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Light Microscopic Features of the Prefrontal Cortices of Adult Male Albino Rats Treated with *Balanites aegyptiaca* Fruit Extract Following Monosodium Glutamate-induced Neurotoxicity

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Abstract

Background: Excess monosodium glutamate (MSG) induces excitatory neurotoxicity. Neurological and mental illnesses share this mechanism. *Balanites aegyptiaca* extract has neuroprotective antioxidants. It treats anxiety, mood disorders, and memory loss. Histological evidence for its usage in such situations is scarce. **Methodology**: Twenty three adult male albino rats were divided into five study groups: a normal saline-only group; an MSG-treated group, which received 4 mg/kg/day intraperitoneal injection (i.p.) of MSG and normal saline by oral gavage (p.o.); a low-dose *Balanites aegyptiaca* (B.A) group (MSG i.p. and 125mg/kg/day B.A), a moderate-dose B.A group, and a high-dose B.A group. We extracted, processed, and stained prefrontal cortices using toluidine blue. Photomicrographs were analysed. Behaviour was assessed using the Y-maze. **Results**: Prefrontal cortices showed morphological abnormalities in pyramidal neurones of MSG-treated rats compared to other study groups. The low-dose and moderate-dose B.A groups had disruptions, but the latter improved. The high-dose B.A group had few morphological changes. In the Y-maze behavioural test, study groups had similar alternation rates. **Conclusion**: The administration of monosodium glutamate disrupts the morphology of prefrontal cortical cells. Treatment with *Balanites aegyptiaca* fruit extract improves their morphology. This provides an additional histological basis for its use in traditional medicine as a remedy for cognitive disorders.

Keywords: *Balanites aegyptiaca*, pyramidal neuron, excitotoxicity, neuropsychiatric, monosodium glutamate.

INTRODUCTION

Monosodium glutamate (MSG) is a food additive that enhances flavour and is widely used as a seasoning in many cuisines around the world (3). Excess MSG causes

neurotoxicity through prolonged excitation of neurons, via production of excess glutamate (1,2). In the prefrontal cortex, excess glutamate results in pyramidal neuron death and glial cell proliferation(6,7). This neurotoxicity has been implicated in the development of many neurological and psychiatric disorders (1,2). In this study, we administered MSG to induce neurotoxicity.

Balanites aegyptiaca, commonly called 'desert dates,' extract has been used for managing anxiety, epilepsy, mood disorders, and memory impairment (8–10). These beneficial effects are attributable to its neuroprotective properties, owing to potent antioxidant activity and anticholinesterase properties of its biocomponents (11). Overexcitation of neurons causes oxidative stress, which underlies the progression of neurodegeneration by promoting free radical attack on neurons (12). *Balanites aegyptiaca* confers neuroprotection by scavenging free radicals and enhancing catecholaminergic-cholinergic balance (13).

The human prefrontal cortex has been associated with neuropsychiatric conditions such as anxiety (15). It serves a critical regulatory function in working memory, spatial memory, and long-term memory, and impairments in this region have been associated with mood disorders (16,17). While the neuroprotective effects of *Balanites aegyptiaca* are known, its impact on the light microscopic features of the prefrontal cortex under MSG-induced neurotoxicity has not been reported. This study therefore aimed to assess these microscopic features in adult male albino rats treated with *Balanites aegyptiaca* fruit extract in an MSG-induced neurotoxicity model.

MATERIALS AND METHODS

This quasi-experimental study employed an adult male albino rat model. Rats are widely used in biomedical research due to their anatomical, physiological, and genetic similarities to humans (18). The Ajinomoto brand's monosodium glutamate (99%) powder was bought from the local market in Nairobi, Kenya. *Balanites aegyptiaca* fruits were collected in Juba, South Sudan, and authenticated by botanists at the department of Botany, University of Nairobi. The fruits were sorted, cleaned, dried and ground to a coarse powder. One kilogram of the powder was soaked in 2.5 L of distilled water for 24 hours under refrigeration. The mixture was filtered through sieves of different sizes, and 1 L of the filtrate was freeze-dried. The resulting powder was stored in a freezer and used throughout the intervention period.

Handling and Treatment of Animals

Twenty-three adult male albino rats were used in this study, which was conducted in the Department of Human Anatomy and Medical Physiology between February and May 2024. Ethical approval was obtained from the Biosafety, Animal Use, and Ethics Committee, Faculty of Veterinary Medicine, University of Nairobi (REF: FVM BAUEC/2024/544). The rats were housed in standard, well-labelled cages measuring 109 cm by 69 cm by 77.5 cm and placed under a 12:12-hour light/dark cycle. Prior to the experiment, they were acclimatised in their cages for 14 days. Throughout the study, the animals had ad libitum access to standard food pellets and water.

The rats were divided into five experimental groups: (i) a normal saline-only control group; (ii) an MSG-treated group, which received intraperitoneal injections (i.p.) of MSG at 4 mg/kg/day together with oral

gavage (p.o.) of normal saline; (iii) a low-dose *Balanites aegyptiaca* (B.A.) group (MSG i.p. plus 125 mg/kg/day B.A.); (iv) a moderate-dose B.A. group (MSG i.p. plus 250 mg/kg/day B.A.); and (v) a high-dose B.A. group (MSG i.p. plus 500 mg/kg/day B.A.). Dosages of *Balanites aegyptiaca* fruit extract were established based on traditional healing practices (one glass daily for adults) and following a screening on mice traditions (9).

Monosodium glutamate was administered following the method described by Waggas (20). Monosodium glutamate was given 30 minutes after administering *Balanites aegyptiaca* fruit extract at doses of 125, 250, and 500 mg/kg daily for 35 days. Each day, 4 mg of MSG powder was freshly dissolved in 0.5 mL of normal saline for intraperitoneal injection. Treatments were given for 35 days.

Y-Maze Test

Following the intervention, behavioural assessments were performed using the Y-maze apparatus prior to euthanasia. The apparatus consisted of a chamber with three arms (A, B, and C), arranged at 120° angles from each other. Each rat was introduced into arm A and allowed 5 minutes to explore all three arms. The frequency of arm entries and the number of alternations - defined as consecutive entries into all three arms in sequence (e.g., ABC, CAB, or BCA, but not BAB or ABA) - were recorded during the trial (21). After each test, the maze was thoroughly cleaned with a 70% ethanol solution to eliminate residual odours and prevent olfactory cues from influencing subsequent trials. Memory performance was evaluated by calculating the percentage of correct alternations using the following formula:

$$(\%)Alternation = \frac{Total\ number\ of\ alternation}{Number\ of\ visits-2} \times 100$$

Tissue Harvesting and Processing

The rats were weighed prior to euthanasia, which was performed by placing them in sealed containers with cotton wool soaked in 1% halothane. Death was confirmed by the absence of heartbeat and ocular reflexes. A longitudinal midline incision was then made, the circulatory system was flushed with normal saline using the transcardiac method, and tissue fixation was initiated with 10% formal saline infusion. The rats were decapitated, and the scalp was cleaned to expose the cranium, which was removed using stainless-steel scissors through the orbit and optic foramen (22). The cerebrum was carefully extracted, immersed in 10% formal saline, and bisected along the midsagittal plane. A digital vernier caliper was used to measure approximately 6 mm from the frontal pole, where the prefrontal cortex was sectioned (23). The cortical slices were processed for light microscopic examination by paraffin wax embedding in the sagittal plane, and one portion was randomly selected and stained with toluidine blue to evaluate pyramidal neuron morphology.

Toluidine Blue Staining

The Nissl technique was used to stain the prefrontal cortex and demonstrate the cell types present because it can stain all neurons and glial cell types in a single section (24). The sections were dipped in toluidine blue stain for one minute. They were removed and passed through distilled water and increasing alcohol concentrations before they were dipped in xylol for five minutes and in xylene for ten minutes. Finally, the sections were mounted for light microscopic examination using the Richter Optica® Model UX1 digital photomicroscope, and histological analysis of the prefrontal cortices was performed.

Data Analysis and Presentation

Metric data were analyzed using the Statistical Package for the Social Sciences (SPSS, Version 29.0, Chicago, Illinois). The dependent variable studied was the percentage of alternations in the Y-Maze behavioural test. The measures were expressed as means ± standard deviation. Data normality was assessed with the Shapiro–Wilk test. Since the data were parametric, a one-way analysis of variance (ANOVA) was applied to compare experimental and control groups. Histological findings were documented with photomicrographs. Morphological comparisons of pyramidal neurons were made across groups using the following parameters: neuronal shape, nuclear apparatus, cellular processes, neuron–astrocyte ratio, solitary astrocytes per high-power field, and the presence of fused cells, binucleated cells, vacuolated cells, and nuclear swelling.

RESULTS

Morphology of Pyramidal Neurons

Shape

Most neurons in the normal saline group were large and pyramidal in shape. In contrast, neurons in the MSG-treated group showed loss of the pyramidal outline, appearing more heterogeneous—some round, others polygonal. Neurons in the low-dose *Balanites aegyptiaca* (B.A.) group were predominantly rounded with occasional ovoid forms, while those in the moderate-dose group showed relatively preserved pyramidal morphology. The high-dose B.A. group exhibited well-preserved pyramidal neurons (Figure 1).

Nuclear apparatus

Neurons in the normal saline group displayed a large euchromatic nucleus with a well-defined nuclear envelope and a prominent nucleolus. Scattered heterochromatin was observed either centrally near the nucleolus or peripherally along the nuclear envelope. In contrast, most neurons in the MSG-treated group showed disintegrated or poorly outlined nuclear membranes with small nucleoli. Neurons in the low-dose B.A. group also exhibited nuclear disintegration, loss of the nuclear membrane, and tiny nucleoli. In the moderate-dose group, nuclear envelopes and nucleoli were indistinct. By comparison, neurons in the high-dose B.A. group showed well-defined nuclear envelopes and prominent nucleoli (Figure 2).

Cellular processes

Neurons in the normal saline group showed evident branching, with 4–5 neurofilaments radiating from the soma and converging into the axonal processes. In the MSG-treated group, branching of axons, dendrites, and neurofilaments within axonal processes was not observed. Neurons in the low-dose *Balanites aegyptiaca* (B.A.) group had thinned dendritic and axonal processes and lacked visible neurofilaments. In the moderate-dose group, cellular processes and neurofilaments were relatively preserved compared with the MSG-treated and low-dose groups. The high-dose B.A. group displayed well-defined cellular processes, with neurofilaments radiating from the soma and converging into the axon (Figure 3).

Neuron astrocyte ratio and solitary astrocytes per high-power field

A neuron-astrocyte ratio of 1:1 and 1-2 solitary astrocytes were observed per

high-power field in all the study groups except the low-dose B.A group. There was neuronal pruning, increased gliosis, and an eyeballing increase in astrocytes per high-power field in this group (Figure 4).

Occasional fused cells, binucleated cells, cells with vacuoles, and nuclear swelling

Microscopic examination of the prefrontal cortices of the MSG-treated and low-dose B.A groups revealed occasional binucleated cells. In the MSG-treated group, fused neurons connected by internuclear bridges were observed, and most neurons exhibited vacuolation with pre-apoptotic changes. These alterations were absent in the other study groups (Figure 5). .

Behavioural Assessment

In the Y-maze behavioural assessment, the normal saline group recorded an average alternation rate of 47%, while the MSG-treated group had 31.4%. The low-, moderate-, and high-dose *Balanites aegyptiaca* (B.A.) groups recorded 23.2%, 49%, and 38% alternations, respectively. The lowest percentage was observed in the low-dose group, followed by the MSG-treated group, whereas the moderate-dose group showed the highest alternation rate. However, these differences were not statistically significant (P = 0.277) (Figure 6).

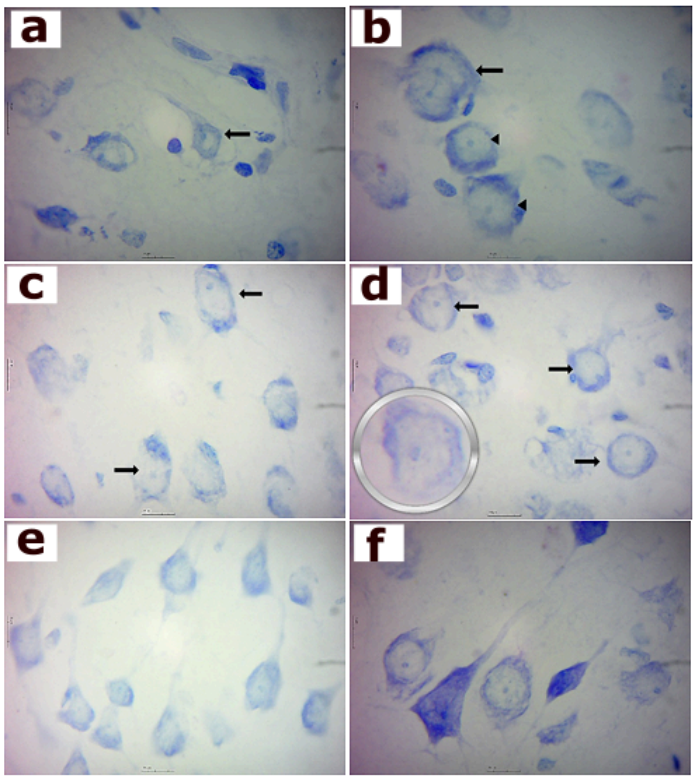

Figure 1 - Morphology of pyramidal neurons in the prefrontal cortex (Shape, Toluidine blue stain, ×1000). *In the normal saline group (a), neurons were large and distinctly pyramidal (black arrow). In the MSG-treated group, neurons appeared heterogeneous, with rounded (b, black arrowheads) and ovoid (c, black arrows) forms. The low-dose Balanites aegyptiaca group (d) showed predominantly oval neurons, while the moderate-dose group (e) displayed relatively preserved pyramidal morphology. In contrast, the high-dose group (f) showed well-preserved pyramidal neurons.*

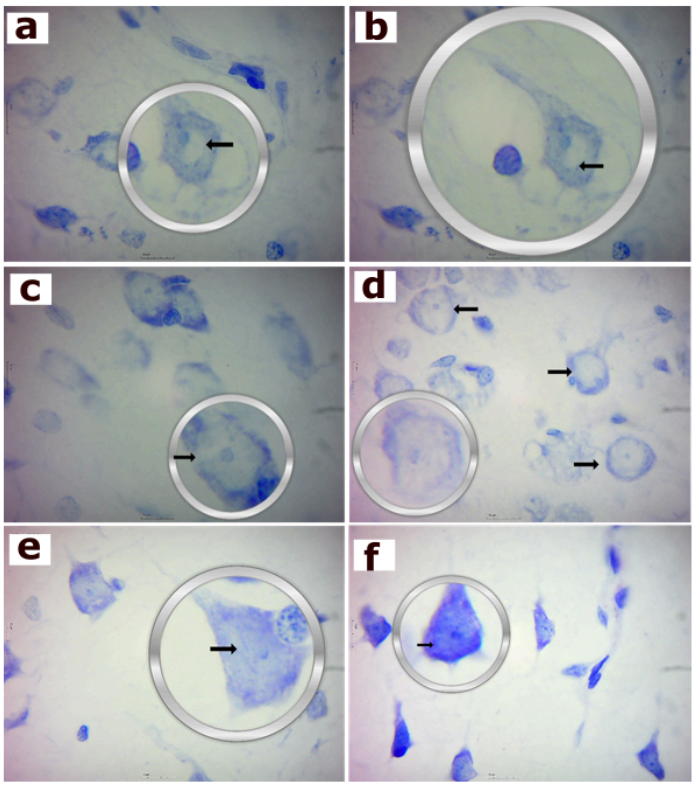

Figure 2 - Morphology of pyramidal neurons in the prefrontal cortex (Nuclear apparatus, Toluidine blue stain, ×1000). *In the normal saline group (a), neurons showed a well-defined nuclear envelope surrounding a large euchromatic nucleus with a prominent nucleolus, while scattered heterochromatin was observed either peripherally along the nuclear envelope (b) or centrally near the nucleolus. In the MSG-treated group (c), the nuclear membrane appeared disintegrated and nucleoli were small. Neurons in the low-dose Balanites aegyptiaca group (d) also exhibited nuclear disintegration with absent envelopes and tiny nucleoli. In the moderate-dose group (e), nuclear envelopes and nucleoli were indistinct. By contrast, the high-dose group (f) displayed prominent nucleoli and clearly visible nuclear envelopes.*

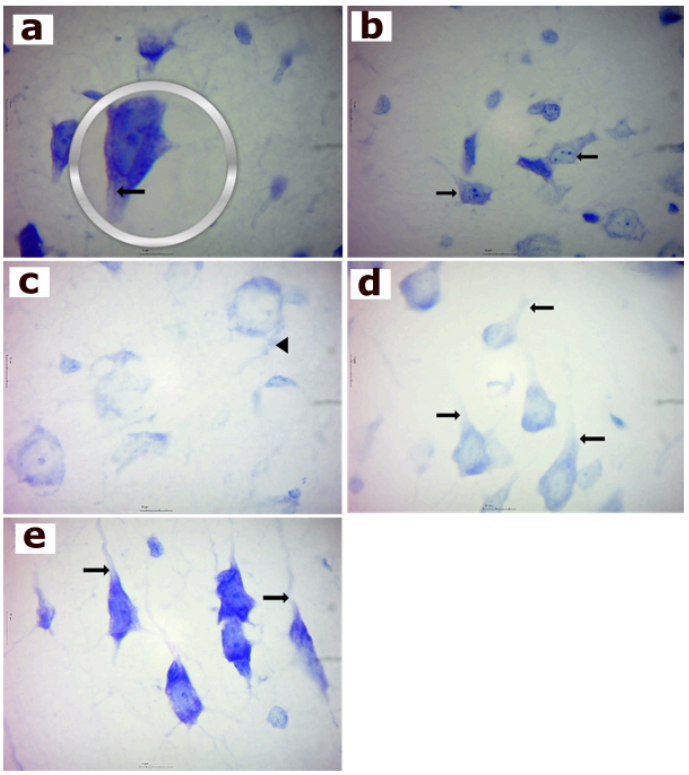

Figure 3 - Morphology of pyramidal neurons in the prefrontal cortex (Cellular processes, Toluidine blue stain, ×1000). *In the normal saline group (a), neurons showed clear branching, with 4–5 neurofilaments radiating from the soma and converging into the axonal processes. In the MSG-treated group (b), axonal and dendritic processes were thinned, and neurofilaments within the axons were not visible. The low-dose Balanites aegyptiaca group (c) also showed thinned processes and lacked visible neurofilaments. In the moderate-dose group (d), axonal and dendritic processes were relatively preserved compared with the MSG-treated and low-dose groups. The high-dose group (e) exhibited well-defined axonal and dendritic processes, with neurofilaments radiating from the soma and converging within the axon.*

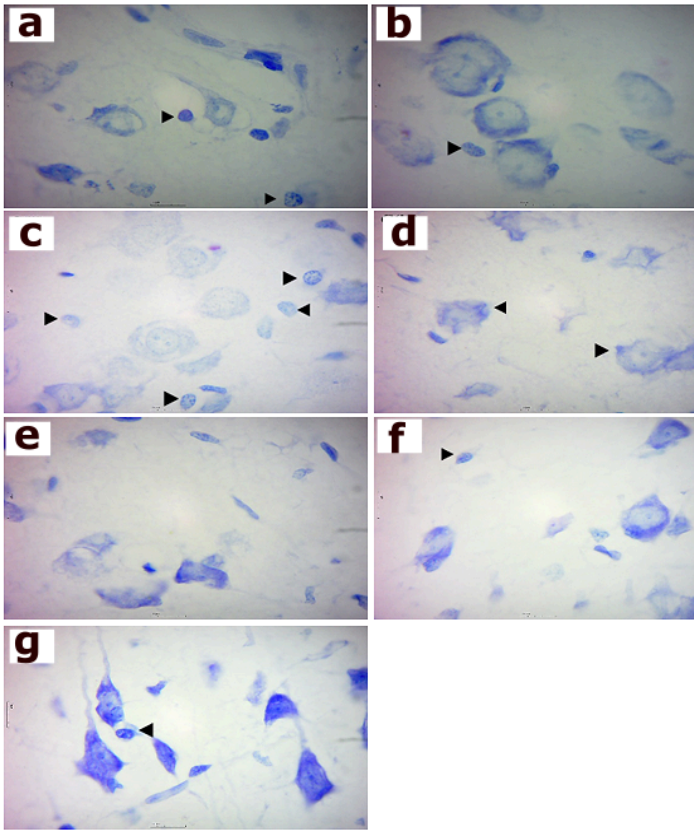

Figure 4 - Morphology of pyramidal neurons in the prefrontal cortex (Neuron–astrocyte ratio and solitary astrocytes per high-power field, Toluidine blue stain, ×1000). *In both the normal saline (a) and MSG-treated (b) groups, the neuron–astrocyte ratio was 1:1, with 1–2 solitary astrocytes observed per high-power field. The low-dose Balanites aegyptiaca group (c - e) showed increased gliosis with a higher number of astrocytes (black arrows), as well as neuronal shrinkage and pruning, reflected in a reduced number of normal pyramidal neurons per field. By contrast, the moderate-dose (f) and high-dose (g) groups maintained a 1:1 neuron–astrocyte ratio with 1–2 solitary astrocytes per high-power field (black arrowhead).*

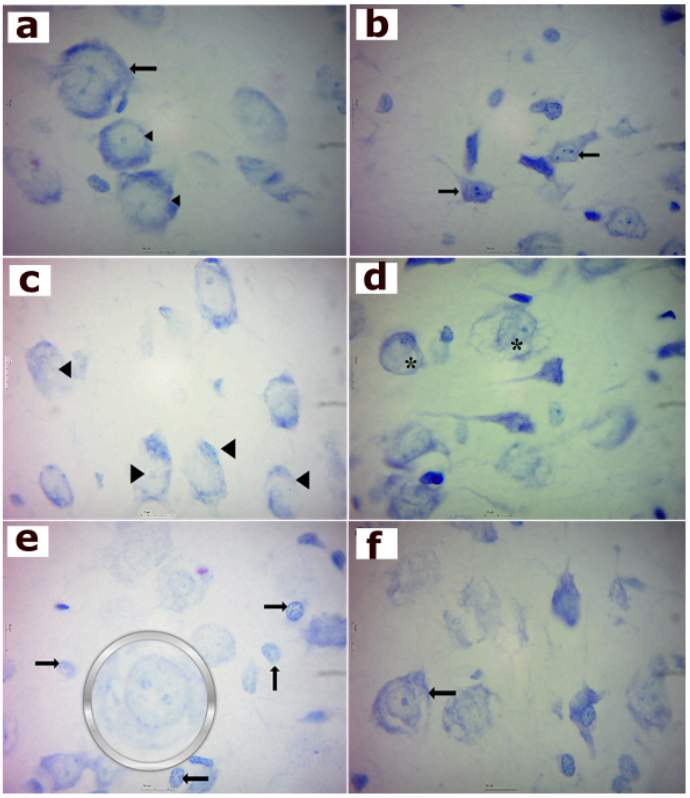

Figure 5 - Morphology of pyramidal neurons in the prefrontal cortex (Fused cells, binucleated cells, vacuoles, and nuclear swelling, Toluidine blue stain, ×1000). *In the MSG-treated group (a-d), neurons displayed several abnormalities, including fusion with internuclear connections (black arrow), karyorrhexis with polygonal cell shapes (black arrows), loss of nuclei with ruptured membranes (black arrowheads), and cytoplasmic vacuolation (black asterisks). In the low-dose Balanites aegyptiaca group (e-f), occasional binucleated cells were observed (inset), along with swollen neuronal nuclei and evidence of adjacent cell disintegration (black arrow).*

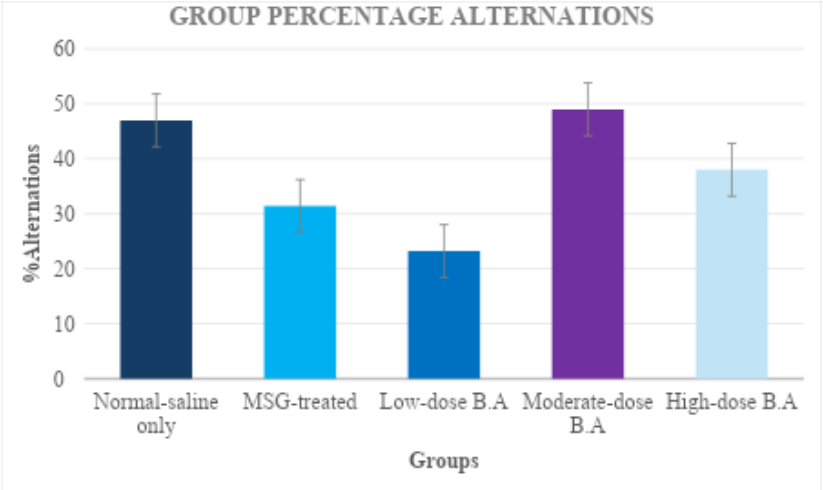

Figure 6 *– Simple bar graph representing group percentage of alternations after the Y-Maze behavioural assessment test.*

DISCUSSION

Excessive monosodium glutamate (MSG) induces neurotoxicity mainly through overactivation of glutamatergic receptors, leading to excitotoxicity and a cascade of intracellular disturbances, including oxidative stress, mitochondrial dysfunction, inflammation, and ultimately neuronal death (25,26). This mechanism is implicated in the pathogenesis of several neurological and psychiatric disorders (1,2). The present study supports prior findings by demonstrating that MSG administration causes profound morphological disruptions in the pyramidal neurons of the prefrontal cortex and is associated with impairments in working memory (17,18).

Histological analysis revealed significant neuronal degeneration, with pyramidal cells adopting abnormal round or polygonal morphologies indicative of cytoplasmic swelling - a hallmark of early neurotoxic insult (27). Vacuolation, disintegration of the nuclear envelope, and loss of nucleolar integrity further point to apoptotic processes, consistent with previously described excitotoxic cascades (28,29). Moreover, the absence of neurofilaments, which are critical for structural stability and synaptic function, suggests cytoskeletal breakdown and heightened vulnerability to neurodegeneration (30). While these findings align with studies linking MSG to excitotoxic cell death and cognitive decline (31,32), this study provides novel evidence implicating MSG in the disruption of neurofilaments, a feature not previously reported.

The therapeutic potential of *Balanites aegyptiaca* fruit extract against MSG-induced neurotoxicity was explored across three dosing regimens. At 125 mg/kg, the extract offered little neuroprotection, as neuronal morphology remained abnormal and evidence of gliosis and pruning suggested an ongoing neuroinflammatory process rather than repair. This finding contrasts with earlier reports of moderate protection at a similar dose (9), possibly due to methodological differences such as the use of whole fruit in this study versus pulp extracts elsewhere.

Conversely, at 250 mg/kg of *Balanites aegyptiaca,* the extract appeared to attenuate cellular injury. Preservation of neuronal architecture and reduced signs of cytoskeletal damage indicate a protective effect, likely mediated by the plant's antioxidant and anticholinesterase

properties (9). Bioactive constituents such as flavonoids, phenolics, and alkaloids may play a central role by buffering oxidative stress and supporting cholinergic transmission—mechanisms crucial for learning and memory (33).

The 500 mg/kg dosage demonstrated the strongest neuroprotection, with neurons maintaining structural integrity and showing no features of degeneration. This suggests that higher doses may stabilize calcium homeostasis, preserve synaptic organization, and reduce oxidative burden through modulation of malondialdehyde levels, superoxide dismutase, and catalase activity (9,34,35). Comparable benefits at this concentration have been reported previously (9), reinforcing the dose-dependent efficacy of *Balanites aegyptiaca*.

Behavioural outcomes from the Y-maze further supported the histological observations. MSG-only animals showed impaired spatial working memory, consistent with prefrontal cortical injury (36,37). Both the moderate- and high-dose groups demonstrated improved performance, with the 250 mg/kg group outperforming all others, including controls. This suggests a possible dose threshold for cognitive enhancement, or a biphasic response, as higher concentrations did not yield further gains. Divergence from prior findings that reported maximal benefits at 500 mg/kg (9) may again reflect differences in plant material or extraction protocols. In contrast, the poorest performance among extract-treated animals occurred in the low-dose group, indicating that subtherapeutic concentrations may be ineffective or even counterproductive.

Interestingly, the low-dose B. A group recorded the lowest cognitive performance among the groups treated with *Balanites aegyptiaca* fruit extract. This underscores that subtherapeutic concentrations may not mitigate MSG-induced cognitive disruptions. Despite variations among groups, the differences in spontaneous alternations were not statistically significant (P = 0.277). Therefore, larger sample sizes or extended observation periods are needed to ascertain the reliability of these behavioural effects.

CONCLUSION

Monosodium glutamate disrupts the morphology of prefrontal cortical neurons, while treatment with *Balanites aegyptiaca* fruit extract helps preserve their structural integrity. These results provide histological support for the plant's traditional use in managing cognitive disorders and highlight its promise as a neuroprotective agent. Future research should focus on clarifying its mechanisms of action, assessing efficacy across diverse neurological models, exploring synergistic effects with established neuroprotectants, and evaluating its potential in the prevention and treatment of cognitive impairment.

Limitations and Future Directions

Variations among animals regarding *Balanites aegyptiaca* fruit extract absorption and metabolism were not established. However, all the rats utilized in the study were inbred to enhance genetic similarity and reduce variations among the animals. Future research should employ stereological and 3D reconstruction techniques for precise quantification of neuronal changes, incorporate immunohistochemical markers to evaluate cell death and treatment response, and investigate the phytochemical constituents responsible for neuroprotection. Standardization of extract preparation will also be critical to advancing the therapeutic potential of *Balanites aegyptiaca* in the prevention and treatment of cognitive impairment.

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DISCLOSURES

The authors have no conflict of interest to declare.

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