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Original Article

Beta Boswellic Acid Reduces Tau Phosphorylation Level and Enhances Reelin Expression in the brain

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ABSTRACT

Objectives: Learning and memory retention involve a permanent change in behavior based on environmental adaptation. Reelin protein plays a role in learning and memory but has not been extensively studied in the presence of herbal components. This study examines the effect of an optimum dose of beta-boswellic acid (BBA) on reducing tau phosphorylation levels and enhancing Reelin expression in the hippocampus to improve cognitive behavioral outcomes..

Methods: Spatial memory, learning, and locomotor activity were assessed. Histological and Western blot analyses were performed.

Results: The findings demonstrate a significant effect of BBA (35 µg/kg body weight) on memory consolidation during the probe trial of the Morris Water Maze (MWM) test. BBA treatment reduced the formation of dark neurons in the hippocampus and promoted Reelin expression.

Conclusion: A specific dose of BBA enhanced memory consolidation in adult rats, with increased Reelin protein expression—likely due to BBA's anti-inflammatory properties, a key factor contributing to improved memory performance.

Keywords: Boswellic Acid, Histological Analysis, Reellin, Memory Consolidation, Learning

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Introduction

Fundamental brain functions, including learning and memory retention, rely on neuronal synaptic activity and the formation of neuronal connections (1). Additionally, the neocortex and hippocampus play key roles in regulating these processes (2). Various medicinal plants, such as *Boswellia* species, have been studied for their effects on spatial learning and memory (3, 4). Traditionally, *Boswellia serrata* dry resin extract has been used to treat inflammatory diseases and memory disorders (5).

Beta-boswellic acid (BBA) primarily targets 5-lipoxygenase (5-LOX), which helps reduce the concentration of various pro-inflammatory cytokines, including leukotriene B_4 (LTB_4) (6). This compound has been reported to inhibit human leukocyte elastase and topoisomerases I and IIα. Additionally, it can reduce PGE_2 formation, leading to decreased inflammation. Furthermore, it has been shown to mitigate oxidative stress, inflammation, complement activation, and cell death in brain endothelial cells exposed to oxygen–glucose deprivation followed by reperfusion (4, 7). BBA also plays a crucial role in brain development by facilitating the proper formation of neuronal compartments such as dendritic trees and axons (8). It effectively promotes hippocampal neurite outgrowth and enhances microtubule polymerization (8). The anti-inflammatory properties of various Boswellia species are widely recognized (9, 10). A previous study demonstrated that an aqueous extract of Boswellia enhances spatial memory, partly through the upregulation of BDNF (11). Its neurotrophic effects are mediated via crosstalk with the Wnt/β-catenin signaling pathway, with GSK-3β serving as the primary factor facilitating this interaction (11). Mahboubi et al. investigated the combined administration of Melissa officinalis and B. serrata extracts in an animal memory model. Their findings revealed a significant statistical difference in both time spent and distance traveled between the group receiving the combined extracts and the scopolamine-treated group, suggesting that the combination may enhance memory, in alignment with traditional medicinal use (12).

Reelin, produced by GABAergic interneurons in the adult brain, plays a crucial role in embryonic neuronal migration. This secreted glycoprotein is closely associated with axons, dendritic spines, and postsynaptic density within the cortex and hippocampus, making it essential for synaptic plasticity in the mature brain (13). Reelin activates numerous neuronal signal transduction pathways, which may play a role in modulating synaptic plasticity (23). Furthermore, Reelin helps regulate neuronal positioning during learning and memory. It activates multiple neuronal signal transduction pathways in the mature Central Nervous System (CNS), ultimately influencing synaptic function and plasticity (14). A previous study showed that Reelin levels increased in rats treated with beta boswellic acid (25). In the present study, we aim to study the role of Reelin expression in hippocampal neuronal cells in the presence of boswellic acid. Therefore, this study evaluates the effect of an optimal dose of boswellic acid on Reelin expression and memory consolidation.

Materials and Methods

Reagents

Beta-Boswellic Acid (BBA) was purchased from Sigma Chemical Co. (St. Louis, USA) and dissolved in 0.05% dimethyl sulfoxide (DMSO). Additionally, the monoclonal rabbit anti-β-actin antibody (ab8229, Abcam, 1:1000 v/v), anti-Reelin antibody (ab139691, Abcam, 1:1000 v/v), and secondary HRP-conjugated antibody (ab6721, Abcam, 1:1000 v/v) were obtained from Abcam Biotechnology Inc. (USA). The chemiluminescent Western blotting detection kit and polyvinylidene difluoride (PVDF) membrane were provided by Amersham Biosciences (Freiburg, Germany). Protease inhibitor cocktail (P8340) and phosphatase inhibitor cocktail 3 (P0044) were acquired from Sigma-Aldrich. All animal experiments were conducted in accordance with the National Institutes of Health's Guide for the Care and Use of Laboratory Animals (NIH Publication No. 80-23, revised 1996). The study was approved by the Ethics Committee of the University of Tehran (ID number: IR.UT.SCIENCE.REC.1400.005).

Animals

A total of 40 male Wistar rats (250–300 g) were obtained from the Pasteur Institute of Iran and housed in groups of five per Plexiglas plastic cage under standard laboratory conditions (temperature: 22 ± 2˚C; humidity: 60–65%). They had unrestricted access to food and water and were maintained on a 12-hour light/dark cycle (lights on at 7:00 a.m.), with testing conducted during the light phase (15). Each animal was used only once, with 10 rats assigned to each experimental group.

Experimental design

Experimental design After one week of adaptation to colony room conditions, 40 rats were randomly assigned to four groups (n = 10). The first group, the sham group, underwent surgery in each ventricle region without treatment. In contrast, the experimental groups received bilateral intracerebroventricular (i.c.v.) infusion of BBA at doses of 25, 35, and 45 µg/kg body weight over four trial days. The injection procedure involved filling a 2-µL syringe and loading the pumps by inserting the needle into the top hole, followed by slow emptying. The subjects were anesthetized via intraperitoneal (i.p.) administration of a ketamine and xylazine mixture (80 and 100 mg/kg BW, respectively).

Stereotaxic coordinates for bilateral i.c.v. injections were set at 0.9 mm posterior to the bregma, 1.5 mm lateral to the mid-sagittal line, and 3.6 mm beneath the cortical surface in the brain (16). Additionally, 2 µL/300 g BW (1 µL/ventricle) was injected using a 30-gauge needle connected to a Hamilton syringe via a polyethylene catheter. Following injection, the needle was kept in place for 2 minutes before being slowly withdrawn.

Behavioral tests

Spatial learning and memory capacity in each group were assessed using the Morris Water Maze (MWM). The tests were conducted between 9.00 am and12 pm.

MWM

Ten minutes after the injections, the rats underwent four training trials per day to locate the hidden platform, each trial lasting 60 seconds, over four consecutive days. Initially, each rat was placed near the pool's border at a designated starting location, facing the wall, and allowed to swim until it found the platform. If a rat failed to locate the hidden platform within the 60-second limit, it was manually guided to the platform, where it remained for 30 seconds before the next trial began. For each animal, three parameters were evaluated: escape latency (time taken to find the platform, in seconds), distance swam (total distance traveled before reaching the platform, in centimeters), and swimming speed (velocity in cm/s).

A single probe trial was conducted in the pool without the platform, during which the time spent in the target quadrant was recorded over 60 seconds. Specifically, the time and frequency spent in quadrant Q3, where the platform had been located during the training phase, were measured. These parameters served as an index of memory consolidation. On the same day that memory consolidation was assessed, a visible test was performed to evaluate visual deficiencies and motivation for finding the platform. Additionally, a computer-based video-tracking system (Ethovision 1.6, Noldus, Wageningen) was used to record all behavioral functions of the animals (17).

Histological analysis

At the conclusion of the behavioral study, five rats were individually placed in a desiccator containing cotton and deeply anesthetized with ether before being perfused with 4% paraformaldehyde (PFA) (v/v). The entire brain was then carefully extracted and preserved in 4% PFA (w/v) overnight. Following fixation, the brain tissue was embedded in paraffin and sectioned into 5-µm slices using a microtome. For each rat, three sections were histologically analyzed. All histological samples were examined using ImageJ software.

Neuron counting

Nissl staining was used to quantify the percentage of pyramidal cell layers in the CA1 and CA3 regions, as well as granule cell layers in the dentate gyrus (DG) area of the dorsal hippocampus. All samples were examined under a Nikon microscope (Nikon H600L, Japan) at 400× magnification.

Cell volume

The paraffin sections were stained with toluidine blue stain and examined under a Nikon microscope at 400× magnification.

Western blot analysis

Each of the four groups (control and varying doses of BBA, n = 5) were sacrificed under CO_2 anesthesia, and one hippocampal tissue sample was collected from each. The samples were homogenized in three volumes of lysis buffer (pH 8) containing 1 mmol/L EDTA, 150 mmol/L NaCl, 1% Triton X-100 (v/v), 50 mmol/L Tris-HCl, 0.1% SDS (v/v), and protease and phosphatase inhibitor cocktails (1:100 v/v). Protein concentration was determined using the Bradford protein assay. The obtained results were based on three independent experiments. Hippocampal lysates were loaded onto a 12% SDS-PAGE and transferred onto a PVDF membrane. The membrane was blocked with 5% BSA (w/v) in TBS at room temperature for 4 hours, followed by overnight incubation at 4°C with primary antibodies (anti-β-actin and anti-Reelin, 1:1000 v/v). After washing, the membranes were incubated with an HRP-conjugated secondary antibody (1:1000 v/v) for 1 hour at room temperature. Chemiluminescent detection was performed using an enhanced chemiluminescence (ECL) system, with β-actin normalization in ImageJ software.

Statistical analysis

Group interactions were evaluated using repeated measurements to determine whether different injection doses significantly affected spatial learning or escape latency over four consecutive days. Additionally, one-way ANOVA was used to analyze cell counts, behavioral criteria, learning, probe trials, and histological data. The effects of dose, time, and dose × time interactions were assessed using two-way ANOVA. Tukey's post-hoc test was performed to compare differences between treated and control groups. Statistical significance was evaluated using GraphPad Prism 7 and SPSS 19 software, with a significance threshold set at $P < 0.05$. All error bars in figures represent mean ± standard deviation (SD). Each experiment was conducted in triplicate.

Results

BBA improves spatial memory

Acquisition test

Different doses of BBA or control were administered to four rat groups to evaluate spatial memory using the Morris Water Maze (MWM) over four trial days. The results showed a 45% and 57% increase in the

distances traveled by rats receiving 25 and 45 µg/kg body weight (BW) of BBA, respectively, compared to the control group (P = 0.000) (Fig. 1A). Additionally, their escape latency increased significantly by 20% and 23%, respectively, compared to the control (P = 0.025) (Fig. 1B). However, there was no significant difference between the BBA-treated and control groups in terms of swimming speed (P = 0.121) (Fig. 1C). These findings suggest that BBA at doses of 25 and 45 µg/kg BW enhanced memory retention, whereas the 35 µg/kg BW dose did not show a significant effect at this stage.

The treatment with BBA and the control group reduced traveled distance and escape latency over four consecutive days of training trials. Based on the traveled distance results for rats administered BBA at 25 µg/kg BW, the smallest effect on spatial memory was observed on the third and fourth days of the training test (P = 0.016). However, a significant difference was detected with BBA at a 45 µg/kg BW dose on day 3 (P = 0.013) (Fig. 2A). Additionally, the effects on escape latency in animals receiving BBA at 45 µg/kg BW were significantly different from the control group (P = 0.021) (Fig. 2B). The results showed no significant difference in swimming speed over the four consecutive days (Fig. 2C). All rats reached the threshold criteria after four days, and traveled distance and escape latency differed significantly between the first and fourth days. Throughout the four days, learning capacity declined following BBA injection at doses of 25 and 45 µg/kg BW.

Probe test

The degree of memory consolidation was evaluated using a probe test conducted one day after the acquisition test. The probe trial results were analyzed based on two parameters: time spent (%) and crossing numbers (sec) in the target quadrant. The first parameter showed a significant decline (40.4%) in the group exposed

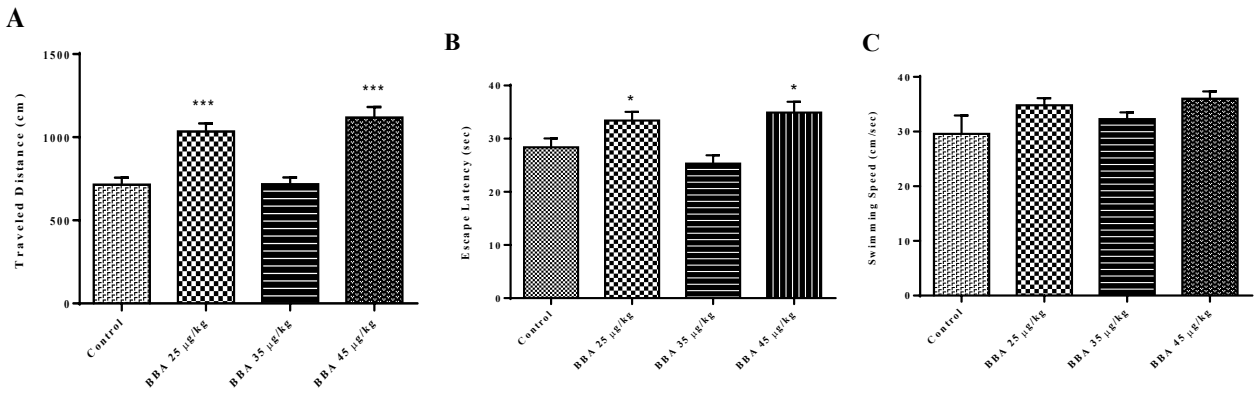

Figure 1. Effects of different doses of BBA treatment on training parameters using the Morris Water Maze (MWM) test. These parameters included: (A) traveled distance (cm), (B) escape latency (sec), and (c) swimming speed (cm/sec). All error bars in the figures represent mean ± SD. Statistical significance was determined as follows based on one-way ANOVA (n = 10 rat/group): ***P < 0.001 indicates a significant difference between treated groups (BBA 25 µg/kg and 45 µg/kg of body weight) and the control group, while *P < 0.05 indicates a significant difference between treated groups (BBA 25 µg/kg and 45 µg/kg of body weight) and the control group. Each group consisted of n = 10 rats.

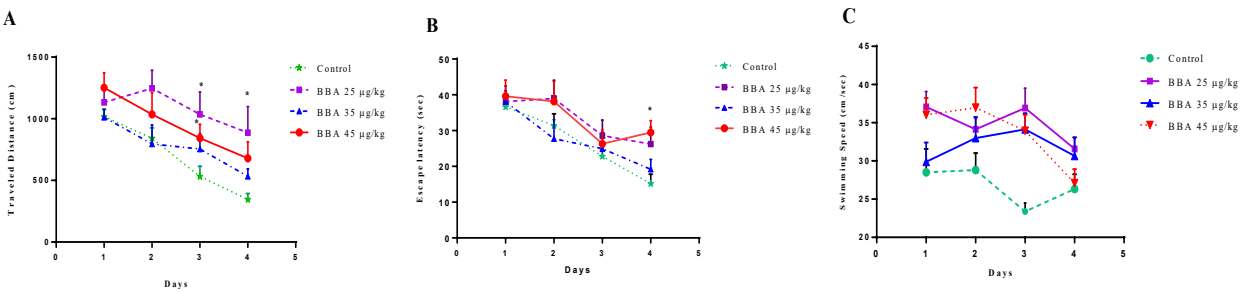

Figure 2. Trials were conducted over four consecutive days to assess the effects of BBA treatment using the Morris Water Maze (MWM) test. The parameters measured included: (A) mean traveled distance (cm), (B) escape latency (sec), and (C) swimming speed (cm/sec) in control and BBA-treated rats. Values are presented as mean ± SD. Statistical significance was determined as follows based on two-way ANOVA (n = 10 rat/group): (a) *P < 0.05 indicates a significant difference between Day 3 (BBA 25 µg/kg and BBA 45 µg/kg of body weight) and the control group, as well as Day 4 (BBA 25 µg/kg of body weight) and the control group; (B) a significant difference was observed between Day 4 of BBA 45 µg/kg of body weight and the control group. Data points are represented by different symbols: closed star (control), closed square (BBA 25 µg/kg), closed diamond (BBA 35 µg/kg), and closed circle (BBA 45 µg/kg).

to BBA at 25 µg/kg BW compared to the control (P = 0.045). In contrast, rats receiving BBA at 35 µg/kg BW (P = 0.038) exhibited significantly greater memory consolidation (48.6%) than the control. Furthermore, a significant difference was observed between the groups treated with BBA at 25 and 35 µg/kg BW (P = 0.000), as well as between those injected with BBA at 35 and 45 µg/kg BW (P = 0.006) (Fig. 3A). Regarding crossing numbers in the target zone, the rats receiving BBA at 35 µg/kg BW demonstrated a significant difference (54%) compared to the control (P = 0.016). Additionally, significant differences were detected between the groups administered BBA at 25 and 35 µg/kg BW (P = 0.003), as well as between those given BBA at 35 and 45 µg/kg BW (P = 0.031) (Fig. 3B). These findings suggest that a BBA dose of 35 µg/kg BW is an effective concentration for memory retention.

Histological observations

Presence of dark neurons at BBA injected rats

The CA1, CA3, and DG regions of the dorsal hippocampus were stained using Nissl reagent and dark neuron (DN) markers. Additionally, the ratio of dark neurons to their total unstained counterparts was determined. Compared to the control group, a significantly lower percentage of dark neurons was observed in the CA1 and CA3 regions of rats administered BBA at 35 µg/kg BW (53% and 48%, respectively) (P = 0.048; P = 0.033). In contrast, treatment with BBA at doses of 25 and 45 µg/kg BW did not lead to significant changes in neuronal appearance within the CA1, CA3, and DG regions (P = 0.252; P = 0.688; P = 0.159, respectively) (Fig. 4A). The Nissl reagent was used to stain neuronal cells in hippocampal subregions (Fig. 4B). These findings suggest that BBA at a dose of 35 µg/kg BW has the potential to reduce the number of dark neurons in various hippocampal regions.

Changes in the cell volume of the BBA-administrated rats

Toluidine blue staining was used to assess the mean neuronal volume in the CA1 and CA3 regions of the hippocampus in both the BBA-treated and control groups. No significant difference in neuronal volume was observed between the control group and the group receiving BBA at 35 mg/kg body weight (BW) (P = 0.256). However, administration of BBA at 45 mg/kg BW led to an increase in neuronal volume by 12% in CA1 and 26% in CA3, respectively (P = 0.011; P = 0.029) (Figs. 5A & B). These results indicate that BBA at 35 mg/kg BW did not alter hippocampal neuronal volume.

Western blot analysis of different doses of BBA

The modification of Reelin protein levels was assessed using Western blot analysis. The analysis identified two molecular weights of Reelin protein (410 and 180 kDa), and results showed significantly higher expression in rats exposed to a 35 µg/kg BW dose of BBA by 30% and 26%, respectively, compared to the control group (P = 0.014; P = 0.26) (Figs. 6A & B). These findings confirm that BBA at 35 µg/kg BW significantly enhances Reelin protein expression.

Discussion

This study aimed to investigate the optimal dose of an herbal agent for enhancing spatial learning and memory. Our objective was to provide nonclinical evidence for establishing a quantitative dose-dependent relationship between BBA concentration in hippocampal regions and neurological performance. Previous studies administered various doses of BBA via subcutaneous

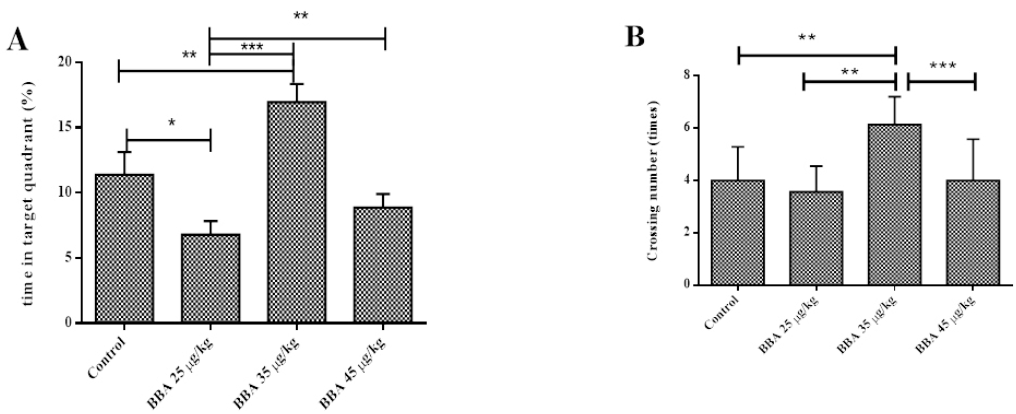

Figure 3. Effects of different doses of BBA treatment in the target quadrant (probe test) using the Morris Water Maze (MWM) test. (A) Time spent in the target quadrant (%) and (B) the number of crossings in the target quadrant. Data are presented as mean ± SD. Statistical significance was determined as follows based on one-way ANOVA (n = 10 rat/group): (a) **P < 0.01 indicates a significant difference between BBA 35 µg/kg of body weight and the control group, as well as between BBA 25 µg/kg and BBA 45 µg/kg groups. ***P < 0.001 indicates a significant difference between BBA 25 µg/kg and BBA 35 µg/kg groups. (b) **P < 0.01 indicates a significant difference between BBA 35 µg/kg and the control group, as well as between BBA 35 µg/kg and BBA 25 µg/kg groups. ***P < 0.001 indicates a significant difference between BBA 35 µg/kg and BBA 45 µg/kg groups.

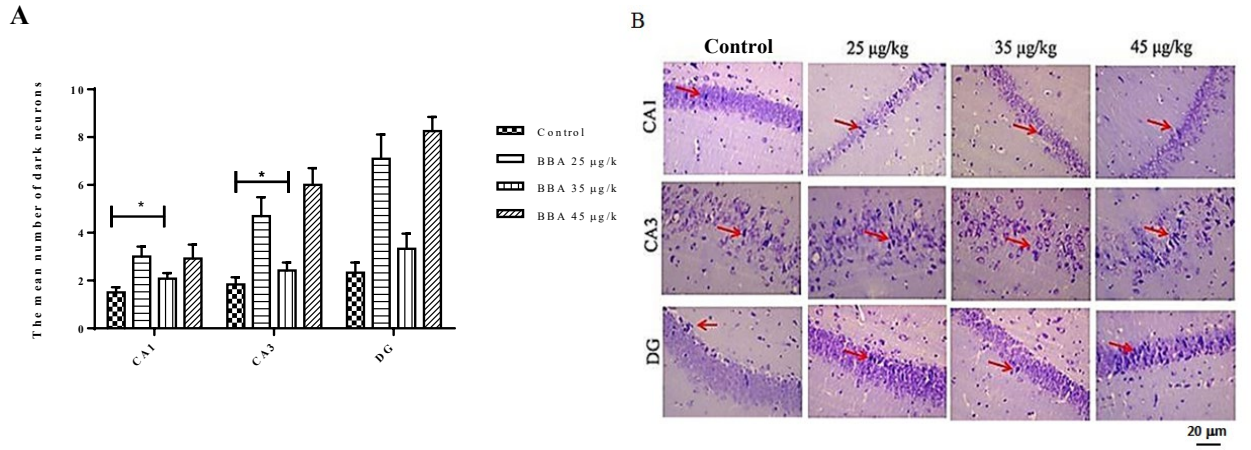

Figure 4. Neuronal counts and characteristic patterns of brain tissue in the CA1, CA3, and DG regions of the hippocampus using Nissl reagent and dark neuron (DN) markers. (A) The percentage of Nissl-stained dark neurons relative to the total neuron count in the CA1, CA3, and DG regions. (B) Photomicrographs showing the effects of different doses of BBA treatment compared to the control group in the CA1, CA3, and DG regions of the hippocampus. Images were captured at a magnification of ×400. Values are presented as mean ± SD. Statistical significance based on one-way ANOVA (n = 5 rat/group): (A) *P < 0.05 indicates a significant difference between BBA 35 µg/kg (CA1 and CA3) and the control group. Scale bar: 20 µm.

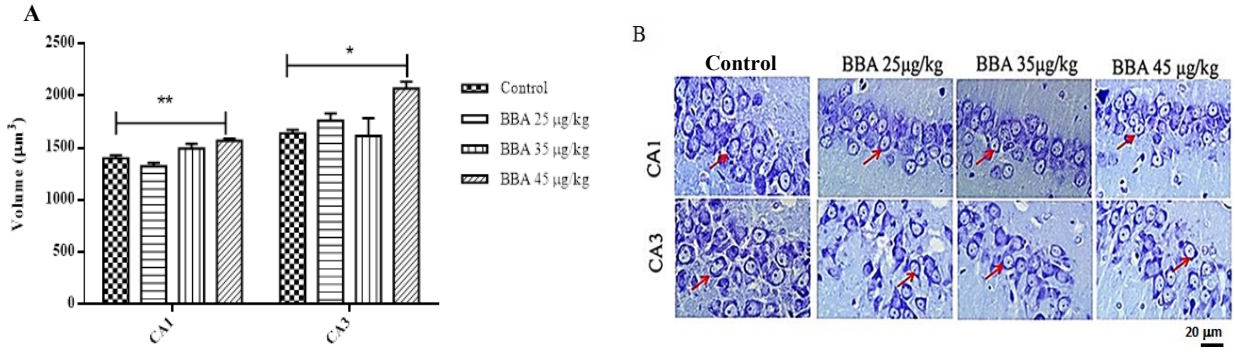

Figure 5. Effects of BBA on neurons in the CA1 and CA3 regions of rat hippocampal slices using toluidine blue staining. (A) Neuronal cell volume. (B) Photomicrographs showing different doses of BBA treatment compared to the control group in the CA1 and CA3 regions of the hippocampus. Images were captured at a magnification of ×400. Values are presented as mean ± SD. Statistical significance based on one-way ANOVA (n = 5 rat/group): (A) *P < 0.05 indicates a significant difference between BBA 45 µg/kg and the control group in both the CA1 and CA3 regions. Scale bar: 20 µm.

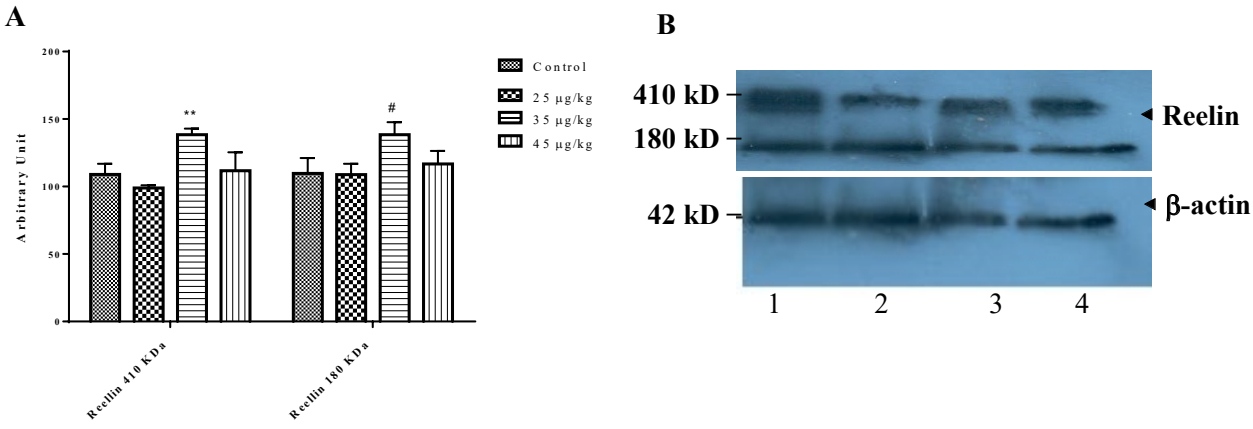

Figure 6. Gel mobility analysis of Reelin protein expression at 410 kDa and 180 kDa using western blot. (A) Reelin protein expression in the hippocampus of rats treated with BBA. (B) Photomicrographs showing different doses of BBA treatment compared to the control group across all hippocampal regions. Groups are labeled as follows: (1) control, (2) BBA 25 µg/kg, (3) BBA 35 µg/kg, and (4) BBA 45 µg/kg of body weight. Statistical significance based on one-way ANOVA (n = 5 rat/group): **P < 0.05 indicates a significant difference between BBA 35 µg/kg and the control group for Reelin at 410 kDa; #P < 0.05 indicates a significant difference between BBA 35 µg/kg and the control group for Reelin at 180 kDa.

and intraperitoneal (i.p.) injections (18, 19), but since BBA undergoes degradation in the liver through these routes, we converted these doses to i.c.v. administration. The final selected concentrations were 25, 35, and 45 µg/kg BW. As a result, the low (25 µg/kg) and high (45 µg/kg) doses of BBA had severely destructive effects, whereas the middle dose (35 µg/kg) nearly normalized neurodegeneration in the brain. Under these conditions, neurobehavioral and neurocognitive parameters, including motor coordination, spatial learning, and memory ability, showed dose-dependent improvements at the optimal dosage. Behavioral, molecular, and pathological findings suggest that BBA at an effective concentration is significantly associated with enhanced learning and memory. In contrast, both higher and lower doses than 35 µg/kg BW led to reduced learning ability and memory retention. All treated animals exhibited greater learning ability and memory, while higher Reelin expression was observed specifically with BBA at 35 µg/kg BW.

According to the literature, *Boswellia serrata* resin influences dendritic density, brain development, and various mental and cognitive functions in rats (20). The medicinal properties of *B. serrata* gum resin extract are primarily attributed to boswellic acids (21), which inhibit 5-lipoxygenase (5-LOX) and the nuclear factor kappa-B (NF-κB) signaling pathway (22). Among the boswellic acid isomers in *B. serrata*, BBA has been shown to promote axonal outgrowth and enhance microtubule polymerization dynamics, although its effects on spatial learning and memory remain uninvestigated (8, 22).

Boswellic acid derivatives, such as 11-keto-β-boswellic acid (23) and 3-acetyl-11-keto-β-boswellic acid (24), may influence brain function and act as bioactive compounds. Previous studies have examined these acids under various experimental conditions. One study investigated the effects of BBA at three concentrations (10, 20, and 30 nM) on hippocampal neurite outgrowth and branching in vitro (8). Other researchers have explored how different doses of BBA affect Reelin expression in human astrocytes (25). To evaluate BBA's direct impact on brain function, i.c.v. injections were employed. Additionally, the effective dose of BBA on the hippocampal regions of adult rats was assessed through behavioral, molecular, and histological analyses. Based on the behavioral analysis in the present study, BBA at 35 mg/kg body weight (BW) did not significantly enhance spatial memory during the training phase but was effective during the recall phase. In contrast, other doses improved spatial memory parameters throughout training. These findings suggest that BBA's efficacy in learning and memory retention is concentration-dependent. The 35 mg/kg BW dose appeared to enhance memory consolidation, possibly through the activation of specific protein kinases involved in the Ca^{2+} signaling pathway (26). Supporting this, previous studies have demonstrated that intracellular Ca^{2+} mobilization can facilitate short-term memory formation (21, 26). Khalaj-Kondori et al. (11) reported that administration of Boswellia aqueous extract significantly reduced escape latency and travel distance in rats, suggesting enhanced spatial memory, a finding consistent with the present study. Similarly, Taghizadeh et al. (27) demonstrated that treatment with tablets containing B. serrata and Melissa officinalis extracts positively affected total memory scores and their subscales (27). Mahboubi et al. (12) also observed memory improvements in an animal model following administration of these herbal supplements. The cognitive-enhancing effects of B. serrata may be attributed to its influence on protein kinase activity, calcium mobilization, and associated signaling pathways (12). In the current study, administration of BBA at all tested concentrations significantly enhanced learning ability and memory retention, without impairing motor function or activity. All BBA-treated rats successfully located the hidden platform during the Morris water maze (MWM) task, indicating preserved intellectual function. Additionally, pro-inflammatory enzymes implicated in modulating learning and memory are present in several herbal compounds, including BBA. BBA is known to inhibit 5-lipoxygenase (5-LO) products such as leukotriene B_4 (LTB_4) and 5-hydroxyeicosatetraenoic acid (5-HETE). Since 5-LO facilitates leukotriene production via calcium displacement, free radical formation, cell adhesion, and recruitment of inflammatory cells to affected tissues, its inhibition may contribute to BBA's neuroprotective and memory-enhancing effects (28).

Histological staining with toluidine blue revealed no significant change in the mean volume of neurons in the hippocampal regions of rats treated with BBA at 35 mg/kg body weight (BW). In contrast, other dosage groups exhibited significant differences compared to the control group. The 35 mg/kg BW dose appears to be the most effective concentration, whereas higher or lower doses may have induced neurotoxic effects, potentially due to osmotic imbalance. In a related study, Hosseini-Sharifabad et al. (29) reported an increase in the size of the pyramidal and radiatum lacunosum-moleculare layers in the CA1 region of the hippocampus in aged rats following eight weeks of daily *B. serrata* gum resin administration.

Western blot analysis further supported the cognitive benefits of the optimal BBA dose (35 mg/kg BW), revealing increased expression of Reelin protein in cerebellar granule cells and pyramidal cells of the entorhinal cortex (25). Previous research has shown that treatment with Reelin enhances expression of the scaffold protein 14-3-3 (30–32). Consistent with this, the current study identified a marked increase in Reelin protein subunits (410 and 180 kDa) in rats administered BBA at 35 mg/kg BW, suggesting upregulation of Reelin in the hippocampus (30).

Conclusion

In summary, the findings revealed that BBA (35 mg/kg BW) is an effective concentration for memory retention. Histological analysis demonstrated the mentioned dose has a potential to reduce the number of dark neurons in various hippocampal regions. It also significantly enhances Reelin protein expression. Therefore, the data suggest a potential mechanism through which it may enhance memory consolidation, possibly mediated by increased Reelin protein expression. The limitations of the current study were the comparison between the effect of other components of *B. serrata* gum resin and the assess their signaling pathways. However, to support the therapeutic application of this herbal compound, further clinical studies are essential.

Conflict of interests

The authors declare no conflict of interest.

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