30 patients with endometriosis referred to the Babol Fatemeh Al-Zahra Infertility Research Center, and any infectious diseases such as hepatitis, diabetes, and thalassemia were excluded. The study was approved by the Ethics Committee of Babol University of Medical Sciences, and the participants gave written consent. The results of this study showed that patients with endometriosis have higher levels of iron and malondialdehyde than the control group (P-value = 0.001).

Conclusion : An increase in the level of iron and malondialdehyde can indicate the severity of oxidative stress damage as an important biomarker. We believe the results of this study show the potential of using malondialdehyde and iron as biomarkers for the diagnosis and treatment of endometriosis.

Keywords: Endometriosis, iron, malondialdehyde

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Abstract: A-10-2673-3

The role of Azolla floating macrophyte plant in the eutrophication phenomenon of Anzali wetland (Gilan province)

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Background: Azolla is a floating macrophyte that covers the water surface of the aquatic ecosystem, thus reducing the penetration of light into the water, which causes a decrease in the amount of oxygen in the deep layers. One of the most important problems of Anzali Wetland is the phenomenon of eutrophication, which has several sources, such as the load of nutrients resulting from the input and distribution of non-native plants, including Azolla. **Methods:** In this research, in order to investigate the effects of Azolla floating plants in three areas of Anzali Wetland, nutrients and biomass of Azolla products were investigated. Water sampling was done at designated stations, and nutrients including total nitrogen, nitrogen-nitrate, ammonium-nitrogen, nitrogen-nitrite, soluble phosphate, and total phosphorus were measured using a standard method with a spectrophotometer. pH and electrical conductivity (EC) of water were measured with a WTW multi-parameter device, and dissolved oxygen (DO) was measured by the Winkler method.
Results: This study showed that the complete coverage of Azolla caused a decrease in dissolved oxygen and pH, and an increase in the concentration of ammonium in the water. The average nitrogen-nitrate and ammonium nitrogen were recorded as 0.332 and 0.129 mg/l, respectively. The low pH level during the Azolla coating causes the release of phosphorus from sediments. The averages of orthophosphate and chlorophyll a were measured as 0.073 mg/l and 6 mg/l, respectively. The results showed that the presence or absence of Azolla has no effect on the number and diversity of benthic organisms, but it increases the amount of organic matter in the bed sediments. **Conclusion:** Considering that 3.5% of the dry weight of the Azolla plant is nitrogen, on average, 50 kg of nitrogen enters the wetland as a result of the decomposition of Azolla, which accelerates eutrophication in the wetland.

Keywords: Eutrificason, Azolla ،nutrients, Anzali wetland, Gilan

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Abstract: A-10-2896-2

Investigating the relationship between carbonated beverages consumption and diabetes in people referring to Sabzevar Persian Cohort Center

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Background: Diabetes is a metabolic disorder characterized by chronic hyperglycemia and disturbances in carbohydrate, fat, and protein metabolism. It arises due to defects in insulin secretion, insulin function, or both. Consuming carbonated, caffeinated, or sweetened soft drinks with artificial sugars has been linked to negative health effects, including obesity. This study aims to evaluate the association between sugar and lipid profiles and diabetes in the population of Sabzevar who consumed carbonated drinks.

Methods: A total of 4,200 individuals who visited the Persian Sabzevar Cohort Center over six months were included in this study. Data were collected through field research and questionnaires. Venous blood samples were obtained following the cohort center's protocol, and biochemical markers were analyzed using an autoanalyzer. LDL levels were calculated using the Friedewald formula. The Kolmogorov-Smirnov test was used for normality, dependent t-tests for intragroup changes, and one-way ANOVA to compare groups. Data analysis was performed using SPSS 18, with a significance level of $P < 0.05$.

Results: A significant relationship was found between diabetes and high blood pressure, cardiac ischemia, fatty liver, and the use of heart and blood pressure medications. Additionally, diabetes was significantly associated with blood lipid levels, including triglycerides, total cholesterol, and LDL. There was also a link between diabetes and body mass index (BMI), with a higher BMI increasing the likelihood of diabetes. However, no significant relationship was found between diabetes and the average consumption of soda or non-alcoholic malt drinks.

Discussion and Conclusion: Several factors, including lipid profiles, BMI, and age, play a direct role in diabetes development. While carbonated drink consumption was associated with diabetes in some individuals, no statistically significant link was found. Reducing carbonated drink consumption through education and promoting healthier alternatives could help lower diabetes rates in society.

Keywords: Diabetes, carbonated drinks

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Abstract: A-10-2644-2

A Review of Association between Endoplasmic Reticulum Stress and diabetic Nephropathy

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Background: Today, diabetic nephropathy, which is the main cause of end-stage renal disease, is presented as one of the most important and common complications of diabetes. Recent studies have shown that stress in the endoplasmic reticulum may be one of the causes of the development and progression of diabetic nephropathy. Hyperglycemia induces ER stress and apoptosis in kidney cells. During ER stress, unfolded proteins accumulate in the ER and activate the unfolded protein response (UPR). The data showed increased expression of UPR genes, including the ER chaperones GRP78, HYOU1 (hypoxia up-regulated 1), and XBP-1 from human biopsies with established diabetic nephropathy compared to normal controls.

Methods: In this review, PubMed, ScienceDirect, and Google Scholar were searched for English-language articles up to July 2024 with the keywords “diabetic nephropathy," “ER stress,” and “unfolded protein response.” After searching for articles, 30 articles related to the title were found and reviewed.

Results: Studies show that endoplasmic reticulum stress can damage various kidney cells in the long term by activating different pathways. Podocytes, specialized epithelial cells in the outer part of the glomerular capillaries, are highly susceptible to endoplasmic reticulum stress due to their high anabolic and catabolic activities. High glucose levels damage podocytes through endoplasmic reticulum stress caused by active mTOR and apoptosis, which can eventually lead to diabetic nephropathy. In addition, other kidney cells are damaged during stress conditions, such as glomerular endothelial cells (GECs), mesangial cells (MCs), and tubular epithelial cells.

Conclusion: The ER maintains proteostasis, which is essential for cellular homeostasis. Induction of ER stress may be cytoprotective or cytotoxic by activating apoptosis. Chronic activation of ER stress can lead to chronic renal damage associated with chronic renal failure.

Keywords: Diabetic Nephropathy, Endoplasmic Reticulum Stress, Unfolded Protein Response (UPR)

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Abstract: A-10-3194-1

Introduction of new methods of removing heavy metals in industrial wastewater based on nanotechnology

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Background :Today, the removal of metal pollutants in industrial wastewater is a serious problem. In this regard, new methods, including nanomaterials, are widely used to remove heavy metals from industrial wastewater due to their special characteristics and very low costs. Among these nanomaterials, there are carbon-based nanomaterials, fine-grained nanomaterials, and silicate-based nanomaterials, as well as zero-valence metals and nanomaterials based on metal oxides.

Methods :In this review, the nanomaterials used include carbon nanotubes due to their special characteristics such as vibration, mechanical and thermal properties, which are divided into single-walled CNTs (SWCNTs) and multi-walled CNTs (MWCNTs), and fine nanomaterials due to their characteristics such as mechanical strength, electrical conductivity, and heat, which exist in the form of graphene oxide (GO) and reduced graphene oxide (RGO). Additionally, silicate-based nanomaterials are discussed due to their special characteristics, including non-toxicity and connection through groups such as NH2 - and -SH, which are used as suitable substrates in nanocomposites for the purification and removal of heavy metals from industrial wastewater.

Results :The results of the investigations showed that, according to the type of industrial wastewater and the chemical structure of nanomaterials, they are able to remove some heavy cations in industrial wastewater. Among the mentioned nanomaterials, carbon tube nanomaterials and silicate-based nanomaterials can remove 75% and 80% of heavy metals in industrial wastewater, respectively.

Conclusion :Purification of heavy metals in industrial wastewater is of great importance from the point of view of environmental and human health. According to the results, the use of modern methods involving nanomaterials to remove heavy metals is much more suitable and economical than other methods and traditional adsorbents.

Keywords: Heavy metals،industrial wastewater،nanomaterials،environment،carbon nanoparticles

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Abstract: A-10-3212-1

Evaluation of the Effect of obesity on omentin gene expression in adipose tissue in type-1 and type-2 diabetic model of C57BL/6 mice

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Background :Omentin, released by adipose tissue, may be related to glucose metabolism. The circulating levels of omentin and the related mRNA expression in visceral adipose tissue are different in types of diabetes, and the exact function of this molecule is still unknown. The aim of this study was to examine omentin gene expression in adipose tissues of type-1 and type-2 diabetic mice to investigate the effects of fat mass and insulin–glucose metabolism.

Methods :In this study, 36 C57BL/6 mice were divided into four experimental groups, including control, type-1 diabetes (induced by streptozotocin), type-2 diabetes with obesity (high-fat diet + low-dose streptozotocin [HFD + STZ]), and type-2 with normal weight (normal-pellet diet + low-dose streptozotocin [NPD + STZ]). The present study involved measurements of the oral glucose tolerance test and the levels of biochemical parameters, including blood glucose, omentin, insulin, lipid profile, as well as aminotransferases. In addition, the omentin mRNA expression was evaluated by real-time polymerase chain reaction.

Results :The results of the omentin gene expression analysis showed a significant difference between mRNA expressions in the experimental groups. The plasma omentin levels were significantly higher in the type-1 diabetes group and lower in type-2 diabetes with NPD + STZ; however, the plasma omentin levels were not changed in the HFD + STZ group. In addition, the findings of the serum biochemical analysis revealed significant differences compared to the control group.

Conclusion :The omentin expression may be affected by insulin and glucose levels in different types of diabetes more than by fat mass, and due to the local activity, the serum omentin may not comply with its gene expression.

Keywords: Obesity, Omentin, Adipose tissue, Type-1 diabetes, Type-2 diabetes, Insulin

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Abstract: A-10-3216-1

Evaluation of the expression pattern and diagnostic value of PPARγ in malignant and benign primary bone tumors

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Background : The quantifiable description of PPARγ expression patterns, alongside mechanistic in vitro evidence, will provide insights into the involvement of this mediator in tumor pathogenesis. This study is focused on illuminating the PPARγ gene and protein expression pattern, its association with tumor deterioration, and its diagnostic value in different types of primary bone tumors.

Methods : The expression pattern of PPARγ was investigated in 180 bone tissues, including 90 bone tumor tissues and 90 non-cancerous bone tissues. The local PPARγ expression level was assessed using real-time qRT-PCR, and the PPARγ protein expression pattern was measured using immunohistochemistry. The correlation of PPARγ expression levels with patients' clinicopathological features, as well as the value of the variables in predicting PPARγ expression levels in tumors and the value of PPARγ to discriminate tumor subtypes, were assessed.

Results : The mean PPARγ mRNA expression was significantly higher in bone tumors compared to healthy bone tissues; also, the malignant tumors, including osteosarcoma and Ewing sarcoma, had elevated levels of PPARγ mRNA compared to GCT tumors. Consistently, the protein expression of PPARγ in the tumor site was significantly higher in the bone tumors and malignant tumors compared to non-cancerous and benign tumors, respectively. The PPARγ protein could predict malignant tumor features, including tumor grade, metastasis, and recurrence, significantly. Moreover, PPARγ could potentially discriminate the patients from the controls, as well as malignant tumors from benign tumors, with significant sensitivity and specificity.

Conclusion :PPARγ might be involved in primary bone tumor pathogenesis, and determining its molecular mechanism regarding bone cancer pathogenesis is of grave importance.

Keywords: PPARγ, Bone tumor, Osteosarcoma, Ewing sarcoma, GCT

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Abstract: A-10-3216-2

The expression changes of PD-L1 and immune response mediators are related to the severity of primary bone tumors

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Background: The expression pattern, diagnostic value, and association of PD-L1, IFN-γ, and TGF-β with bone tumor type, severity, and relapse are determined in this study. Three hundred human samples from patients with osteosarcoma, Ewing sarcoma, and GCT were enrolled.
Methods: The PD-L1 gene and protein expression were assessed by qRT-PCR and immunohistochemistry, respectively. ELISA and flow cytometry were used to detect cytokines and CD4/CD8 T cell percentages, respectively.
Results: A considerable increase in PD-L1 level was detected in bone tumor tissues at both gene and protein levels, which was significant in osteosarcoma and Ewing sarcoma. A positive correlation was detected regarding PD-L1 and tumor metastasis and recurrence in osteosarcoma and Ewing sarcoma. The increased IFN-γ level was detected in patients with metastatic and recurrent osteosarcoma tumors, which was in accordance with the level of TGF-β in these samples. The simultaneous elevation of IFN-γ and TGF-β was detected in Ewing sarcoma and GCT; also, the CD4+/CD8+ ratio was decreased significantly in patients with osteosarcoma compared to GCT tumors.
Conclusion: The elevated levels of PD-L1, TGF-β, and IFN-γ were associated with bone tumor severity, which can provide insights into the possible role of this axis in promoting immune system escape, suppression, and tumor invasion.

Keywords: Bon tumors, osteosarcoma, Ewing sarcoma, Giant cell tumors, PD-L1, IFN-γ, TGF-β.

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Abstract: A-10-3217-1

The Effect of Coenzyme Q10 Supplementation on Oxidative Stress: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Background: Coenzyme Q10 (CoQ10) has been suggested to have beneficial effects on oxidative stress, but findings from studies on its impact remain inconsistent. This systematic review and meta-analysis aimed to assess the effects of CoQ10 supplementation on oxidative stress markers, including total antioxidant capacity (TAC), malondialdehyde (MDA), glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase (CAT).

Methods: A comprehensive search of databases including PubMed, Web of Science, Google Scholar, and Scopus was performed to identify relevant randomized controlled trials (RCTs) up to January 23, 2019. The analysis included 19 eligible RCTs. A random-effects model was applied to calculate the standardized mean difference (SMD) and 95% confidence intervals (CI) for the impact of CoQ10 on oxidative stress markers. The heterogeneity of studies was assessed using Cochran's Q test and the I^2 statistic to ensure robustness. Subgroup analyses and publication bias tests were conducted to explore variability in study outcomes.

Results: The meta-analysis revealed that CoQ10 supplementation significantly improved TAC (SMD = 1.29; 95% CI = 0.35–2.23; p = .007), GPx (SMD = 0.45; 95% CI = 0.17–0.74; p = .002), SOD (SMD = 0.63; 95% CI = 0.29–0.97; p < .0001), and CAT (SMD = 1.67; 95% CI = 0.29–3.10; p = .018). MDA levels were significantly reduced (SMD = −1.12; 95% CI = −1.58 to −0.65; p < .0001). However, results for SOD and CAT should be interpreted with caution due to potential publication bias.

Conclusion: CoQ10 supplementation shows promising effects on improving oxidative stress markers, particularly in enhancing antioxidant capacity and reducing oxidative damage. However, further well-designed studies with larger sample sizes are needed to validate these findings.

Keywords: antioxidant enzymes, coenzyme Q10, malondialdehyde, meta-analysis, oxidative stress, total antioxidant capacity

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3217-2

Comparison of Laser and Ultrasound Effects on Temperature Increase in Graphene Oxide Nanoparticle Solutions for Thermal Treatment of Osteosarcoma Cancer Cells

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Background: Ultrasound and laser waves, when used with nanoparticles, have been identified as effective methods for thermal cancer treatment due to their reduced side effects, faster results, and improved treatment efficiency. In this study, 2D graphene oxide nanoparticles were employed as thermal nano-converters to enhance the effectiveness of thermal cancer therapy.

Methods: The temperature changes in graphene oxide (GO) solutions at concentrations of 0.2 and 0.4 mg/ml, as well as in deionized water, were measured under various conditions, including heating, bath sonication, probe sonication (at power levels of 2-3.5 W), and exposure to a continuous wave laser at 808 nm (with a power range of 0-2 W) over 10 minutes. The effects of laser and ultrasound radiation on temperature were also simulated using a data mining approach based on experimental data.

Results: Both experimental and simulated results indicated that graphene oxide nanoparticles are ineffective at converting ultrasound waves into heat. However, GO nanoparticles act as strong absorbers of electromagnetic waves at 808 nm, with the ability to raise temperatures up to 85°C. The combination of laser and GO significantly improved the efficacy of cancer cell treatment, increasing the mortality rate of MG63 osteosarcoma cells by up to 85%. Fluorescence microscopy confirmed the uptake of GO by cancer cells.

Conclusion: The findings demonstrate that graphene oxide is highly effective in laser-based photothermal therapy but not in ultrasound-based treatments. GO serves as an excellent photothermal agent for localized thermal therapy of osteosarcoma cells when irradiated by an 808 nm laser, with minimal side effects.

Keywords: Cancer, Graphene oxide, Laser, Thermal therapy, Ultrasound

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3217-3

Assessment of Demographic and Clinical Characteristics of COVID-19 Patients Referred to Khatam Al-Nabi'a (PBUH) Hospital in Shirvan

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Background: The COVID-19 pandemic, originating in Wuhan, China, in December 2019, has created global health challenges, with around 14% of cases requiring hospitalization and 5% progressing to critical conditions. This study aimed to examine the demographic and clinical characteristics of COVID-19 patients referred to Khatam Al-Nabi'a (PBUH) Hospital in Shirvan.

Methods: This cross-sectional descriptive study included 665 confirmed COVID-19 patients. Data on demographic factors, clinical symptoms, and comorbidities were extracted from patient records using a structured checklist. Variables such as age, gender, body mass index (BMI), hospitalization duration, and common symptoms (e.g., shortness of breath, fever) were analyzed using SPSS software version 22. Statistical significance was set at $P<0.05$ to examine relationships between demographic factors and clinical outcomes.

Results: The average age of the 665 patients was 56.8 years, with a mean BMI of 26.4. Females made up 54.3% of the sample, and the average hospitalization duration was 5.3 days. The most common symptoms were shortness of breath (59.4%), fever (42.7%), and weakness (38.6%). Hypertension (31.3%), heart disease (19%), and diabetes (16.1%) were the most prevalent comorbidities. Older patients showed more severe symptoms, with a significant correlation between age and clinical severity ($P<0.05$). Males exhibited slightly more severe symptoms than females, although the difference was marginal.

Conclusion: Older individuals and those with pre-existing comorbidities, such as hypertension, heart disease, and diabetes, are at higher risk of severe COVID-19 complications. This study suggests that health policies should focus on these vulnerable groups to improve care outcomes during pandemics. Further research is recommended to explore additional risk factors.

Keywords: COVID-19, Clinical Symptoms, Demographic Characteristics, Comorbidities, Hospitalization Duration

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3222-1

The Impact of Dark Chocolate on C-Reactive Protein Levels: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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4. Department of Biochemistry, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.

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Conclusion: Older individuals and those with pre-existing comorbidities, such as hypertension, heart disease, and diabetes, are at higher risk of severe COVID-19 complications. This study suggests that health policies should focus on these vulnerable groups to improve care outcomes during pandemics. Further research is recommended to explore additional risk factors.

Keywords: Dark chocolate, C-Reactive Protein, Inflammation, Meta-analysis, Randomized controlled trials

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3222-2

Association Between Low Carbohydrate Diets and Non-Alcoholic Fatty Liver Disease: A Case-Control Study

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5. Department of Biochemistry, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.

Background: Non-alcoholic fatty liver disease (NAFLD) is characterized by the excessive buildup of fat in liver cells in individuals who do not consume alcohol. This study aimed to investigate the relationship between adherence to low carbohydrate diets (LCDs) and the risk of NAFLD.

Methods: This age- and gender-matched case-control study included 120 newly diagnosed NAFLD patients and 120 healthy controls without NAFLD. NAFLD diagnosis was confirmed through laboratory tests and abdominal ultrasound. The low carbohydrate diet score was calculated based on the percentage of energy derived from carbohydrates, fats, and proteins. Participants who consumed the highest proportion of fat and protein, along with the lowest carbohydrate intake, were assigned the highest scores (10 points). Multivariable logistic regression was used to assess the association between LCDs and NAFLD.

Results: The study revealed that individuals in the highest tertile of LCD adherence had higher intakes of zinc and vitamin B12 compared to those in the lowest tertile. Additionally, protein ($p = 0.02$), carbohydrate ($p < 0.02$), and cholesterol ($p = 0.02$) intake were significantly higher in NAFLD patients compared to the control group. However, there was no significant association between LCD adherence and the risk of developing NAFLD in both crude (OR: 1.36; 95% CI: 0.97–1.92; P-trend = 0.13) and adjusted models (OR: 1.31; 95% CI: 0.84–2.04; P-trend = 0.23).

Conclusion: Although protein, carbohydrate, and cholesterol intake were higher in individuals with NAFLD, adherence to low carbohydrate diets, characterized by higher intakes of protein and fat, was not significantly associated with the risk of NAFLD. Further prospective studies are needed to confirm these findings.

Keywords: Diet, Carbohydrate-Restricted, Fatty Liver, Non-Alcoholic Fatty Liver Disease

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3222-3

The Impact of Quercetin on Oxidative Stress Markers: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Conclusion: Although protein, carbohydrate, and cholesterol intake were higher in individuals with NAFLD, adherence to low carbohydrate diets, characterized by higher intakes of protein and fat, was not significantly associated with the risk of NAFLD. Further prospective studies are needed to confirm these findings.

Keywords: Quercetin, Oxidative Stress, Malondialdehyde, Total Antioxidant Capacity, Ferric Reducing Ability of Plasma

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2257-2

Protective effect of herniarin against gentamicin-induced nephrotoxicity by improvement of oxidative stress

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Background: In order to determine the reasons for patients' renal disease, practitioners ought to attempt to understand drug-induced nephrotoxicity, a prevalent clinical issue. An effective antibiotic for gram-negative bacterial infections is gentamicin. This medication's extremely dangerous adverse effect, nephrotoxicity, has limited its effectiveness. Thus far, it has been determined that gentamicin accumulation in the renal tubules results in oxidative stress, which is the cause of the negative effects. One compound that has been found to have antioxidant properties is herniarin. In this article, we evaluated its impact for the first time on nephrotoxicity induced by gentamicin.

Methods: Four groups of twenty-four C57/BL6J mice were established. First Group: Control; Group 2: A dose of 100 mg/kg of gentamicin for ten days; Group 3 was administered injections of gentamicin for the final ten days along with a 15-day dose of herniarin at a dosage of 25 mg/kg. For 15 days, Group 4 was administered a 50 mg/kg injection of herniarin, along with gentamicin for the final 10 days. The investigation of renal function involved the measurement of creatinine and plasma urea levels in addition to a histological analysis. Furthermore, oxidative stress markers were assessed in kidney tissues.

Results: Our results show that treatment with herniarin improves kidney function by reducing levels of urea and creatinine. Herniarin treatment is associated with the improvement of oxidative stress by reducing MDA and increasing TAC, but it did not affect SOD.

Conclusion: As a conclusion, it may be inferred that herniarin may have a nephroprotective effect by substantially reducing the kidney damage produced by gentamicin in mice through its antioxidant properties in a dose-dependent way.

Keywords: Nephrotoxicity, Gentamicin, Herniarin, Oxidative Stress.

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3228-1

Protective effect of herniarin against gentamicin-induced nephrotoxicity in C57BL/6 mice

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Background: Triple-negative breast cancer (TNBC) is an aggressive subtype characterized by the absence of estrogen receptors, progesterone receptors, and HER2. This lack of targeted therapies results in poor prognosis and limited treatment options. Conventional chemotherapy can be effective but often leads to severe side effects and resistance. Natural compounds like Calebin A, derived from turmeric, have shown promise in enhancing existing treatments while minimizing toxicity. Notably, the NF-κB signaling pathway is frequently activated in TNBC, promoting tumor progression and metastasis. Inhibiting this pathway may provide a novel therapeutic approach.
Methods: This study explored the synergistic anti-cancer effects of Calebin A and cisplatin in TNBC MDA-MB-231 cells. Cell viability assays assessed the combined effects, and a combination index was calculated for synergy evaluation. Flow cytometry was used to measure apoptosis and necrosis, while real-time PCR analyzed NF-κB expression and its downstream targets, including survivin, MYC, VEGF, and MMP9/2. Wound healing assays evaluated the impact on cell migration.
Results: The combination treatment significantly induced apoptosis, inhibited cell proliferation, and suppressed migration compared to single agents. Mechanistic studies indicated that the combination effectively reduced NF-κB activation and downregulated its downstream targets. This suggests that Calebin A and cisplatin together may offer a promising strategy for TNBC by specifically targeting the NF-κB pathway.
Conclusion: Our findings underscore the potential of combining natural compounds like Calebin A with conventional chemotherapy to address the challenges of TNBC. By targeting critical pathways involved in cancer progression, this combination could enhance therapeutic efficacy. Further clinical investigations are needed to validate these results and explore the full potential of this strategy in patient care.

Keywords: Triple-negative breast cancer, Calebin A, Cisplatin, NF-κB, Apoptosis

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Abstract: A-10-3228-2

Synthesis, characterization, and protective activity of Selenium-Chitosan nanoparticles loaded with Diosmin

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Background : Glutamate-induced toxicity is a significant contributor to neurodegenerative disorders, necessitating the development of effective neuroprotective agents. Diosmin, a flavonoid known for its antioxidant and anti-inflammatory properties, has shown promise in protecting neuronal cells from glutamate toxicity. However, its low bioavailability and stability hinder its therapeutic efficacy. This study aimed to synthesize diosmin-loaded selenium nanoparticles (SeNPs) stabilized by chitosan (CS) to enhance the neuroprotective effects of diosmin against glutamate-induced toxicity in PC12 cells.

Methods : Diosmin-loaded SeNPs were synthesized using a co-precipitation method, followed by stabilization with chitosan. The nanoparticles were characterized through various techniques, including dynamic light scattering (DLS) for size distribution, scanning electron microscopy (SEM) for morphology, and Fourier-transform infrared spectroscopy (FTIR) for functional group identification. The neuroprotective effects were evaluated by exposing PC12 cells to glutamate and subsequently treating them with diosmin-loaded SeNPs. Cell viability was assessed using the MTT assay, while oxidative stress and inflammatory markers were measured.

Results : The synthesized diosmin-loaded SeNPs exhibited a uniform size distribution and spherical morphology. Characterization confirmed the successful loading of diosmin onto SeNPs. Treatment with diosmin-loaded SeNPs significantly improved cell viability in glutamate-exposed PC12 cells compared to controls. Additionally, there was a notable reduction in oxidative stress markers and inflammatory cytokines in treated cells, indicating enhanced neuroprotection.

Conclusion : The study demonstrates that selenium-chitosan nanoparticles loaded with diosmin effectively enhance the neuroprotective properties of diosmin against glutamate-induced toxicity in neuronal cells. This nanotechnology-based approach not only improves the stability and bioavailability of diosmin but also offers a promising strategy for developing novel treatments for neurodegenerative disorders.

Keywords: protect effect, PC12 cell line, Diosmin, Selenium, Chitosan, Glutamate.

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-3228-3

Investigating the combined effect of resveratrol and metformin on gentamicin-induced nephrotoxicity in C57BL/6 mice

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Background: Gentamicin is a potent antibiotic widely used in clinical settings, but its application is often limited by nephrotoxicity. This study aimed to evaluate the protective effects of resveratrol and metformin, both known for their antioxidant and anti-inflammatory properties, against gentamicin-induced kidney damage in male C57BL/6 mice.

Methods: A total of 30 male C57BL/6 mice were randomly assigned to five groups (n=6 each): control (saline), gentamicin, resveratrol + gentamicin, metformin + gentamicin, and the combination of resveratrol and metformin + gentamicin. The treatment lasted for 15 days, after which blood samples and kidney tissues were collected. Biochemical analyses focused on serum creatinine and urea levels, while histopathological evaluations assessed oxidative stress and inflammation in kidney tissues.

Results: Gentamicin administration significantly elevated serum creatinine and urea levels, indicating impaired renal function. Additionally, it increased oxidative stress and inflammatory markers in kidney tissues. Conversely, treatment with resveratrol and metformin resulted in marked reductions in these harmful effects. Notably, the combined treatment of resveratrol and metformin provided enhanced protective effects compared to either agent alone, significantly lowering oxidative stress and inflammation while improving renal function.

Conclusion: The findings suggest that resveratrol and metformin effectively mitigate gentamicin-induced nephrotoxicity in C57BL/6 mice. Their combined use could represent a promising therapeutic strategy to protect against kidney damage associated with gentamicin treatment, warranting further investigation for potential clinical applications.

Keywords: Nephrotoxicity, Gentamicin, Resveratrol, Metformin, Oxidative stress

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2397-1

The impact of circulating exosomes obtained from young and old men on P53, P21 and stress oxidative in hematopoietic stem cells

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4. Department of Medical Laboratory Sciences, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran.
5. Department of Hematology and Transfusion Sciences, Faculty of Allied Medical Sciences, Tehran University of Medical Sciences, Tehran, Iran.

Background: Gentamicin is a potent antibiotic widely used in clinical settings, but its application is often limited by nephrotoxicity. This study aimed to evaluate the protective effects of resveratrol and metformin, both known for their antioxidant and anti-inflammatory properties, against gentamicin-induced kidney damage in male C57BL/6 mice.

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Conclusion: The findings suggest that resveratrol and metformin effectively mitigate gentamicin-induced nephrotoxicity in C57BL/6 mice. Their combined use could represent a promising therapeutic strategy to protect against kidney damage associated with gentamicin treatment, warranting further investigation for potential clinical applications.

Keywords: Aging, Exosome, Extracellular vesicles, Hematopoietic stem cell, Stress oxidative, Senescence

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2397-2

CCN5/WISP2 serum levels in patients with coronary artery disease and type 2 diabetes and its correlation with inflammation and insulin resistance; A machine learning approach

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5. Department of Hematology and Transfusion Sciences, School of Allied Medical Sciences, Tehran University of Medical Sciences, Tehran, Iran.

Background: This study investigates the relationship between serum levels of CCN5/WISP2 and the risk of coronary artery disease (CAD) and type 2 diabetes mellitus (T2DM). Previous research has explored CCN5's effects on metabolic pathways, but no studies have linked its serum levels to CAD or T2DM. This study aims to fill that gap by comparing individuals with CAD, T2DM, and CAD-T2DM against healthy controls.

Methods: A case-control design was employed with 160 participants divided into four groups: T2DM, CAD, CAD-T2DM, and healthy controls. Serum levels of CCN5, TNF-α, IL-6, adiponectin, and fasting insulin were analyzed. Statistical analyses included Chi-square tests, ANOVA, Spearman correlation, and logistic regression. Receiver Operating Characteristic (ROC) curves assessed CCN5's diagnostic potential. Machine learning algorithms—Decision Tree, Gradient Boosted Trees, Random Forest, Naïve Bayes, and KNN—were used to predict disease states and evaluated through 10-fold cross-validation.

Results: The CAD, T2DM, and CAD-T2DM groups had significantly higher CCN5 concentrations compared to the healthy control group (CAD: 336.87 ± 107.36 ng/mL, T2DM: 367.46 ± 102.15 ng/mL, CAD-T2DM: 404.68 ± 108.15 ng/mL, control: 205.62 ± 63.34 ng/mL; $P < 0.001$). A significant positive correlation was found between CCN5 and cytokines IL-6 and TNF-α across all patient groups ($P < 0.05$). Multinomial logistic regression highlighted a significant association between CCN5 and the conditions of T2DM-CAD, T2DM, and CAD ($P < 0.001$), even after adjusting for confounding factors. Among machine learning models, Naïve Bayes excelled in T2DM classification (AUC: 0.938), while Random Forest performed best for CAD prediction (AUC: 0.994).

Conclusion: Our study has revealed, for the first time, a positive connection between CCN5 serum levels and the risk of developing T2DM and CAD. Nonetheless, more research is needed to ascertain whether CCN5 can serve as a predictive marker.

Keywords: Adipokine, Coronary artery disease, Diabetes, Machine learning, Artificial Intelligence

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Journal Homepage: https://abi.tums.ac.ir/index.php/abi

Abstract: A-10-2397-3

Circulating CCN6/WISP3 in Type 2 Diabetes Mellitus Patients and its Correlation with Insulin Resistance and Inflammation; Statistical and Machine Learning Analyses

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Background: Cellular Communication Network Factor 6 (CCN6) is an adipokine whose production undergoes significant alterations in metabolic disorders. Given the established connection between the dysfunction of adipose tissue secretions and metabolic disorders, along with the observed negative correlation of CCN6 with insulin levels, the present study aimed to investigate the association between serum CCN6 levels and type 2 diabetes mellitus (T2DM) as well as its risk factors for the first time.

Methods: A total of 80 individuals diagnosed with T2DM and 80 healthy control subjects were included in the study. The circulating levels of CCN6, adiponectin, TNF-α, IL-6, and insulin were quantified using ELISA. The Gini Index was utilized to determine the weight of each factor in T2DM classification. Additionally, various machine learning models were employed to develop classifiers for predicting T2DM.

Results: T2DM patients demonstrated significantly lower levels of CCN6 (1259.76 ± 395.02 pg/ml) compared to controls (1979.17 ± 471.99 pg/ml, $P < 0.001$), as well as lower levels of adiponectin ($P < 0.001$) and higher levels of TNF-α and IL-6 ($P < 0.001$) compared to non-T2DM individuals. In the T2DM group, CCN6 exhibited negative correlations with insulin, HOMA-IR, BMI, IL-6, and TNF-α. Logistic regression analysis indicated an increased risk of T2DM, with a CCN6 cutoff value of 1527.95 pg/mL distinguishing T2DM patients with 86.3% sensitivity and 73.8% specificity. The Gini Index highlighted that HOMA-IR, IL-6, and CCN6 had the highest weighting on T2DM.

Conclusion: Our research identified a significant and negative association between serum CCN6 levels and the likelihood of T2DM, as well as inflammation biomarkers (IL-6 and TNF-α). CCN6 shows promise as a potential biomarker for T2DM; however, further investigations are necessary to validate this finding and assess its clinical utility.

Keywords: WISP3/CCN6, Type 2 diabetes mellitus, Inflammatory cytokines, Insulin resistance, Adiponectin

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Abstract: A-10-3242-1

Exercise improves hippocampal klotho and parkin levels in a rat model exhibiting cognitive decline induced by streptozotocin

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Background: The oxidative status of the brain plays a significant role in the onset of Alzheimer's disease (AD). Klotho, a protein associated with anti-aging, reduces oxidative stress through the activation of antioxidant enzymes. Parkin-mediated mitophagy is the dominant mitophagy pathway in neural cells. Consequently, compounds that enhance klotho and parkin expression may serve as potential therapeutic options for Alzheimer's disease in the context of oxidative imbalance. It has been proposed that physical activity may promote the up-regulation of klotho and parkin expression.

Methods: In this investigation, we evaluated the neuroprotective effects of pretreatment exercise in rats, which involved treadmill running at a speed of 15 m/min for 25 minutes per day, six days a week, over a period of four weeks. We investigated the impact of exercise on the expression levels of klotho, parkin, SOD, and GPX in the hippocampus of an animal model exhibiting cognitive decline, which was induced through intracerebroventricular (ICV) administration of streptozotocin (STZ). Cognitive function was evaluated using the Morris Water Maze test.

Results: The findings revealed that the average escape latency and distance were significantly extended in the STZ group in comparison to the sham group. Additionally, the levels of klotho, parkin, SOD, and GPX were found to be reduced in the hippocampus. Notably, exercise mitigated the enhanced spatial performance. This improvement may be associated with an increase in oxidative stress tolerance, as indicated by the up-regulation of klotho, parkin, SOD, and GPX.

Conclusion: Our present study suggests that the upregulation of klotho and parkin may serve as a neuroprotective mechanism of exercise against neural injuries following cognitive decline associated with Alzheimer's disease.

Keywords: Klotho, Parkin, Alzheimer's disease, streptozotocin, oxidative stress

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Abstract: A-10-2616-2

Covalent Drug Design Strategy and molecular dynamic simulation and MMGBSA Calculation against COVID-19 Mpro

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Background: The viral main protease (Mpro) is a key drug target due to its integral role in the life cycle of SARS-CoV-2. Given the urgent need for effective therapeutics against COVID-19, extensive research has focused on the development of inhibitors targeting this enzyme. This study focuses on the exploration of covalent docking for Mpro inhibition.

Methods: Using computational methods, the interactions between potential inhibitors and SARS-CoV-2 Mpro are investigated. Using protein structures (7JKV and 7TDU), fragment-based ligand selection and covalent docking via SeeSAR were performed. Pharmacokinetic properties, toxicity assessments using SwissADME and molecular dynamics simulations were performed using GROMACS. Molecular dynamics simulations were performed and parameters such as RMSD, RMSF, and MM/GBSA were analyzed for two specific ligands.

Results: These inhibitors exhibit pharmacological properties that may affect drug interactions and metabolism in vivo.

Conclusion: In addition, the toxicity profiles of covalent ligands highlight complex interactions across physiological systems and underscore the need for comprehensive safety evaluations prior to therapeutic considerations.

Keywords: COVID-19, Main Protease (Mpro), Computational Drug Desig, Covalent Drug Design

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Abstract: A-10-3032-1

The Effect of Simultaneous Use of Opium and Ischemic Preconditioning on Ischemia/Reperfusion Injury in the Rat Liver

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Background: Ischemia preconditioning (IPC) is a protective procedure against the injury induced by ischemia/reperfusion (IR). There is evidence that the administration of opioids may have the same effects on the injury. It was aimed to investigate the ameliorating effects of concurrent use of opium and IPC on lobar IR injury in the rat liver.

Methods: Twenty-five adults male Wistar rats were randomly divided into 5 groups: 1) sham-operated, 2) IR, 3) IR+IPC, 4) opium+IPC+IR, and 5) naloxone+opium+IPC+IR. At the end of the reperfusion, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in the blood were assayed and oxidative stress was determined by measuring malondialdehyde (MDA), total antioxidant capacity (TAC), superoxide dismutase (SOD) and catalase (CAT) activities in the liver tissues.

Results: ALT, AST and MDA levels were significantly increased in the IR group compared to the sham-operated group ($P<0.05$). However, the application of IPC and IPC+opium significantly decreased the release of these enzymes, while the simultaneous application of opium and IPC had a stronger restorative effect on the IR injury ($P<0.05$). The recovery effects induced by opium+IPC in terms of TAC, SOD and catalase were also higher than that of the IPC alone. However, the use of naloxone significantly inhibited the protective effects induced by the opium.

Conclusion: It was concluded that the simultaneous use of opium and IPC was able to accelerate the protective effects of IPC on the IR injury.

Keywords: Ischemia preconditionin, Ischemia/reperfusion, Liver, Opium, Rat.

Abstract: A-10-2906-2

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The Effects of Fisetin on Blood Glucose Regulation:

A Systematic Review of In Vivo Evidences

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Background: High blood glucose is a major health concern in patients with diabetes and metabolic disorders. Fisetin, a natural flavonoid, has garnered significant attention due to its anti-inflammatory and antioxidant potential. Preliminary evidence suggests that fisetin may play a positive role in blood glucose regulation. The objective of this review is to report the latest evidence on the effects of fisetin on blood glucose levels in existing literature and to summarize the evidence related to its efficacy.

Methods: A systematic search was conducted in the databases of PubMed, Scopus, and Web of Science for articles published from 2010 to 2024. Studies examining the effects of fisetin on blood glucose levels in both in vivo models and humans were reviewed, with inclusion criteria focused on those that specifically investigated fisetin's impact on blood glucose. This systematic review evaluated the quality, study design, sample characteristics, differences in animal species, established disease models, dose and duration of fisetin treatment, and the outcomes of the eligible studies.

Results: A total of 18 studies involving 630 laboratory rats or mice and 51 human participants were identified and analyzed. Most studies indicated that fisetin significantly reduces fasting blood glucose level. Various biochemical hypotheses, such as the antioxidant and anti-inflammatory effects of fisetin, were explored to explain these results.

Conclusion: This systematic review indicates that fisetin may have a positive impact on lowering blood glucose levels in patients with diabetes and metabolic disorders. However, further research with randomized controlled designs is needed to confirm these findings and determine the optimal dosage.

Keywords: Fisetin; Glucose; In vivo; Diabetes; Hyperglycemia.

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Investigating the Therapeutic Effects of Fisetin and Hydroxychloroquine on Fatty Pancreatic Disease: Implications for Insulin Sensitivity and Autophagy Modulation

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Background: Fatty pancreas, characterized by fat accumulation in the pancreas, is linked to obesity and can progress to prediabetes and type 2 diabetes. Therapeutic strategies aimed at reducing endoplasmic reticulum stress and promoting autophagy may provide beneficial outcomes. This study investigates the impact of fisetin (FST) and hydroxychloroquine (HCQ) on fatty pancreas in an experimental setting.

Methods: Forty-eight male C57BL/6J mice were allocated to either a standard chow diet (SCD) or a high-fat diet (HFD) for a total of 16 weeks. The HFD group was subdivided into five groups of eight mice each: HFD, HFD+V (Vehicle), HFD+FST, HFD+HCQ, and HFD+FST+HCQ. FST was administered daily at a dose of 100 mg/kg, while HCQ was injected intraperitoneally at a dose of 50 mg/kg twice a week for an additional 8 weeks. Insulin resistance was evaluated using the oral glucose tolerance test (OGTT) and the homeostasis model assessment of insulin resistance (HOMA-IR). Histological analysis of pancreatic tissues was performed, and protein and mRNA levels of markers related to endoplasmic reticulum stress and autophagy were quantified through PCR and immunoblotting techniques.

Results: Both FST and HCQ significantly mitigated weight gain, pancreatic adipocyte accumulation, and insulin resistance in obese mice subjected to HFD, with their combined administration yielding even more pronounced therapeutic effects. The HFD diet elevated the expression of UPR markers ATF4 and CHOP, with HCQ amplifying this response. Conversely, FST effectively reduced the UPR by modulating GRP78 levels. Moreover, the HFD resulted in a notable decrease in the LC3II/LC3I ratio and an accumulation of p62 protein due to diminished p-AMPK levels. Treatment with FST reversed these alterations, leading to decreased mTOR expression and increased levels of autophagy markers such as ATG5 and Beclin1.

Conclusion: Our findings demonstrate that FST and HCQ are effective in countering fatty pancreas, enhancing insulin sensitivity, and addressing pancreatic fat deposition associated with metabolic syndrome. While HCQ may induce endoplasmic reticulum stress, FST appears to confer protective effects, highlighting the potential benefits of their combined application for improved treatment outcomes.

Keywords: Metabolic syndrome, Fatty pancreas, ER stress, Autophagy, Fisetin, Hydroxychloroquine

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Serotonin paradox in AUTISM disorder spectrum via vitamin D

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Background: Autism spectrum disorder (ASD), a common neurodevelopmental disorder characterized by impaired communication and repetitive behaviors, has increased extensively in the last 20 years. Imbalanced serotonin regulation and blood levels of vitamin D have been considered in autism; however, there is no an exact mechanism in this case. This systematic review and meta-analysis demonstrate evidence regarding the role of vitamin D in the expression of the tryptophan hydroxylase 2 (TPH2) in the brain and TPH1 in tissues that can improve autism symptoms and helps to treatment.

Methods: Medline, Scopus, and Web of Science were searched for literature from 2001-01-01 to 2024-08-29. Meta-analyses were performed by implementing continuous random-effects models and outcomes were reported by Mean Differences (MDs) or Standardized Mean Differences (SMDs).

Results: 20 studies involving 162 participants were included in this analysis. Test group received vitamin D doses below 4000 IU/day lasting 10 weeks or longer against control group receiving placebo. There were significant changes in serotonin levels between the test group and control group ($p < 0.05$). Meta-analysis showed that, compared with placebo, vitamin D modified Serotonin synthesis via direct genetic regulation of serotonin synthesis enzymes, both peripheral Tryptophan hydroxylase-1 (TPH1) and central Tryptophan hydroxylase-2 (TPH2). Activated vitamin D down-regulates peripheral TPH1 while upregulates central TPH2. [MD = 0.365; 95 % CI (0.254, 0.436), I2 = 0 %].

Conclusion: In this meta-analysis, we demonstrated that vitamin D can induce TPH2 synthesis but repress TPH1 to improve the symptoms of the core symptoms of autism in about 75% of autistic children.

Keywords: Serotonin, AUTISM, vitamin D, Tryptophan hydroxylase

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Evaluating The Effectiveness of Quercetin Nanoparticles in The Prevention and Treatment of Oral Mucositis During Radiotherapy for Head and Neck Cancers

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Background: Oral mucositis is a debilitating side effect of head and neck radiotherapy, impacting up to 85% of patients. Quercetin, a flavonoid with significant antioxidant and anti-inflammatory properties, has yet to be thoroughly investigated for its potential in mitigating radiation-induced oral mucositis. This study aims to evaluate the preventive and therapeutic efficacy of quercetin and quercetin nanoparticles on radiation-induced oral mucositis in a murine model.

Methods: Thirty Wistar rats were subjected to a single 13 Gy dose of radiation to induce mucositis. The rats were then divided into six groups (n=5/group): non-irradiated control, vehicle control, 10 mg/kg quercetin, 10 mg/kg quercetin nanoparticles, and dexamethasone. Treatments were administered from day 7 to day 13 post-irradiation. Outcome measures included daily oral injury scoring, serum TNF-α levels, total antioxidant capacity, weight changes, and scar area. Additionally, histological examination of oral mucosal samples was performed using hematoxylin and eosin (H&E) staining to assess the extent of tissue damage after the treatment period.

Results: Administration of 10 mg/kg quercetin significantly reduced TNF-α levels and increased antioxidant capacity compared to the vehicle group ($p<0.001$). Both quercetin and quercetin nanoparticles significantly attenuated the progression of oral injury scores compared to other treatments ($p<0.01$). Additionally, quercetin nanoparticles and dexamethasone effectively protected against weight loss compared to the vehicle ($p<0.001$). Dexamethasone also significantly reduced scar area compared to the control group ($p=0.0438$). Histopathological evaluation revealed that eight days post-radiation, untreated groups exhibited significant tissue damage and endothelial cell apoptosis, whereas treated groups showed marked improvement.

Conclusion: Quercetin nanoparticles at a 10 mg/kg dose demonstrated significant protective effects against radiation-induced oral mucositis, likely through antioxidant and anti-inflammatory mechanisms. These findings suggest that quercetin, particularly in nanoparticle form, warrants further investigation as a potential adjuvant therapy for radiotherapy induced mucositis in head and neck cancer patients.

Keywords: Antioxidant, Quercetin, Head and Neck Cancer, Oral mucositis, Radiotherapy

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EXPRESSION LEVELS OF FOXO-1MIR-27 IN WOMEN WITH ENDOMETRIAL CANCER AND HYPERPLASIA: IMPLICATIONS FOR THE HUMAN REPRODUCTIVE SYSTEM

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Background: Despite extensive research on endometrial cancer (EC) and endometrial hyperplasia, there is still a gap in understanding the molecular mechanisms underlying their development and progression. The aim of this study was to investigate the expression levels of FOXO-1 and miR-27 in patients with EC and endometrial hyperplasia compared to control subjects.

Methods: Endometrial tissue of patients with cancer, hypoplasia, and controls were applied for expression levels of FOXO1 gene and microRNA-27 by qRT- PCR. The data were analyzed, using t-test, Mann -Whitney U, Pearson correlation coefficient analysis, ANCOVA, and ANOVA.

Results: There was a significant decrease in FOXO-1 in endometrial tissue of patients with cancer AND hyperplasia compared to control tissue ($p<0.01$). Whereas miR-186 expression level increased significantly only in patients with EC ($p<0.05$). There was a significant association between expression levels of miR-27 with FOXO-1 in patients with EC.

Conclusion: Our findings suggest that FOXO-1, miR-27 the potential to serve as tissue biomarkers for early diagnosis, prognosis, and progression of EC in the human reproductive system.

Keywords: FOXO-1, ENDOMETRIAL CANCER, HYPERPLASIA, REPRODUCTIVE SYSTEM

Abstract: A-10-2778-1

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Antioxidant and anticancer effects of Astragalus baba-alliar methanolic extract against breast and prostate cancer cells through apoptosis induction

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Background: This study aims to examine the anticancer and antioxidant effects of Astragalus baba-alliar methanolic extract (ABME) on breast (MCF-7) and prostate (LNCaP) cancer cell lines.
Methods: Phytochemical analysis of the ABME was conducted to identify the secondary compounds present in the baba-alliar methanolic extract. An MTT test was performed to assess the effects of ABME on the viability of MCF-7 and LNCaP cell lines. The impact of ABME on DNA synthesis, gene expression, and the protein levels of apoptotic genes was evaluated using Real-time PCR and western blot analysis. The antioxidant capacity of ABME was determined by measuring its free radical scavenging ability through the DPPH assay.
Results: The phytochemical analysis revealed the presence of flavonoids, phenols, saponins, terpenoids, and polysaccharides in ABME. The CC50 values measured for ABME were 242.3 and 285.4 µg/mL for MCF-7 and LNCaP cells, respectively, while the CC50 value for normal THLE-3 cells was 612.7 µg/mL. Treatment of the cell lines with ABME resulted in a dose-dependent decrease in DNA production. Real-time PCR and western blot analyses showed that the gene and protein expression levels of Bax and caspase-3 were significantly increased following treatment of MCF-7 and LNCaP cells, whereas exposure to ABME led to a notable reduction in the expression levels of the gene and protein of Bcl-2.
Conclusion: The findings of this study revealed the potential anticancer and antioxidant effects of ABME. These effects may be attributed to alterations in DNA synthesis and the induction of apoptosis. However, further research is necessary to evaluate the precise mechanisms and efficacy of ABME in animal models.

Keywords: prostate cancer, breast cancer, apoptosis, DNA, western blot

Abstract: A-10-2887-1

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Serum levels of C1q/TNF-related protein (CTRP) 1 and CTRP-3 are associated with the presence and severity of coronary artery disease

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Background: Recent research indicates that the disruption of adipokines is associated with the development of obesity-related illnesses such as coronary artery disease (CAD). In this study, we examined whether the plasma levels of two adipokines, C1q/TNF-related protein (CTRP) 1 and CTRP-3, are linked to the occurrence and severity of CAD.
Methods: This study included a total of 88 patients who underwent coronary angiography. Among them, there were 39 patients without coronary artery disease (CAD), 31 patients with stable CAD, and 18 patients with unstable CAD. The levels of CTRP-1 and CTRP-3, fasting blood glucose, lipid parameters, hs-CRP, and hematological indices were measured.
Results: The levels of CTRP-1 were significantly elevated in both the unstable (6.28 ± 2.64 ng/ml) and stable (6.12 ± 2.22 ng/ml) groups compared to the control group (4.20 ± 2.08 ng/ml). However, there was no significant difference in CTRP-1 levels between patients with stable and unstable CAD. The levels of CTRP-3 in the serum were markedly higher in both the unstable (18.00 ± 7.68 ng/ml) and stable (14.90 ± 4.73 ng/ml) groups compared to the control group (10.80 ± 2.40 ng/ml). In all participants of the study, there was a positive correlation between serum CTRP-1 levels and the coronary artery score ($r = 0.443$, $p < 0.001$). Furthermore, a notable and favorable correlation was observed between CTRP-3 and the coronary artery score in all participants of the study ($r = 0.330$, $p = 0.002$). Correlation analysis using multiple regression revealed that both CTRP-1 and CTRP-3 were independently associated with the coronary artery score.
Conclusion: Elevated levels of serum CTRP-1 and CTRP-3 were strongly associated with both the occurrence and severity of coronary artery disease (CAD), suggesting that they could serve as reliable indicators for CAD.

Keywords: Coronary artery disease, Adipokines, CTRP1 protein, CTRP1 protein.

Abstract: A-10-2887-2

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Comparison of serum levels of inflammatory factors and vitamin B9, B12 and D levels in patients with Obsessive-Compulsive disorder (OCD) and without OCD

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Background: The main mechanisms involved in Obsessive-Compulsive Disorder (OCD) are still unclear. However, immune system disorders are one of the proposed mechanisms in the pathophysiology of OCD. Considering the potential role of vitamins in regulating levels of inflammatory markers, this study examined the levels of IL-1, TNF-α, hs-CRP, and vitamins B9, B12, and D in patients with OCD and healthy individuals.

Methods: The research included 40 individuals diagnosed with and an equal number of healthy volunteers serving as control subjects. The concentrations of IL-1, TNF-α, vitamin B9, vitamin B12, and vitamin D in the blood were measured using Enzyme-Linked Immunosorbent Assay (ELISA). The lipid profile, hematological indices, and hs-CRP were evaluated using standard procedures.

Results: The concentration of IL-1ß in the blood of individuals with OCD was significantly higher compared to the control group. Furthermore, the serum levels of TNF-α and hs-CRP were higher in OCD patients than controls. The examination of serum levels of vitamins D, B12, and folate using the ELISA method revealed that the level of vitamin D in serum samples of individuals with OCD was significantly lower compared to those without the disorder. This was while the level of vitamin B12 among individuals with OCD did not statistically differ from those without obsessions. Similarly, no difference was observed in serum vitamin B9 levels between cases and controls. Vitamin D showed a significant negative correlation with both IL-1ß and TNF-α values.

Conclusion: Based on the obtained data, it seems that inflammatory cytokines and the indicated vitamins may play a significant part in the development of OCD. Additionally, the analysis of these markers might potentially be utilized as indicators to anticipate the occurrence of OCD. Nevertheless, more research is advised to get more definitive findings.

Keywords: Obsessive-Compulsive Disorder, Inflammatory cytokines, Inflammation Mediators, Vitamin D, Vitamin B12, Vitamin B9

Abstract: A-10-2887-3

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Evaluation of membrane fatty acid profiles in erythrocytes of patients with major depressive disorder and comparison with normal individuals

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Background: The lack of omega-3 fatty acids in one's diet has been associated with the emergence of several neuropsychiatric conditions, such as major depressive disorder (MDD). Erythrocyte fatty acids are more reliable indicators of fat consumption than serum lipids, primarily because they have a slower turnover rate. Nevertheless, the fatty acid content of erythrocyte membranes in Iranian individuals with MDD has not yet been examined. Objectives: This study aimed to examine the fatty acid composition of erythrocyte membranes in individuals diagnosed with MDD. Moreover, a study was carried out to investigate the relationship between the ratio of fatty acids in the membrane and the severity of the disease.

Methods: The research included 38 persons who were diagnosed with MDD based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-V-TR). Additionally, 35 mentally healthy volunteers served as the control group. Analyzed utilizing reverse-phase high-performance liquid chromatography (HPLC), the fatty acid composition of the red blood cell membrane was determined as a percentage.

Results: The research showed a notable increase in the amounts of arachidonic acid (AA) in the cell membranes of red blood cells in patients, as compared to the control group. In contrast, the concentration of eicosapentaenoic acid (EPA) in the membrane of red blood cells was significantly greater in the normal group than in the group of patients. In people with severe depressive illness, the ratio of AA to EPA (AA/EPA) in red blood cells was considerably higher compared to the control group.

Conclusion: This study showed that the erythrocyte membrane fatty acid composition in MDD patients differs from that of healthy controls, which might be a part of the pathogenic mechanism of MDD and could be considered a possible risk factor for the disease.

Keywords: Keywords: Major depression disorder, erythrocyte membrane fatty acids, polyunsaturated fatty acids, omega-3 fatty acids

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Abstract: A-10-2543-1

Reduced Mitochondrial Translocator Protein and Voltage-Dependent Anion Channel-1 in Granulosa Cells Are Associated with the Lower Estradiol Levels and Presence of Immature Follicles in Polycystic Ovary Syndrome

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Background: Granulosa cells (GCs) play key roles in oocyte maturation by providing required steroid hormones. Since the presence of immature oocytes has been reported in polycystic ovary syndrome (PCOS), this study determined levels of mitochondrial membrane cholesterol transporter proteins involved in estradiol (E2) synthesis and measured E2 concentration and parameters of oxidative status in follicular fluids of PCOS women.
Methods: Forty-three women with PCOS and 43 control women were enrolled in this case-control study. GCs and follicular fluids were collected from all participants. The gene expression and protein levels of mitochondrial translocator protein (TSPO) and voltage-dependent anion channel 1 (VDAC1) were determined in GCs. Total cholesterol, E2 level, total antioxidant capacity (TAC), total oxidant status (TOS), oxidative stress index (OSI), and malondialdehyde (MDA) were determined in follicular fluids.
Results: VDAC1 and TSPO were significantly lower both at mRNA and protein levels in PCOS patients. Cholesterol, estradiol and TAC levels were lower in PCOS whereas higher TOS and MDA contents were observed in PCOS compared with control group. E2 level was in direct correlations with VDAC1 and TSPO expressions and with TAC level but was inversely correlated with TOS, OSI and MDA (all $p<0.001$). Higher E2 levels were found associated with greater number of high-quality oocytes and higher number of conceived embryos.
Conclusion: We showed that lower VDAC1 and TSPO expression and reduced E2 level are involved in the pathogenesis of PCOS. Thus, increasing of E2 level and reducing oxidative stress in follicular fluid may be envisioned as therapeutic strategies in PCOS women.

Keywords: Estradiol, Granulosa Cells, Oxidative Stress, Polycystic Ovary Syndrome, TSPO protein human, Voltage-Dependent Anion Channel 1

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Abstract: A-10-2543-2

Granulosa Cells Isolated from Immature Follicles Are Associated with Restricted Glycolysis and Reduced Energy Production: A Dominant Problem in Polycystic Ovary Syndrome

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Background: We hypothesized that immature oocytes are associated with impaired energy production in surrounding granulosa cells (GCs) in polycystic ovary syndrome. Thus, this study investigated mitochondrial function, determined expression of glycolytic regulatory enzymes, and measured ATP level in GCs of PCOS patients.
Methods: GCs were isolated from forty-five PCOS patients and 45 control women. Intracellular concentration of reactive oxygen species (ROS), mitochondrial membrane potential (Dym), the rate of glycolysis, total antioxidant capacity (TAC), activities of catalase (CAT) and superoxide dismutase (SOD), and ATP level were measured in GCs. The gene expression and protein levels of glycolytic enzymes (hexokinase, muscular phosphofructokinase, platelet derived phosphofructokinase, and muscular pyruvate kinase) were determined. Association of GCs energy level with oocyte maturation was further validated by measuring glycolysis rate and ATP level in GCs isolated from mature and immature follicles from new set of fifteen PCOS patients and 15 controls.
Results: PCOS patients showed higher ROS level, declined TAC, reduced CAT and SOD activities, and lower Dym together with reduced expression of key glycolytic enzymes. ATP concentration and fertilization rate were lower in PCOS compared with control group. ATP level was significantly correlated with ROS and Dym (r=–0.624 and r=0.487, respectively). GCs isolated from immature follicles had significantly lower ATP level and rate of glycolysis compared with the GCs separated from mature follicles in both PCOS patients and control.
Conclusion: Declined energy due to the mitochondrial dysfunction and restrained glycolysis in GCs is associated with the immature oocytes and lower fertilization rate in PCOS.

Keywords: Granulosa cells, Glycolysis, In vitro fertilization, Polycystic ovary syndrome, Reactive oxygen species

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Ndufs8: Specific Potential Gene Based on TCGA Datasets in Acute Myeloid Leukemia and Bioinformatics Analysis of Its Cerna Network

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Background: Acute myeloid leukemia (AML) is a heterogeneous hematological malignancy characterized by diverse genetic alterations. This study aimed to investigate crucial miRNAs, transcription factors (TFs), and circular RNAs (circRNAs) associated with hub genes involved in AML survival, focusing on identifying potential biomarkers for diagnosis and treatment.

Methods: The TCGA LAML dataset from GEPIA2 was utilized to identify differentially expressed genes (DEGs) associated with AML through high-throughput RNA sequencing data. A protein-protein interaction (PPI) network of significant genes was constructed using STRING and analyzed in Cytoscape. Hub genes with higher connectivity were selected, and pan-cancer analysis using GEPIA2 and UALCAN revealed NDUFS8 as a key gene. The hTFtarget database was employed to identify transcription factors associated with NDUFS8, relevant to blood and bone marrow. Additionally, miRNAs regulating NDUFS8 were identified using miRTarBase, TargetScan, miRDB, and miRWalk, while circRNAs were sourced from the circBank database. A competing endogenous RNA (ceRNA) network encompassing selected genes, their TFs, miRNAs, and circRNAs was established in Cytoscape, with hub nodes identified for further analysis.

Results: From the 7,965 genes obtained from the TCGA RNA-seq data, 843 genes were considered significant. Eight hub genes were identified, with pan-cancer analysis showing that NDUFS8 was significantly downregulated compared to normal samples and other cancers. A total of 93 transcription factors associated with blood and bone marrow were identified, along with 25 miRNAs from three databases (16 from TargetScan, eight from miRWalk, and one from miRTarBase), and seven circRNAs (including hsa_circ_0023138, hsa_circ_0023139, hsa_circ_0096261, hsa_circ_0023140, hsa_circ_0023141, hsa_circ_0023142, and hsa_circ_0023143). The ceRNA network was designed, and hub nodes were identified.

Conclusion: This study highlights NDUFS8 as a differentially expressed gene in AML, demonstrating a significant negative impact on overall survival. The diagnostic potential of NDUFS8 and its involvement in the ceRNA network suggest that it may serve as a reliable biomarker for diagnosing AML and monitoring treatment responses. Furthermore, NDUFS8 represents a promising target for future AML therapies.

Keywords: Acute myeloid leukemia, TCGA, bioinformatics, miRNA, circRNA, transcription factors

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Combination of Calebin A and Cisplatin as a Promising Therapeutic Strategy for Triple-Negative Breast Cancer through NF-κB Pathway Inhibition

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Background: Triple-negative breast cancer (TNBC) is an aggressive subtype characterized by the absence of estrogen receptors, progesterone receptors, and HER2. This lack of targeted therapies results in poor prognosis and limited treatment options. Conventional chemotherapy can be effective but often leads to severe side effects and resistance. Natural compounds like Calebin A, derived from turmeric, have shown promise in enhancing existing treatments while minimizing toxicity. Notably, the NF-κB signaling pathway is frequently activated in TNBC, promoting tumor progression and metastasis. Inhibiting this pathway may provide a novel therapeutic approach.
Method: This study explored the synergistic anti-cancer effects of Calebin A and cisplatin in TNBC MDA-MB-231 cells. Cell viability assays assessed the combined effects, and a combination index was calculated for synergy evaluation. Flow cytometry was used to measure apoptosis and necrosis, while real-time PCR analyzed NF-κB expression and its downstream targets, including survivin, MYC, VEGF, and MMP9/2. Wound healing assays evaluated the impact on cell migration.
Result: The combination treatment significantly induced apoptosis, inhibited cell proliferation, and suppressed migration compared to single agents. Mechanistic studies indicated that the combination effectively reduced NF-κB activation and downregulated its downstream targets. This suggests that Calebin A and cisplatin together may offer a promising strategy for TNBC by specifically targeting the NF-κB pathway.
Conclusion: Our findings underscore the potential of combining natural compounds like Calebin A with conventional chemotherapy to address the challenges of TNBC. By targeting critical pathways involved in cancer progression, this combination could enhance therapeutic efficacy. Further clinical investigations are needed to validate these results and explore the full potential of this strategy in patient care.

Keywords: Triple-negative breast cancer, Calebin A, Cisplatin, NF-κB, Apoptosis