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Original Article

Protective effects of *Sclerocarya birrea in vivo*

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Abstract

Background and objectives: *Sclerocarya birrea* (A. Rich) Hochst (Anacardiaceae) is a plant widely used by traditional healers in several African countries to treat numerous illnesses such as Alzheimer's disease, schizophrenia, inflammation, infections, arterial hypertension, headaches, and others. This study aimed to determine the therapeutic efficacy of *Sclerocarya birrea* (*S. birrea*) against glutamate-induced neurotoxicity.

Methods: Thirty naïve white mice (*Mus musculus* Swiss, Muridae), of both genders and weighing between 18 and 25 g, were used in the experiments. Different doses (102.5, 205, and 410 mg/kg) of the extract and vitamin C (100 mg/kg) were administered to the animals one hour before administration of monosodium glutamate (4 mg/kg) for 15 consecutive days. T-maze and Y-maze tests were conducted over three days to assess the animals' behavioral performance. After behavioral testing, the animals were sacrificed and their brains removed for analysis of oxidative stress parameters.

Results: *S. birrea* extract reversed glutamate-induced behavioral alterations by significantly ($P < 0.001$) reducing the latency to reach the platform in the T-maze and significantly increasing the percentage of spontaneous alternation in the Y-maze. The extract also significantly counteracted ($P < 0.001$) glutamate-induced oxidative stress parameters. The 102.5 and 205 mg/kg doses of the extract significantly ($P < 0.001$) reduced catalase and reduced glutathione levels, as well as the increase in malondialdehyde levels induced by glutamate.

Conclusions: *S. birrea* root bark extract exhibits neuroprotective properties that facilitate memory and ameliorate glutamate-induced cognitive deficits in white mice. The results provide partial justification for the traditional medicinal use of *S. birrea* extract.

Introduction

Neurodegenerative diseases and cognitive disorders represent a major global public health challenge, particularly among the elderly population. One of the key mechanisms implicated in the pathogenesis of these conditions is oxidative stress, which arises from an imbalance between the production of reactive oxygen species and the body's antioxidant defenses. This imbalance leads to neuronal damage, impaired synaptic function, and ultimately, cognitive decline.

The brain, a critical organ for perception and environmental adaptation,[1] is not immune to aging or degenerative diseases,[2,3] which cause the progressive deterioration of nerve cells.

Glutamate, the primary excitatory neurotransmitter in the central nervous system, plays a fundamental role in brain function. However, despite its widespread use as a food additive, monosodium glutamate (MSG) has been shown to exhibit neurotoxic effects in rodents.[4,5] Studies confirm that exposure to MSG induces significant neurochemical toxicity, notably through the induction of oxidative stress and neuronal damage.[5] It is important to emphasize, however, that these mechanisms differ qualitatively from the complex pathogenic processes involved in Alzheimer's

Keywords: *Sclerocarya birrea*; Neuroprotection; Monosodium glutamate; Oxidative stress; Neurotoxicity; Memory; Traditional medicine.

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disease, which involve amyloid protein aggregation, abnormal tau phosphorylation, and specific synaptic alterations. Therefore, direct or simplistic extrapolation of MSG's neurotoxic effects to Alzheimer's-like neurodegeneration should be avoided to maintain scientific rigor and preserve the validity of conclusions.[6]

In the search for new therapeutic strategies, medicinal plants with anthelmintic, antibacterial, antidiabetic, anti-inflammatory, antioxidant, and neuroprotective properties have garnered increasing interest.[7] *Sclerocarya birrea* (A. Rich) Hochst (Anacardiaceae), commonly known as marula, is traditionally used in African medicine to treat various ailments, including memory and neurological disorders.[8] It also possesses nutritional benefits, supporting its inclusion in local diets.

This species, widely distributed across Saharan and Sub-Saharan Africa,[9] exhibits vigorous growth during the dry season and slower growth during the rainy season. Various parts of the plant, particularly the leaves, are used to treat conditions such as sexual impotence, malaria, agalactia, pain, diarrhea, and trypanosomiasis. *S. birrea* has demonstrated anti-inflammatory, analgesic, antioxidant, antidepressant, antihypertensive, and antipyretic activities.[10]

Phytochemical analyses of *S. birrea* root bark have identified the presence of bioactive compounds such as tannins, flavonoids, alkaloids, saponins, and triterpenes, all known for their antioxidant properties.[11] Recent studies have shown that aqueous extracts of this bark can mitigate MSG-induced cognitive deficits and oxidative stress in mice. Oral administration of these extracts reverses behavioral disturbances, restores antioxidant enzyme activity, and reduces oxidative brain damage, thus supporting the traditional use of *S. birrea* in managing neurodegenerative diseases.

This study aimed to further evaluate the neuroprotective and antioxidant effects of orally administered aqueous extracts of *S. birrea* root bark in a mouse model of MSG-induced oxidative stress and memory impairment. By highlighting the therapeutic potential of this plant, the research seeks to contribute to the development of alternative interventions for cognitive disorders and neurodegeneration.

Materials and methods

Plant material and extract preparation

The root bark of *S. birrea* was collected in Moundou (Chad) and identified at the National Herbarium of Yaoundé. After grinding, 2.5 g of the powder was boiled in 50 mL of distilled water and then filtered to obtain a stock solution. Evaporation of 23 mL of this solution yielded 0.9435 g of dry extract, with a yield of 37.74%, corresponding to a concentration of 41 mg/mL. The initial administered dose was 410 mg/kg, and two additional doses (205 and 102.5 mg/kg) of the dry extract were subsequently prepared.

Preliminary phytochemical tests of the *S. birrea* extract were performed using qualitative colorimetric methods to identify the chemical groups.[12]

These tests showed the presence of alkaloids (white or orange precipitate with Dragendorff's reagent), tannins (blue-black coloration with FeCl3), flavonoids (orange, red, or purple coloration depending on type), triterpenes or steroids (purple or green-black coloration after treatment with chloroform, H2SO4, and acetic anhydride), anthraquinones (red coloration with petroleum ether/chloroform mixture and NaOH), and phenolic compounds (green or bluish coloration with FeCl3). These results confirm that *S. birrea* is rich in bioactive molecules that may explain its therapeutic effects.

Assessment of bioactive compound content in S. birrea root bark extract

Polyphenol content

The bioactive compound content of *S. birrea* root bark extract was evaluated using spectrophotometric methods. Polyphenols were measured using the Folin-Ciocalteu reagent,[13] tannins by a vanillin reaction using catechin as a standard,[14] and triterpenes following a lupeol-based protocol.[15] These analyses allowed quantification of key molecules contributing to the plant's therapeutic effects.

Determination of plant antioxidant capacity *in vitro;* Ferric reducing ability of plasma (FRAP) test: quantification of antioxidant potential by reduction of Fe^{3+} to Fe^{2+}

The FRAP method is based on the ability of an extract to reduce ferric iron (Fe^{3+}) to ferrous iron (Fe^{2+}).[16] A fresh FRAP reagent solution was prepared by mixing 2.5 mL of TPTZ (2,4,6-Tris(2-pyridyl)-s-triazine) solution (10 mM in 40 mM HCl) with 2.5 mL of FeCl3·6H2O (20 mM) and 25 mL of acetate buffer (300 mM sodium acetate, pH adjusted to 3.6 with acetic acid). Then, 900 µL of FRAP reagent, pre-incubated at 37°C, was mixed with 70 µL distilled water and 30 µL of plant extract at different concentrations (0.1 to 0.5 mg/mL). After 30 m of incubation, absorbance was measured at 593 nm at 37°C against the blank. Ascorbic acid was used as a positive control, and its absorbance was measured under the same conditions.

The percentage reducing power of the extract and vitamin C was calculated using the formula:

$$PR\ (\%) = \frac{A_0 - A_1}{A_0} \times 100$$

where PR is the reducing power, A_0 the absorbance of the control, and A_1 the absorbance of the sample.

Behavioral tests

Naïve white Swiss mice (*Mus musculus*, Muridae), aged eight to ten weeks, were used to study the effects of *S. birrea* on memory in an MSG-induced neurotoxicity model. Animals were divided into control and test groups and treated for 15 days with different doses of the plant extract or controls.[17] A T-maze test,[18] comprising three phases (habituation, acquisition, retention), was conducted to assess exploration, spatial preference, and memory. Parameters measured included latency time, time spent in maze arms, and number of entries, allowing evaluation of the extract's impact on cognitive functions.

Y-maze test

The spontaneous alternation test in a Y-maze started on treatment day 14 and comprised two phases: habituation and retention.[19]

During habituation (day 14), animals were individually placed at the starting compartment end and allowed to explore the maze freely for 5 m. Mice spontaneously explored the less recently visited arm, demonstrating their ability to alternate visits across the three arms.

The retention phase (day 15) began 24 h later. The parameter recorded was the number of successive entries into the three different arms of the Y-maze.

An animal was considered to have entered an arm only if all four paws were inside. After each animal, the maze was cleaned with 70% ethanol. Spontaneous alternation was defined as three successive entries into different arms (e.g., ABC, CAB, or BCA). The percentage of spontaneous alternation (% AS) and the alter-

nation index were used as indices of working memory performance:

$$\%\ AS = \frac{\text{Number of alternations performed}}{\text{Total number of arms visited} - 2} * 100$$

The number of possible alternations corresponds to the total number of arms visited minus 2.

$$\text{Alternation index} = \frac{\text{Number of alternations performed}}{\text{Number of arms visited}} * 100$$

Evaluation of the antioxidant capacity of the extract in vivo

Brain sampling and homogenate preparation

Immediately after behavioral tests, animals were sacrificed by cervical decapitation. Brains were removed, rinsed in 0.9% NaCl solution, blotted dry, weighed, and placed in a ceramic mortar. 500 µL of phosphate-buffered saline (PBS) was added, and the tissue was homogenized. The homogenate was centrifuged at 10,000 rpm for 15 m. The supernatant was collected and stored in labeled tubes for oxidative stress parameter assays.

Determination of oxidative stress markers

Malondialdehyde (MDA) assay

MDA presence leads, under hot acidic conditions (100°C), to the formation of aldehydes that react with thiobarbituric acid to form a pink complex. Absorbance was read at 530 nm against a blank following the protocol by Wilbur *et al*.[20] Briefly, 0.5 mL homogenate was mixed with 0.25 mL Tris-HCl buffer (blank tube) or test tubes; then 0.25 mL 20% trichloroacetic acid and 0.5 mL 0.67% thiobarbituric acid were added. Tubes were sealed with glass beads and incubated at 90°C for 10 m, cooled, then centrifuged at 3,000 rpm for 15 m at room temperature. Absorbance of the supernatant was measured at 530 nm. MDA concentration was calculated as:

$$[\text{MDA}]\ (\text{mol/g tissue}) = \frac{\text{DO} \times \text{Vt}}{\varepsilon \times \text{L} \times \text{Vi} \times \text{m}}$$

where: OD: optical density; Vt: total volume in tube (mL) = 1.25 mL; Vi: volume of supernatant used for assay (mL) = 0.5 mL; m: mass of tissue used (g) = 0.4 g; L: length of cell = 1 cm; ε: molar extinction coefficient = 1.56×105 $mol^{-1}.cm^{-1}$.

Determination of catalase activity

Catalase activity was determined by the method of Beers and Sizer in 1952.[21] Two hundred and fifty microliters of distilled water and 250 µL of seahorse homogenate were added to cuvettes, followed by 250 µL phosphate buffer (0.1 M, pH 7.2) and 1,000 µL 30 mM H2O2. After rapid mixing at room temperature, absorbance was read at 240 nm after 30 s and 90 s. Catalase activity was calculated using Beer-Lambert law.

$$\text{Catalase activity} = \frac{\text{Am} \times 10^3 \times \text{Vt}}{1 \times \varepsilon \times \text{m} \times \text{Ve}}$$

where: Am = mean absorbance at 240 nm; ε = molar extinction coefficient = 40 M^{-1}; cm^{-1}; Vt is the total volume of the reaction medium; Ve is the volume of the homogenate; t is the reaction time (m); l is the optical path of the cell.

Reduced glutathione assay

Reduced glutathione was quantified using Ellman's method (1959).[22] 2,2-dithio-5,5′-dinitrobenzoic acid reacts with –SH groups to form a yellow complex, measured at 412 nm. Three milliliters of reagent were mixed with 200 µL of homogenate (test) or Tris-HCl buffer (control). After vortexing and 1-h incubation at room temperature, absorbance was read. Glutathione concentration was calculated as:

$$[\text{Reduced glutathione}]\ (\text{mol/g tissue}) = \frac{\text{DO} \times \text{Vt}}{\varepsilon \times \text{L} \times \text{Vi} \times \text{m}}$$

where: OD: optical density; Vt: total tube volume = 3.2 mL; Vi: volume of supernatant used for assay = 0.2 mL; m: mass of tissue used = 0.4 g; L: length of cell = 1 cm; ε: molar extinction coefficient = 13,600 $mol^{-1}.cm^{-1}$.

Superoxide dismutase activity (SOD)

SOD activity was measured by its inhibition of adrenaline oxidation to adrenochrome, monitored by absorbance increase at 480 nm between 20 and 80 s. The Misra and Fridovich method (1972) was used to calculate SOD units per mg protein,[23] where one unit corresponds to 50% inhibition.

$$\text{Activité SOD} = \frac{\text{U}}{\text{mg}} \text{de protéine}$$

$$= \frac{\text{Nombred d'unités de } \frac{\text{SOD}}{\text{aL}}}{\text{mg de protéine}}$$

$$* \text{Facteur de dilution}$$

SOD unit = (100 - ((Δ DOessay x 100)) / ΔDOwhite = % inhibition; 50% inhibition corresponds to 1 SOD unit; OD variation: ΔDOm = DO20s - DO80s.

Determination of the cholinergic transmission system

Acetylcholinesterase (AchE) activity

AChE activity, which degrades acetylcholine, was determined by Ellman's method.[22] Absorbance at 412 nm was recorded over 2 m to calculate enzyme activity expressed in units per minute per mg protein. One unit corresponds to the enzyme amount hydrolyzing 1 µmol acetylthiocholine iodide per minute.

$$\text{AchE} = \frac{\frac{\text{A}}{\text{m}} \times \text{Vt}}{\varepsilon \times \text{b} \times \text{Vs}}$$

where: A/m is absorbance variation per minute; ε is 1.361 X 104 M^{-1}; cm^{-1}; b is the length of the cell (1 cm); Vt is the total volume (3.2 mL); Vs is the sample volume (0.4 mL). Enzyme activity is expressed in U/m/mg protein in brain tissue (1 U/m/mg AchE was defined as the amount of enzyme that as the amount of enzyme hydrolyzing 1 µmol acetylthiocholine iodide).

Statistical analysis

Data were analyzed using descriptive statistics with Microsoft Excel 2016 to determine mean ± standard error of the mean. Analysis of variance followed by Tukey's multiple comparison test was performed using GraphPad Prism version 8.3.1. Differences were considered significant at $P \leq 0.05$.

Results

Qualitative phytochemical screening of S. birrea extract

Phytochemical characterization tests of *S. birrea* extract revealed the presence of the following major chemical families: polyphe-

Table 1. Main chemical families in *Sclerocarya birrea* extract

Chemical compound families	Existence (scale 1–3)
Alkaloids	2
Flavonoids	1
Saponins	1
Tannins	3
Triterpenes	3
Anthraquinones	2
Steroids	2
Polyphenols	3

Rating: 1 = low; 2 = moderate; 3 = high.

nols, tannins, anthraquinones, alkaloids, saponins, and triterpenes. These results are summarized in Table 1 below.

Content of bioactive compounds in S. birrea extract

The bioactive compound assay showed a high polyphenol content of 194.75 ± 0.05 mg EAG/g (gallic acid equivalent per gram) extract, followed by tannins at 6.65 ± 0.30 mg EqCat/g extract. The triterpene content was relatively low, at 1.60 ± 0.29 mg EqLu/g extract.

Anti-free radical activity of *S. birrea* extract Iron reducing power

The reducing power of the extract increased proportionally with concentration and is expressed in milligrams of ascorbic acid equivalent per gram of dry extract Equivalent antioxidant activity per gram (mg EAA/g dry extract). The results are presented in Table 2.

Effects of S. birrea on MSG-induced memory loss in the T-maze test

Effects on latency to enter the first arm

A significant increase ($P < 0.001$) in latency to enter the first arm (Fig. 1) was observed during all three phases of the T-maze (habituation, acquisition, retention), increasing from 9.4 ± 0.84 s in normal controls to 19 ± 0.74 s in negative controls. *S. birrea* extract antagonized the effects of MSG, significantly ($P < 0.001$) reducing latency to 2.8 ± 0.88 s and 4 ± 0.83 s in animals treated with 410 mg/kg and vitamin C, respectively, compared with the negative control during habituation.

During acquisition, latency increased from 7.8 ± 0.72 s (nor-

Table 2. Reducing power of extracts

Extract concentrations (mg/mL)	Reducing power of Vit C (mg AAE/g dry extract)	Reducing power of decoctate (mg AAE/g dry extract)
0.5 mg/mL	85,63 ± 0,07	69,09 ± 0,17
0.4 mg/mL	81,81 ± 0,10	54,54 ± 0,25
0.3 mg/mL	66,27 ± 0,18	44,54 ± 0,30
0.2 mg/mL	56,90 ± 0,23	40,54 ± 0,32
0.1 mg/mL	47,90 ± 0,28	34,54 ± 0,36

Each value represents mean ± MSE, n = 3. AAE, ascorbic acid equivalent; MSE, methanol stem extract; Vit C, Vitamin C.

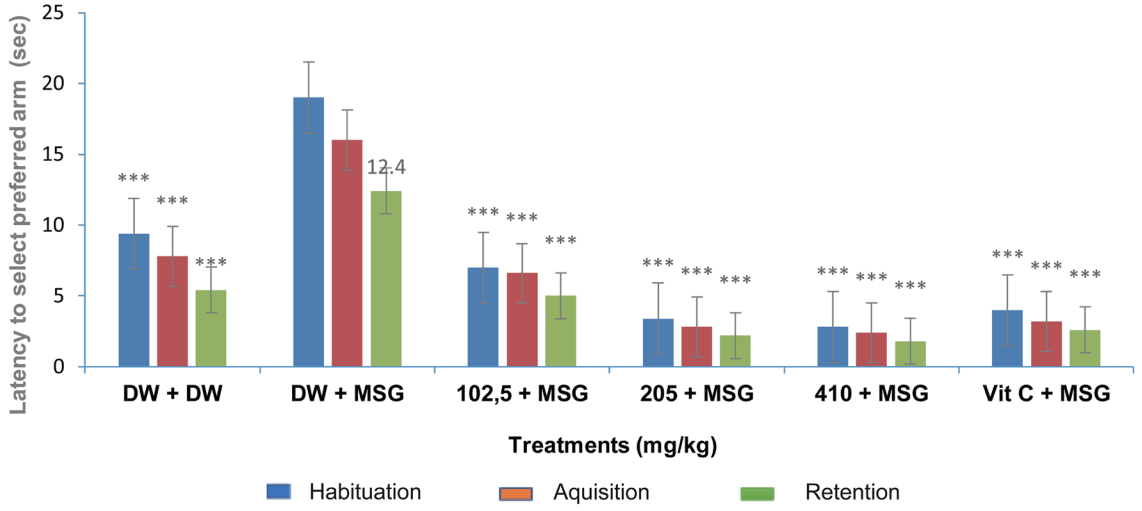

Fig. 1. Latency for choosing the preferred arm in the T-maze. Each bar represents mean ± standard error of the mean (SEM) of five animals. Data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's multiple comparisons test. ***$P < 0.001$ vs. monosodium glutamate-treated group (DW + MSG). DW, distilled water (normal control); MSG, monosodium glutamate (4 mg/kg). 102.5, 205, and 410: *S. birrea* doses (mg/kg). Vit C, vitamin C (100 mg/kg, positive control).

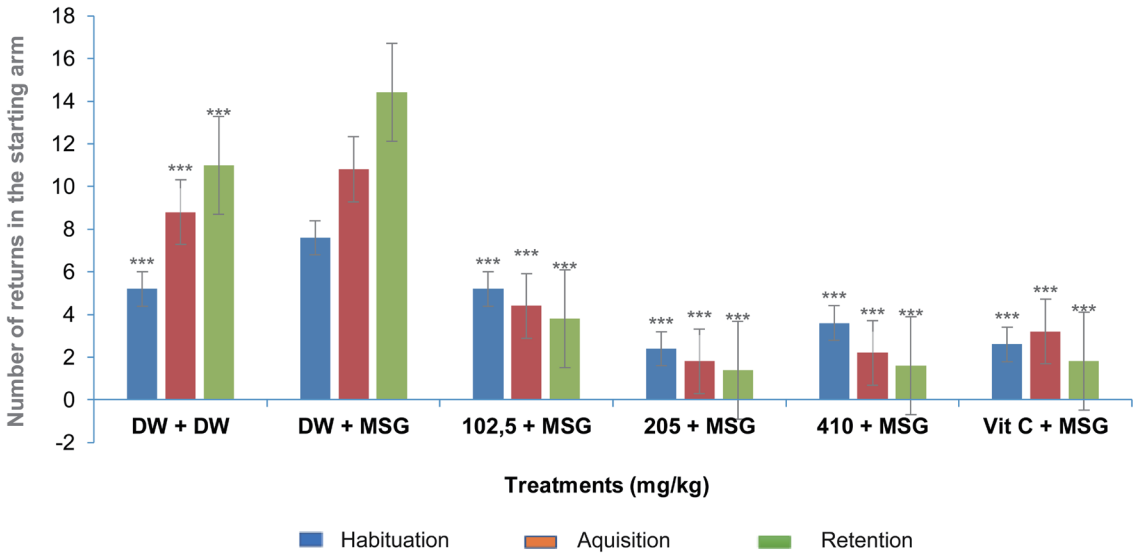

Fig. 2. Number of returns in the starting arm of the T-maze. Each bar represents mean ± standard error of the mean (SEM) of five animals. Data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's multiple comparisons test. ***$P < 0.001$ vs. monosodium glutamate-treated group (DW + MSG). DW, distilled water (normal control); MSG, monosodium glutamate (4 mg/kg). 102.5, 205, and 410: *S. birrea* doses (mg/kg). Vit C, vitamin C (100 mg/kg, positive control).

mal controls) to 16 ± 0.72 s (negative controls). Treatment with *S. birrea* at 410 mg/kg and vitamin C significantly ($P < 0.001$) decreased this to 2.4 ± 0.88 s and 3.2 ± 0.42 s, respectively.

During retention, latency rose from 5.4 ± 0.88 s (normal controls) to 12.4 ± 0.50 s (negative controls). *S. birrea* at 205 mg/kg and vitamin C significantly ($P < 0.001$) reduced latency to 1.8 ± 0.66 s and 2.6 ± 0.44 s, respectively.

Effects on the number of returns to the baseline arm

Daily administration of MSG induced a significant increase ($P < 0.001$) in the number of returns to the starting arm (Fig. 2), rising from 7.4 ± 0.88 in normal controls to 8.8 ± 0.64 in negative controls. Treatment with *S. birrea* significantly ($P < 0.001$) reduced this number to 3.4 ± 0.88 and 4.4 ± 0.88 at 410 mg/kg and with vitamin C, respectively, during habituation.

During acquisition, the number of returns increased from 5.6 ± 0.88 (normal controls) to 9.8 ± 0.64 (negative controls). Treatment with *S. birrea* (410 mg/kg) and vitamin C significantly ($P < 0.001$) decreased this to 2.6 ± 0.88 and 3.4 ± 0.88, respectively.

During retention, returns rose from 4.6 ± 0.48 (normal controls) to 10.4 ± 0.48 (negative controls). *S. birrea* and vitamin C significantly ($P < 0.001$) lowered returns to 1.8 ± 0.32 and 2.4 ± 0.48, respectively.

Effects on time spent in the preferred arm

Daily MSG administration significantly ($P < 0.001$) decreased time spent in the preferred arm (Fig. 3), from 117.4 ± 0.64 s in normal controls to 88.2 ± 0.84 s in negative controls. Treatment with *S. birrea* significantly ($P < 0.001$) increased this time to 172 ± 0.55 s and 150.4 ± 0.66 s at 410 mg/kg and with vitamin C, respectively, during habituation.

During acquisition, time spent decreased from 78.6 ± 0.72 s (normal controls) to 69 ± 0.32 s (negative controls). *S. birrea* treatment significantly ($P < 0.001$) increased this time to 195.4 ± 0.66 s and 159 ± 0.66 s at 410 mg/kg and with vitamin C, respectively.

During retention, time spent decreased from 57.8 ± 0.64 s (normal controls) to 49 ± 0.66 s (negative controls). *S. birrea* reversed these effects, significantly ($P < 0.001$) increasing time to 203.6 ± 0.44 s and 186 ± 0.83 s at 410 mg/kg and with vitamin C, respectively.

Effects of S. birrea on MSG-induced neurotoxicity in the Y-labyrinth test

Effects on the number of spontaneous alternations

After 15 days of treatment, Figure 4 shows that MSG significantly ($P < 0.001$) reduced the number of alternations in the Y-maze from 4.2 ± 0.83 in normal controls to 1.4 ± 0.44 in negative controls. *S. birrea* extract antagonized this effect by significantly ($P < 0.001$) increasing the number of alternations at all doses, with optimal values of 7 ± 0.55 and 5.2 ± 0.27 in mice treated with 102.5 mg/kg and vitamin C, respectively, compared to the negative control.

Effects on the percentage of spontaneous alternation

Figure 5 shows the effect of *S. birrea* extract on the percentage of spontaneous alternation in MSG-treated animals. MSG caused a significant decrease ($P < 0.001$) in spontaneous alternation percentage, from 12.6 ± 0.66% in normal controls to 4.8 ± 0.27% in negative controls. *S. birrea* extract significantly ($P < 0.001$) increased this percentage to peak values of 23.2 ± 0.55% and 13.8 ± 0.27% in animals treated with 410 mg/kg and vitamin C, respectively, compared to the negative control.

Effects on the spontaneous alternation index

Figure 6 shows that daily administration of MSG significantly ($P < 0.001$) decreased the alternation index from 11.4 ± 0.77 in normal controls to 7.4 ± 0.44 in negative controls. *S. birrea* extract antagonized this effect by significantly ($P < 0.001$) increasing the index at all doses, with maximum values of 19.8 ± 0.55 and 12.8 ± 0.55 in animals treated with 410 mg/kg and vitamin C, respectively, compared to the negative control.

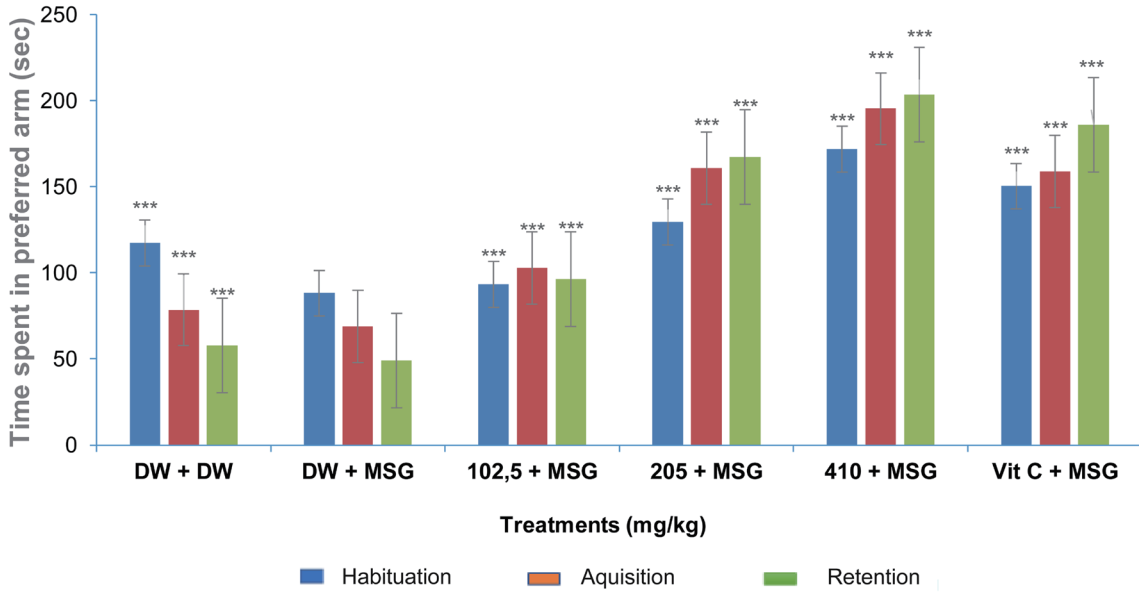

Fig. 3. Time spent in the preferred arm in the T-maze. Each bar represents mean ± standard error of the mean (SEM) of five animals. Data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's multiple comparisons test. ***$P < 0.001$ vs. monosodium glutamate-treated group (DW + MSG). DW, distilled water (normal control); MSG, monosodium glutamate (4 mg/kg). 102.5, 205, and 410: *S. birrea* doses in mg/kg; Vit C, vitamin C 100 mg/kg (positive control).

Effects on MDA concentration

Table 3 shows that MSG caused a significant increase ($P < 0.001$) in MDA levels, from 4.65 ± 0.51 µmol/g tissue in normal controls to 10.39 ± 0.21 µmol/g tissue in negative controls. *S. birrea* extract significantly ($P < 0.001$) inhibited this increase, reducing MDA concentration to 8.60 ± 0.19 µmol/g tissue at 102.5 mg/kg and 4.97 ± 0.29 µmol/g tissue in the vitamin C-treated group, compared to negative controls.

Effects on catalase concentration

Table 3 also shows that MSG significantly ($P < 0.001$) decreased catalase levels from 13.88 ± 0.34 µmol/g tissue in normal controls to 10.61 ± 0.45 µmol/g tissue in negative controls. Treatment with *S. birrea* extract significantly ($P < 0.001$) increased catalase concentration at all doses, with optimal values of 14.44 ± 0.92 and 14.52 ± 1.30 µmol/g tissue in mice treated with 102.5 mg/kg and vitamin C, respectively, compared to negative controls.

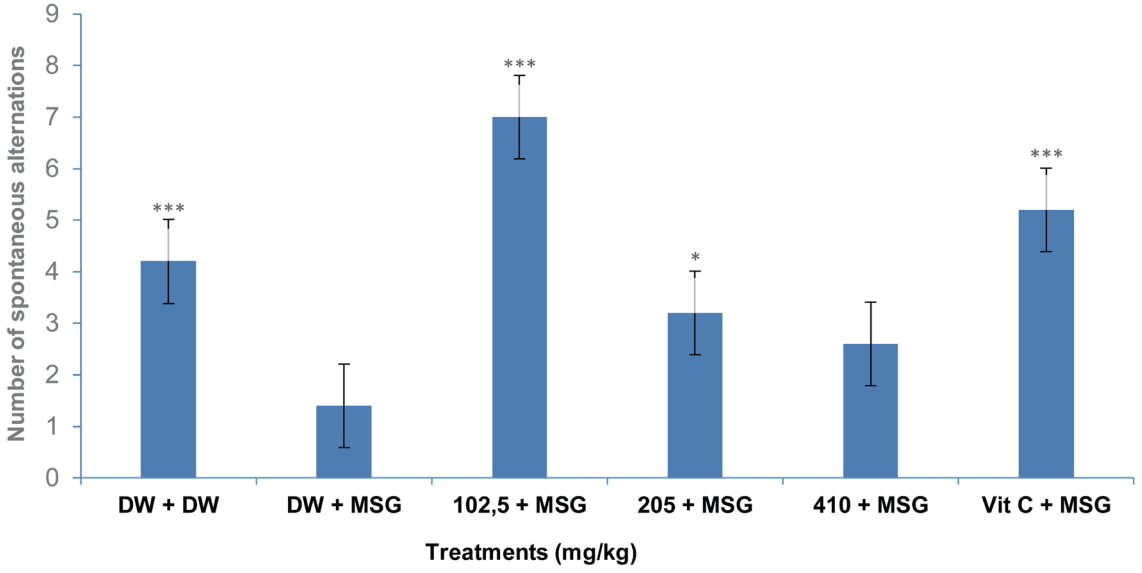

Fig. 4. Effects of *Sclerocarya birrea* on the number of spontaneous alternations in the Y-maze. Each bar represents mean ± standard error of the mean (SEM) of five animals. Data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's multiple comparisons test. *$P < 0.05$; ***$P < 0.001$ vs. monosodium glutamate-treated group (DW + MSG). DW, distilled water (normal control); MSG, monosodium glutamate (4 mg/kg). 102.5, 205, and 410: *S. birrea* doses in mg/kg. Vit C, vitamin C 100 mg/kg (positive control).

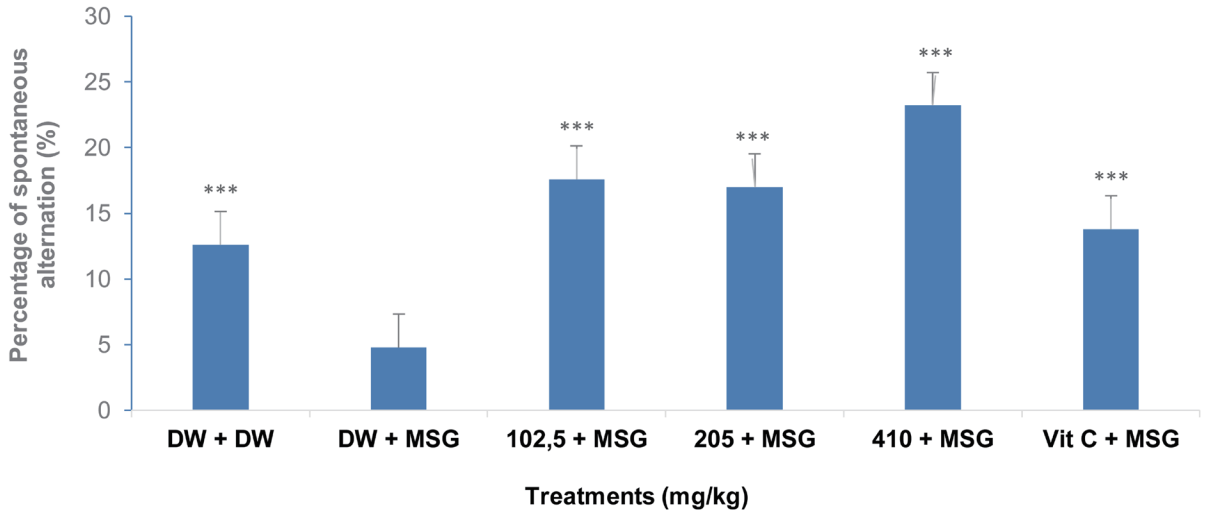

Fig. 5. Effects of *Sclerocarya birrea* extract on the percentage of spontaneous alternation in the Y-maze. Each bar represents mean ± standard error of the mean (SEM) of five animals. Data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's multiple comparisons test. ***$P < 0.001$ vs. monosodium glutamate-treated group (DW + MSG). DW, distilled water (normal control); MSG, monosodium glutamate (4 mg/kg). 102.5, 205, and 410: *S. birrea* doses in mg/kg. Vit C, vitamin C 100 mg/kg (positive control).

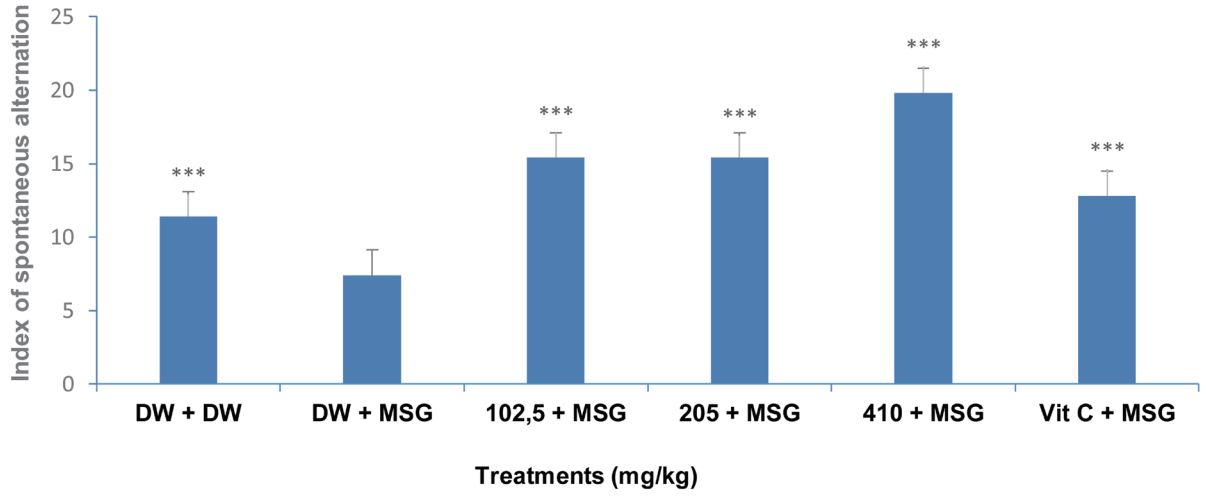

Fig. 6. Effects of *Sclerocarya birrea* on the spontaneous alternation index in the Y-maze. Each bar represents mean ± standard error of the mean (SEM) of five animals. Data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's multiple comparisons test. ***$P < 0.001$ vs. monosodium glutamate-treated group (DW + MSG). DW, distilled water (normal control); MSG, monosodium glutamate (4 mg/kg). 102.5, 205, and 410: *S. birrea* doses in mg/kg. Vit C, vitamin C 100 mg/kg (positive control).

Table 3. Effects of *Sclerocarya birrea* on oxidative stress markers

	Treatments (mg/kg)					
	DW + DW	**DW + MSG**	**102,5 + MSG**	**205 + MSG**	**410 + MSG**	**Vit C+ MSG**
MDA (mol/g)	4,65 ± 0,51***	10,39 ± 0,21	8,60 ± 0,19*	9,88 ± 0,24*	10,80 ± 0,17	4,97 ± 0,29***
CAT (mol/g)	13,88 ± 0,34***	10,61 ± 0,45	14,44 ± 0,92***	12,14 ± 0,71**	11,57 ± 0,50*	14,52 ± 1,30***
Reduced GSH (mol/g)	0,06 ± 0,00***	0,04 ± 0,00	0,05 ± 0,00**	0,06 ± 0,00***	0,03 ± 0,00	0,07 ± 0,00***
SOD (SOD/mg)	5,02 ± 0,69***	4,07 ± 0,61	5,08 ± 0,34***	5,09 ± 0,22***	4,86 ± 0,32	5,13 ± 0,11***

Results are expressed as mean ± standard error of the mean (SEM) for five animals. Data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's multiple comparisons test. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ vs. monosodium glutamate-treated group (DW + MSG). DW, distilled water (normal control); MSG, monosodium glutamate (4 mg/kg). 102.5, 205, and 410: *S. birrea* doses in mg/kg. Vit C, vitamin C 100 mg/kg (positive control). CAT, catalase; GSH, glutathione; MDA, malondialdehyde; SOD, superoxide dismutase.

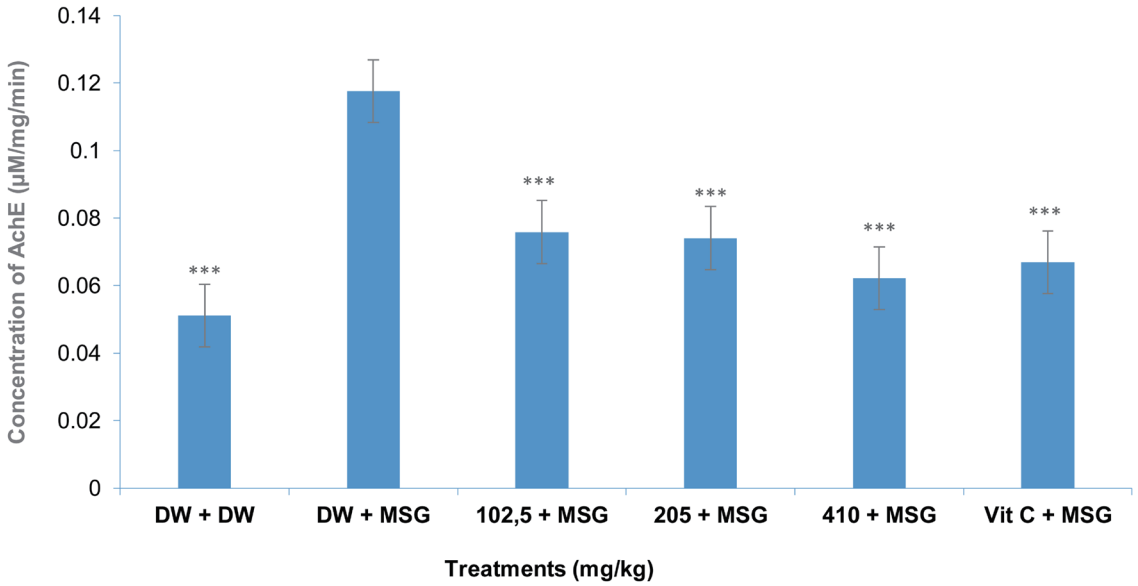

Fig. 7. Effects of *Sclerocarya birrea* extract on brain acetylcholinesterase levels in white mice. Each bar represents mean ± standard error of the mean (SEM) of five animals. Data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's multiple comparisons test. **P* < 0.05; ***P* < 0.01; ****P* < 0.001 vs. monosodium glutamate-treated group (DW + MSG). DW, distilled water (normal control); MSG, monosodium glutamate (4 mg/kg). 102.5, 205, and 410: *S. birrea* doses in mg/kg. Vit C, vitamin C 100 mg/kg (positive control). AchE, acetylcholinesterase.

Effects on reduced glutathione concentration

MSG significantly ($P < 0.001$) reduced glutathione levels from 0.06 ± 0.00 µmol/g tissue in normal controls to 0.04 ± 0.00 µmol/g tissue in negative controls. *S. birrea* extract treatment significantly ($P < 0.001$) reversed this decrease, raising glutathione concentrations to 0.06 ± 0.00 and 0.07 ± 0.00 µmol/g tissue in animals treated with 205 mg/kg and vitamin C, respectively, compared to negative controls.

Effects on SOD concentration

MSG caused a significant ($P < 0.001$) reduction in SOD activity, decreasing from 5.02 ± 0.69 U/mg protein in normal controls to 4.07 ± 0.61 U/mg protein in negative controls. Treatment with *S. birrea* extract significantly ($P < 0.001$) mitigated this decline at all doses, with peak activities of 5.09 ± 0.22 and 5.13 ± 0.11 U/mg protein in mice treated with 205 mg/kg and vitamin C, respectively, compared to negative controls.

Effects of S. birrea on parameters of the MSG-induced cholinergic transmission system; Effects on AchE concentration

Figure 7 illustrates that MSG caused a significant ($P < 0.001$) increase in AchE activity, from 0.05 ± 0.03 µM/mg/m in normal controls to 0.11 ± 0.07 µM/mg/m in negative controls. *S. birrea* extract significantly ($P < 0.001$) reduced AchE activity, reaching minimum values of 0.06 ± 0.05 and 0.06 ± 0.03 µM/mg/m in animals treated with 410 mg/kg and vitamin C, respectively, compared to negative controls.

Discussion

S. birrea is extensively used in traditional medicine due to its numerous therapeutic properties,[24] largely attributed to its rich content of phytochemicals and antioxidants such as alkaloids, flavonoids, tannins, terpenoids, saponins, and phenolic compounds.[25] The objective of this study was to evaluate the neuroprotective and antioxidant effects of oral administration of aqueous extracts from *S. birrea* root bark in a mouse model of oxidative stress and memory impairment induced by MSG.

Our findings confirm that the *S. birrea* extract contains a substantial amount of phenolic compounds, including polyphenols, tannins, and triterpenes,[26] secondary metabolites well recognized for their diverse beneficial effects,[26] particularly their antioxidant and neuroprotective properties.[27] These compounds are responsible for the radical scavenging activity observed in the FRAP assay, demonstrating the extract's ability to neutralize free radicals and enhance the enzymatic antioxidant defense system.[28]

Behaviorally, administration of the extract significantly reversed MSG-induced impairments.[29] In the T-maze test, the extract reduced latency and increased the time spent in the preferred arm, indicating improved memory performance along with reduced stress and anxiety,[30] which facilitated exploratory behavior. These results align with those reported by Boix *et al*.,[31] who observed similar neuroprotective effects of fisetin on neurodegeneration and memory deficits induced by lipopolysaccharides. Furthermore, in the spontaneous alternation test using the Y-maze, the extract enhanced the number, percentage, and index of alternation, reflecting a significant improvement in short-term memory consistent with the protective effects of wogonin reported by Huang *et al*.[32] in Alzheimer's disease models. Biochemical analyses revealed that treatment with *S. birrea* extract mitigated glutamate-induced cerebral oxidative stress, as evidenced by decreased MDA levels and increased concentrations of reduced glutathione, SOD, and catalase. These findings corroborate the work of Lobo *et al*.,[33] highlighting the critical role of antioxidants in protecting against oxidative damage. Given that oxidative stress is a key contributor to Alzheimer's disease pathogenesis,[34] these data suggest a promising neuroprotective potential of *S. birrea* extract in preventing brain degeneration.[35]

Additionally, we observed a significant increase in AchE in the

brains of glutamate-exposed mice, indicative of cholinergic system dysfunction associated with oxidative stress and cholesterol degradation.[36] Treatment with the extract significantly reduced this enzymatic activity, suggesting restoration of cholinergic function and neuroprotection. In summary, *S. birrea* extract acts as a potent antioxidant and neuroprotective agent capable of attenuating cognitive deficits and oxidative stress induced by glutamate. These results support its traditional use and open avenues for its development as a complementary therapy for neurodegenerative disorders.[37]

However, despite these promising findings, several limitations must be acknowledged for a rigorous interpretation of the extract's effects. The MSG-induced neurotoxicity model only partially replicates the complex mechanisms underlying human neurodegenerative diseases.[38] The behavioral tests employed (T-maze and Y-maze) primarily assess spatial memory and exploratory behavior but do not encompass the full spectrum of cognitive or emotional functions. The biochemical markers measured (MDA, glutathione, SOD, catalase, AchE) provide insight into oxidative stress and neuroprotection but do not address other relevant mechanisms such as inflammation, apoptosis, or neurotransmission. Furthermore, variability in administered doses of both neurotoxic agents and therapeutic compounds may compromise the reproducibility and stability of the results obtained *in vivo*. In addition, the precise molecular mechanisms underlying the observed effects remain only partially elucidated, requiring further research, particularly through the use of transgenic animal models dedicated to neurodegenerative diseases. Finally, the study compares *S. birrea* extract only to vitamin C as a positive control; the absence of comparison with other established neuroprotective agents or reference drugs limits the relative assessment of its efficacy.[39,40] In summary, although *S. birrea* extract demonstrates noteworthy antioxidant and neuroprotective potential in this animal model, further studies are warranted to confirm these effects, elucidate underlying mechanisms, evaluate long-term safety, and explore clinical applicability in humans.

Future directions

Regarding future avenues, it would be relevant to further utilize transgenic animal models to deepen our understanding of the molecular pathways involved and better target the pharmacological potential of *S. birrea* in various neurodegenerative diseases. Furthermore, it is important to analyze the stability, consistency, and reproducibility of the observed effects in order to standardize its therapeutic use. Finally, confirming clinical efficacy, clarifying mechanisms of action, and exploring the integration of this extract into innovative therapeutic strategies represent key steps before any practical medical application.

Conclusions

This study highlights the significant potential of *S.* aqueous extract as a neuroprotective and antioxidant agent. Its effects effectively counteract neurotoxicity, oxidative stress, and behavioral alterations induced by MSG. These results provide a scientific basis for the traditional use of *S. birrea* in the prevention and treatment of cognitive deficits, thus confirming its promising therapeutic value.

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Conflict of interest

The authors declare no conflict of interest.

Author contributions

Study design (RN, AHM), manuscript drafting, data analysis, and interpretation (RN, AHM, ENB), and supervision and guidance to ensure that the manuscript met quality standards (ENB). All authors listed made valuable contributions to the manuscript design, data collection, analysis, and interpretation. All authors reviewed the final version of the manuscript and approved it for publication. Each author was sufficiently involved in the work to assume overall responsibility for appropriate portions of its content.

Ethical statement

The *in vivo* experimental protocols were fully reviewed and approved by the Animal Experimentation Ethics Committee of the University of Ngaoundéré. All animal experimental procedures strictly adhere to current national and international recommendations, including guidelines issued by the Ministry of Research, to ensure the protection, welfare, and dignity of animals used for scientific purposes. We implement rigorous measures to minimize pain, suffering, and stress in animals, fully applying the 3Rs (Replacement, Reduction, Refinement) to minimize the number of animals used while optimizing the quality of care provided.

Data sharing statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

References

[1] Liu F, Bai Q, Tang W, Zhang S, Guo Y, Pan S, *et al*. Antioxidants in neuropsychiatric disorder prevention: neuroprotection, synaptic regulation, microglia modulation, and neurotrophic effects. Front Neurosci 2024;18:1505153. doi:10.3389/fnins.2024.1505153, PMID:39703344.

[2] Baerends E, Soud K, Folke J, Pedersen AK, Henmar S, Konrad L, *et al*. Modeling the early stages of Alzheimer's disease by administering intracerebroventricular injections of human native Aβ oligomers to rats. Acta Neuropathol Commun 2022;10(1):113. doi:10.1186/s40478-022-01417-5, PMID:35974377.

[3] Chen C, Lu J, Peng W, Mak MS, Yang Y, Zhu Z, *et al*. Acrolein, an endogenous aldehyde induces Alzheimer's disease-like pathologies in mice: A new sporadic AD animal model. Pharmacol Res 2022;175:106003. doi:10.1016/j.phrs.2021.106003, PMID:34838693.

[4] Shivasharan BD, Nagakannan P, Thippeswamy BS, Veerapur VP. Protective Effect of Calendula officinalis L. Flowers Against Monosodium Glutamate Induced Oxidative Stress and Excitotoxic Brain Damage in Rats. Indian J Clin Biochem 2013;28(3):292–298. doi:10.1007/s12291-012-0256-1, PMID:24426226.

[5] Essawy AE, Jimmiey EM, Abdel-Wahab WM, Ali RG, Eweda SM, Ab-

dou HM. The protective efficacy of omega-3 polyunsaturated fatty acids on oxidative stress, inflammation, neurotransmitter perturbations, and apoptosis induced by monosodium glutamate in the brain of male rats. Metab Brain Dis 2025;40:114. doi:10.1007/s11011-025-01539-4.

[6] Pradhan B, Jit BP, Maharana S, Ramchandani S, Jena M. Bio-nano Interface and Its Potential Application in Alzheimer's Disease. In: Arakha M, Pradhan AK, Jha S (eds). Bio-Nano Interface. Singapore: Springer; 2022:209–224. doi:10.1007/978-981-16-2516-9_12.

[7] Atoki AV, Aja PM, Ondari EN, Aja PM, Nyakundi E. Advances in Alz heimer's disease therapeutics: biochemistry, exploring bioactive compounds and novel approaches. Int J Food Prop 2023;26(1):2091–2127. doi:10.1080/10942912.2023.2243050.

[8] Cisse A, Gueye M, Ka A, Ndiaye F, Koma S, Akpo LE. Ethnobotanique des plantes médicinales chez les bergers peuls de Widou Thiengoly de la commune de Téssékéré (Ferlo-Nord Sénégal). J Appl Biosci 2016;98:9301–9308. doi:10.4314/jab.v98i1.6.

[9] Boubacar H, Zoubeirou AM. Croissance de Leptadenia hastata (Pers.) Decne., (Asclepiadaceae) en pépinière, une liane comestible au Niger. Int J Adv Res 2023;11(2):81–90.

[10] El-Fitiany RA, Khasawneh MA. Leptadenia pyrotechnica (Forsk.) Decne: from edibility to drug discovery (comprehensive review). Food Rev Int 2022;39(9):6834–6886. doi:10.1080/87559129.2022.2126853.

[11] Russo D, Miglionico R, Carmosino M, Bisaccia F, Andrade PB, Valentão P, *et al*. A Comparative Study on Phytochemical Profiles and Biological Activities of Sclerocarya birrea (A.Rich.) Hochst Leaf and Bark Extracts. Int J Mol Sci 2018;19(1):186. doi:10.3390/ijms19010186.

[12] Harborne JB. Phytochemical methods: A guide to modern techniques of plant analysis. 2nd ed. London: Chapman & Hall; 1973:5–11.

[13] Hebi M, Eddouks M. Évaluation de l'activité antioxydante de Stevia rebaudiana. Phytothérapie 2016;14(1):17–22. doi:10.1007/s10298-015-0999-y.

[14] Enneb H, Belkadhi A, Cheour F, Ferchichi A. Comparaison des composés phénoliques et du pouvoir antioxydant de la plante de henné (Lawsonia inermis L.). J New Sci 2015;20(2):788–793. doi:10.14719/pst.2015.2.1.92.

[15] Simões RR, Dos Santos Coelho I, do Espírito Santo CC, Morel AF, Zanchet EM, Santos AR. Oral treatment with methanolic extract of the root bark of Condalia buxifolia Reissek alleviates acute pain and inflammation in mice: Potential interactions with PGE2, TRPV1/ASIC and PKA signaling pathways. J Ethnopharmacol 2016;185:319–326. doi:10.1016/j.jep.2016.03.050, PMID:27013097.

[16] Benzie IF, Strain JJ. The ferric reducing ability of plasma (FRAP) as a measure of "antioxidant power": the FRAP assay. Anal Biochem 1996;239(1):70–76. doi:10.1006/abio.1996.0292, PMID:8660627.

[17] Rujjanawate C, Kanjanapothi D, Panthong A. Pharmacological effect and toxicity of alkaloids from Gelsemium elegans Benth. J Ethnopharmacol 2003;89(1):91–95. doi:10.1016/s0378-8741(03)00267-8, PMID:14522437.

[18] Fernandes RM, Eiró LG, Chemelo VDS, Alvarenga MOP, Lima RR. Alu minum toxicity and oxidative stress. In: Patel VB, Preedy VR (eds). Toxicology: Oxidative Stress and Dietary Antioxidants. New York, NY: Academic Press; 2021:127–135. doi:10.1016/B978-0-12-819092-0.00014-5.

[19] Xue JS, Li JQ, Wang CC, Ma XH, Dai H, Xu CB, *et al*. Dauricine alleviates cognitive impairment in Alzheimer's disease mice induced by D-galactose and AlCl(3) via the Ca(2+)/CaM pathway. Toxicol Appl Pharmacol 2023;474:116613. doi:10.1016/j.taap.2023.116613, PMID:37414289.

[20] Wilbur KM, Bernheim F, Shafiro OW. Determination of lipid peroxidation. Arch Biochem Biophys 1949;24:305–310.

[21] Beers RF Jr, Sizer IW. A spectrophotometric method for measuring the breakdown of hydrogen peroxide by catalase. J Biol Chem 1952; 195(1):133–140. doi:10.1016/S0021-9258(19)50881-X, PMID:14938361.

[22] Ellman GL. Tissue sulfhydryl groups. Arch Biochem Biophys 1959; 82(1):70–77. doi:10.1016/0003-9861(59)90090-6, PMID:13650640.

[23] Ellman GL, Courtney KD, Andres V Jr, Feather-Stone RM. A new and rapid colorimetric determination of acetylcholinesterase activity. Biochem Pharmacol 1961;7:88–95. doi:10.1016/0006-2952(61)90145-9, PMID:13726518.

[24] Olas B. Marula [Sclerocarya birrea (A. Rich.) Hochst.] products as a food and medicine. Front Pharmacol 2025;16:1552355. doi:10.3389/fphar.2025.1552355, PMID:40041496.

[25] Machu L, Misurcova L, Ambrozova JV, Orsavova J, Mlcek J, Sochor J, *et al*. Phenolic content and antioxidant capacity in algal food products. Molecules 2015;20(1):1118–1133. doi:10.3390/molecules20011118, PMID:25587787.

[26] Taha M, Mosaddik A, Rahim F, Ali S, Ibrahim M, Almandil NB. Synthesis, antiglycation and antioxidant potentials of benzimidazole derivatives. Journal of King Saud University-Science 2020;32(1):191–194. doi:10.1016/j.jksus.2018.04.003.

[27] Jiang T, Sun Q, Chen S. Oxidative stress: A major pathogenesis and potential therapeutic target of antioxidative agents in Parkinson's disease and Alzheimer's disease. Prog Neurobiol 2016;147:1–19. doi:10.1016/j.pneurobio.2016.07.005, PMID:27769868.

[28] Liao R, Wood TR, Nance E. Superoxide dismutase reduces monosodium glutamate-induced injury in an organotypic whole hemisphere brain slice model of excitotoxicity. J Biol Eng 2020;14:3. doi:10.1186/s13036-020-0226-8, PMID:32042309.

[29] Ngbolua KN, Mihigo SO, Liyongo CI, Ashande MC, Tshibangu DST, Zoawe BG, *et al*. Ethno-botanical survey of plant species used in traditional medicine in Kinshasa city (Democratic Republic of the Congo). Trop Plant Res 2016;3(2):413–417.

[30] Nonmarmbaye R, Kouemou N, Neteydji S, Njapdounke JSK, Willy TNS, Bum EN. Mnemonic and neuroprotective properties of *Sclerocarya birrea* root bark decoction on mouse model of monosodium glutamate induced neurotoxicity in volve by its antioxidant activities. GSC Biological and Pharmaceutical Sciences 2021;17(1):193–203. doi:10.30574/gscbps.2021.17.1.0318.

[31] Boix CP, Lopez-Font I, Cuchillo-Ibañez I, Sáez-Valero J. Amyloid precursor protein glycosylation is altered in the brain of patients with Alzheimer's disease. Alzheimers Res Ther 2020;12(1):96. doi:10.1186/s13195-020-00664-9, PMID:32787955.

[32] Huang DS, Yu YC, Wu CH, Lin JY. Protective Effects of Wogonin against Alzheimer's Disease by Inhibition of Amyloidogenic Pathway. Evid Based Complement Alternat Med 2017;2017:3545169. doi:10.1155/2017/3545169, PMID:28680449.

[33] Lobo V, Patil A, Phatak A, Chandra N. Free radicals, antioxidants and functional foods: Impact on human health. Pharmacogn Rev 2010;4(8):118–126. doi:10.4103/0973-7847.70902, PMID:22228951.

[34] Firdaus Z, Kumar D, Singh SK, Singh TD. Centella asiatica Alleviates AlCl (3)-induced Cognitive Impairment, Oxidative Stress, and Neurodegeneration by Modulating Cholinergic Activity and Oxidative Burden in Rat Brain. Biol Trace Elem Res 2022;200(12):5115–5126. doi:10.1007/s12011-021-03083-5, PMID:34984596.

[35] Fitzgerald PJ. Neurodining: Common dietary factors may be substrates in novel biosynthetic pathways for monoaminergic neurotransmitters. Med Hypotheses 2020;138:109618. doi:10.1016/j.mehy.2020.109618, PMID:32070787.

[36] Zhao Y, Dang M, Zhang W, Lei Y, Ramesh T, Veeraraghavan VP, *et al*. Neuroprotective effects of Syringic acid against aluminium chloride induced oxidative stress mediated neu roinflammation in rat model of Alzheimer's disease. J Funct Foods 2020;71:104009. doi:10.1016/j.jff.2020.104009.

[37] Varshavskaya KB, Mitkevich VA, Makarov AA, Barykin EP. Synthetic, Cell-Derived, Brain-Derived, and Recombinant β-Amyloid: Modelling Alzheimer's Disease for Research and Drug Development. Int J Mol Sci 2022;23(23):15036. doi:10.3390/ijms232315036, PMID:36499362.

[38] Lee KH, Cha M, Lee BH. Neuroprotective Effect of Antioxidants in the Brain. Int J Mol Sci 2020;21(19):7152. doi:10.3390/ijms21197152, PMID:32998277.

[39] Nonmarmbaye R, Neteydji S, Mahamt AH, Amboussidi FB, Gadou AH, Willy TNS, *et al*. Antioxidant Properties of Sclerocarya birrea (Anacardiaceae) on Monosodium Glutamate-Induced Memory Loss in the Mus musculus Swiss (Murideae). Journal of Diseases and Medicinal Plants 2025;11(1):12–23. doi:10.11648/j.jdmp.20251101.12.

[40] Wang Y, Li M, Jiang Y, Ji Q. Comparative efficacy of neuroprotective agents for improving neurological function and prognosis in acute ischemic stroke: a network meta-analysis. Front Neurosci 2025;18:1530987. doi:10.3389/fnins.2024.1530987.