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# Targeting Hypothalamic Oxidative Stress and Neuroinflammation: A Novel Neuroprotective Role for Annona Muricata Seed Extract in Aluminium-Induced Alzheimer-Like Neurodegeneration

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## ABSTRACT

Alzheimer's disease (AD) is increasingly recognized as a multisystem neurodegenerative disorder involving oxidative stress and neuroinflammation beyond classical hippocampal pathology. The hypothalamus, a key regulator of metabolic and neuroendocrine homeostasis, remains comparatively underexplored in experimental AD models. This study investigated the effects of aqueous Annona muricata seed extract (SSE) on hypothalamic oxidative injury in an aluminium chloride ($AlCl_3$)-induced Alzheimer's disease–like model in Wistar rats. Adult Wistar rats of both sexes were randomly assigned to five groups (n = 5): control, $AlCl_3$ (100 mg/kg), SSE alone (200 mg/kg), $AlCl_3$ + SSE, and $AlCl_3$ + donepezil (10 mg/kg). Treatments were administered orally for 28 days with blinded outcome assessment. Spatial learning and memory were assessed using the Morris Water Maze. Hypothalamic tissues were stereotaxically dissected and analyzed for oxidative stress markers (superoxide dismutase, catalase, reduced glutathione, malondialdehyde), pro-inflammatory cytokines (TNF-$\alpha$, IL-B), and histomorphological integrity using hematoxylin-eosin and Cresyl violet staining with quantitative morphometry. $AlCl_3$ exposure impaired spatial learning, reduced antioxidant defenses, elevated lipid peroxidation and inflammatory cytokines, and induced neuronal degeneration within the hypothalamus. SSE co-administration significantly attenuated these alterations and preserved neuronal architecture, with effects comparable to donepezil. However, classical AD hallmarks such as amyloid-$\beta$ and tau pathology were not assessed, and findings therefore reflect protection against oxidative and inflammatory neurodegeneration rather than comprehensive AD pathology. These results highlight the hypothalamus as a vulnerable target in experimental Alzheimer-like neurodegeneration and suggest that Annona muricata seed extract warrants further mechanistic and translational investigation.

**Keywords:** Alzheimer's disease, Hypothalamus, Oxidative stress, Neuroinflammation, *Annona muricata*

## 1. Background

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized clinically by cognitive decline and neuropathologically by extracellular amyloid-$\beta$ (A$\beta$) plaques, intracellular neurofibrillary tangles composed of hyperphosphorylated tau, synaptic dysfunction, and progressive neuronal loss. Beyond these classical hallmarks, accumulating evidence indicates that oxidative stress, mitochondrial dysfunction, and chronic neuroinflammation are central drivers of disease progression and neuronal

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vulnerability [1]. While AD research has historically focused on hippocampal and cortical degeneration, emerging data suggest that subcortical regulatory centers, particularly the hypothalamus, are also significantly affected during disease evolution.

The hypothalamus plays a critical role in maintaining metabolic, endocrine, autonomic, and circadian homeostasis. Disruption of hypothalamic integrity has been linked to sleep disturbances, appetite dysregulation, hormonal imbalance, and metabolic abnormalities observed in patients with AD [2]. Neuropathological and imaging studies indicate that hypothalamic dysfunction may occur early in the disease course, potentially contributing to systemic and cognitive decline. Despite this emerging recognition, experimental studies examining targeted hypothalamic vulnerability and protection in AD-related models remain limited, leaving a significant gap in understanding region-specific neurodegenerative mechanisms.

Experimental models employing aluminium chloride ($AlCl_3$) are widely used to induce Alzheimer-like neurodegenerative changes in rodents. Aluminium exposure promotes oxidative stress, impairs mitochondrial function, disrupts proteostasis, and stimulates pro-inflammatory cytokine production, resulting in cognitive deficits and neuronal injury [3, 4]. Although the translational relevance of aluminium models to sporadic AD remains debated, these models reliably reproduce oxidative and inflammatory neurotoxicity with behavioral impairments, making them useful for mechanistic exploration and screening of neuroprotective agents. Importantly, most aluminium-based investigations have focused on the hippocampus and cortex, with comparatively little attention given to hypothalamic pathology.

Annona muricata (soursop) has attracted considerable interest due to its rich phytochemical composition, including flavonoids, phenolic compounds, alkaloids, and acetogenins. Extracts of this plant have demonstrated antioxidant and anti-inflammatory activities in various experimental models [5]. A. muricata may attenuate lipid peroxidation, restore endogenous antioxidant enzymes, and reduce inflammatory mediator production in neurotoxicity paradigms [6]. However, most investigations have examined leaf or pulp extracts, while seed-derived preparations remain comparatively undercharacterized. Furthermore, no study to date has specifically evaluated the effects of A. muricata seed extract on hypothalamic oxidative stress and neuroinflammation in an aluminium-induced neurodegeneration model.

Given the central role of oxidative stress and inflammation in aluminium-induced neurotoxicity, and the emerging recognition of hypothalamic vulnerability in AD-related pathology, investigating targeted neuroprotection within this region is warranted. The present study therefore evaluated the effects of an aqueous Annona muricata seed extract on behavioral performance, hypothalamic oxidative stress markers, pro-inflammatory cytokines, and histomorphological integrity in an $AlCl_3$-induced Alzheimer-like oxidative neurodegeneration model in Wistar rats.

## 2. Materials and methods

### 2.1. Ethical approval

All experimental procedures followed the National Institutes of Health *Guide for the Care and Use of Laboratory Animals* (2011) and were approved by the University Ethical Review Committee (UERC), Olabisi Onabanjo University, Ago-Iwoye (Approval No: OOU/SCIENG/EC/241084). All methods were performed in accordance with ARRIVE 2.0 guidelines [7]. All efforts were made to minimize animal suffering and reduce the number of animals used. A randomized, controlled, blinded design was employed.

### 2.2. Experimental animals and housing conditions

Adult male and female Wistar rats (180–220 g) were obtained from the Animal House Unit, Olabisi Onabanjo University. Sex identification was based on external genitalia and confirmed by testicular palpation in males. Animals were housed in ventilated polypropylene cages under controlled conditions (temperature 28–31°C, relative humidity 40–70%, 12 h light/dark cycle) with ad libitum access to water and standard chow. Rats were acclimatized for two weeks prior to the experiment.Animals were stratified by body weight and sex before randomization to minimize baseline variability. To minimize biological variance, animals were stratified by sex and weight before randomization [8]. Sex distribution per group was balanced. Sex was not analyzed as an independent factor in statistical testing and is acknowledged as a limitation.

### 2.3. Sample size determination

Sample size (n = 5 per group) was determined based on previous aluminium-induced neurotoxicity studies reporting large effect sizes in oxidative stress and behavioral outcomes [8]. Using an expected large effect size ($f \geq 0.40$), $\alpha = 0.05$, and power $(1\text{-}\beta) = 0.80$ for one-way ANOVA, a minimum of five animals per group was considered sufficient.

### 2.4. Plant collection, authentication, and extract preparation

Fresh *Annona muricata* fruits were purchased from Sabo Market, Sagamu, Ogun State, Nigeria, and authenticated at the Herbarium, Department of Plant Biology and Biotechnology, University of Benin (Voucher No: UBHa 0205). Seeds were washed, air-dried (10–14 days), and milled to fine powder.

Aqueous extraction was performed by macerating 200 g of powdered seed in 1000 mL distilled water for 48 hours with intermittent agitation. The filtrate was concentrated using a rotary evaporator at 40–45 °C and stored at 4 °C until use. Extract yield (%) was calculated to enhance reproducibility [9].

Extraction yield (%) was calculated as:

$$\text{Yield (\%)} = \{\text{Weight of dried extract} / \text{Weight of powdered material}) \times 100\}$$

Microbial screening and contamination checks were performed according to WHO guidelines [10].

### 2.5. Phytochemical screening

Qualitative phytochemical tests (flavonoids, tannins, alkaloids, steroids, triterpenoids, saponins, cardiac glycosides, reducing sugars) were performed using standard methods adopted in the Pharmacology Department, Olabisi Onabanjo University. For high-impact reproducibility, tests were performed in triplicate and validated using reagent blanks [11].

### 2.6. Standard drug

Donepezil hydrochloride (10 mg; Wockhardt) equivalent to 9.12 mg was obtained from Skybet Pharmaceuticals, Sagamu, Nigeria. Purity was confirmed by checking batch certification and manufacturer COA [12].

### 2.7. Experimental design

Twenty-five rats were randomly assigned to five groups (n = 5):

**C (Control):** distilled water
**T1:** $AlCl_3$ (100 mg/kg)
**T2:** *A. muricata* seed extract (200 mg/kg)
**T3:** $AlCl_3$ (100 mg/kg) + seed extract (200 mg/kg)
**T4:** $AlCl_3$ (100 mg/kg) + donepezil (10 mg/kg)

All treatments were administered orally for 28 days. The $AlCl_3$ dose was selected based on established protocols inducing Alzheimer-like oxidative and inflammatory changes [13]. Randomization was performed using a computer-generated block-randomization schedule [14]. All outcome assessors (behavioral, biochemical, histological) were blinded to treatment groups.

### 2.8. Neurobehavioral assessment (Morris water maze)

Spatial learning and memory were evaluated on day 28 using the Morris

Spatial learning and memory were assessed on days 25–28 using the Morris Water Maze [15].

- Training protocol:

Four acquisition trials per day for four consecutive days.
Escape latency recorded for each trial.
Swim speed recorded to control for motor impairment.

- Probe trial:

Platform removed.
Time spent in target quadrant recorded.
Directional errors documented.
Water temperature was maintained at 25 ± 1°C. Visual cues remained constant throughout testing.

### 2.9. Sample collection

After overnight fasting, rats were euthanized by cervical dislocation. Brains were rapidly excised, and the hypothalamus was dissected using anatomical landmarks (optic chiasm, mammillary bodies, hypothalamic sulcus).

Dissection followed stereotaxic coordinates from Paxinos & Watson's Rat Brain Atlas [16].

Each hypothalamus was divided into two portions:
Biochemical assays (stored at –20°C)
Histology (fixed in 10% neutral-buffered formalin)

### 2.10. Hypothalamic tissue homogenization

Samples were homogenized in ice-cold phosphate-buffered saline (pH 7.4), centrifuged at 3000 rpm for 15 min at 4°C, and supernatants stored for assays. Standard ELISA kits typically detect in the range of <10 pg/mL, while ultra-sensitive kits can detect <0.5 pg/mL. Protein concentration was quantified using the Bradford method for normalization [17].

### 2.11. Oxidative stress biomarkers

#### 2.11.1. Catalase activity

Catalase activity was measured using the method described by Sinha [18]. The assay involved the

reaction of catalase with hydrogen peroxide, and the resulting decrease in absorbance was monitored to quantify enzyme activity. Expressed in mass units per volume, U/mg protein.

#### 2.11.2. Glutathione (GSH) measurement

Glutathione levels were determined using the DTNB method as outlined by Giustarini et al. [19]. This spectrophotometric assay involves the reduction of DTNB (5,5'-dithiobis(2-nitrobenzoic acid)) in the presence of glutathione, allowing for the quantification of GSH concentration. Expressed in mass units per volume, nmol/mg protein.

#### 2.11.3. Superoxide dismutase (SOD) activity

Superoxide dismutase activity was assessed by evaluating the inhibition of pyrogallol autoxidation, as described by Sun et al. [20]. The rate of increase in absorbance at 420 nm was measured, as it reflects the enzyme's ability to scavenge superoxide radicals. Expressed in mass units per volume, mg/dl.

#### 2.11.4. Malondialdehyde (MDA) level determination

Malondialdehyde levels were determined using the thiobarbituric acid reactive substances (TBARS) assay, following the methodology developed by Gutteridge and Halliwell [21]. This method quantifies MDA, a byproduct of lipid peroxidation, through its reaction with thiobarbituric acid to form a colored complex that can be measured spectrophotometrically. Expressed in mass units per volume, mg/dl.

Assays were run in duplicate, and intra-assay CV $<$ 10% was required for acceptance [22].

### 2.12. Inflammatory cytokines

Hypothalamic TNF-$\alpha$ and IL-1$\beta$ were quantified using rat-specific ELISA kits following manufacturer protocols. Typically expressed in mass units per volume, pg/g. Sensitivity and precision were confirmed as described by Robak et al. [23]. Calibration curves ($R^2 > 0.99$) and spike-recovery tests were performed [24].

### 2.13. Histological and morphometric analysis (H&E and Cresyl violet)

Fixed hypothalamic tissues were processed through graded alcohols, cleared in xylene, embedded in paraffin, and sectioned at 5 $\mu$m. Hematoxylin & Eosin: assessed neuroarchitecture, vascular integrity, neuronal density. Cresyl Violet (Nissl stain): evaluated neuronal morphology, Nissl substance distribution, chromatolysis.

Sections were examined using a light microscope with digital imaging. Quantitative morphometry was performed using ImageJ (cell counts per mm$^2$, Nissl intensity index) following blinded scoring [25]. A minimum of three non-overlapping fields per animal were analyzed.

Three non-overlapping fields per section per animal were analyzed using ImageJ software.

Quantitative measures:
Neuronal density (cells/mm$^2$)
Nissl staining intensity index (arbitrary units)

Sampling was performed at standardized anatomical levels; however, stereology was don using Image J.

### 2.14. Statistical analysis

Data were analyzed with GraphPad Prism 10.1. Normality was assessed using the Shapiro–Wilk test. Group differences were evaluated with one-way ANOVA followed by Tukey's post hoc test. Data are presented as mean $\pm$ SD, with significance at $p < 0.05$. Sex was not included as an independent variable in the statistical model.

## 3. Result

### 3.1. Effect of soursop seed aqueous extract on weight evaluation and neurobehavioural in aluminium chloride-induced rats

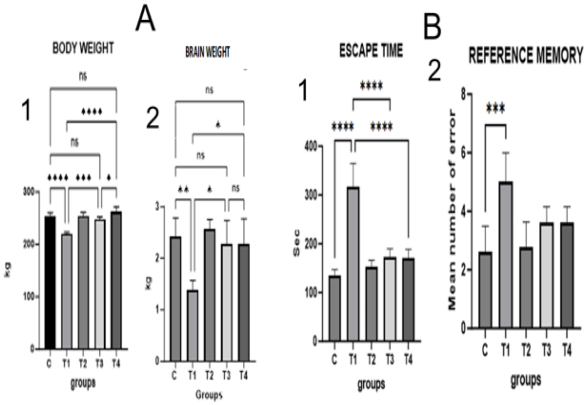


**Fig. 1.** A. Effect of soursop seed aqueous extract on body and brain weight in aluminium chloride-induced rats. (A1) Body weight, (A2) Brain weight. B. Assessment of spatial learning and reference memory using Morris Water Maze in aluminium chloride-induced rats. (B1) Time to detect safe zone (spatial learning), (B2) Directional errors toward safe zone (reference memory). Groups: C (physiological saline), T1 (Aluminium Chloride), T2 (soursop extract), T3 (combination T1+T2), T4 (T1 + Donepezil). Values expressed as mean $\pm$ SD. (ns = not significant; *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001).

### 3.2. Effect of soursop seed aqueous extract on hypothalamic oxidative stress and proinflammatory biomarkers in aluminium chloride-induced rats

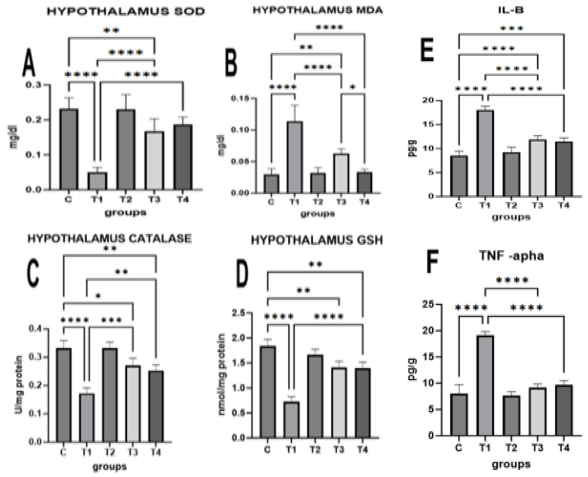


**Fig. 2.** Effect of soursop seed aqueous extract on hypothalamic oxidative stress and pro-inflammatory cytokines biomarkers in aluminium chloride-induced rats. (A) SOD activity, (B) MDA levels, (C) Catalase activity, (D) GSH levels (E) Interleukin-1$\beta$ levels, (F) TNF-$\alpha$ levels. Groups: C (physiological saline), T1 (Aluminium Chloride), T2 (soursop extract), T3 (combination T1+T2), T4 (T1 + Donepezil). Values expressed as mean ± SD. (*p<0.05; **p<0.01; ***p<0.001; ****p<0.0001).

### 3.3. Photomicrograph of hypothalamic tissue sections stained with Hematoxylin and Eosin (H&E) in aluminium chloride-induced rats

Group C (Control): The control group demonstrates preserved hypothalamic cytoarchitecture. Black arrows indicate neurons with vesicular nuclei and prominent nucleoli. Orange arrows point to glial cells. The neuropil exhibits homogeneous eosinophilic staining with no evidence of gliosis or inflammatory infiltration.

Group T1 ($AlCl_3$-induced Alzheimer model): This group exhibits severe neuropathological alterations. The red circle highlights neuronal chromatolysis with nuclear pyknosis. Yellow arrows indicate extensive cytoplasmic vacuolation and spongiosis. Red arrows point to inflammatory cell infiltration Fig. 4. Black arrows show dark neurons with loss of Nissl bodies and neuronal dropout.

Group T2 (Soursop extract alone): The histological architecture closely resembles the control group with well-preserved neuronal integrity. Black arrows indicate neurons with euchromatic nuclei and visible Nissl granules. Orange circles highlight intact neurons with no cytoplasmic vacuolation or pathological features.

Group T3 (Combination treatment): This group demonstrates significant neuroprotective alterations. The orange circle shows neurons with restored cellular architecture and reduced chromatolytic changes. Black arrows point to neurons with recovered Nissl substance. The neuropil shows diminished spongiosis and minimal inflammatory presence.

Group T4 (Donepezil treatment): Similar cytoprotective effects are evident. The red circle highlights neurons with preserved morphology. White arrows indicate reversal of tissue rarefaction. Black arrows show neurons with improved structural integrity and reduced nuclear pyknosis compared to T1.

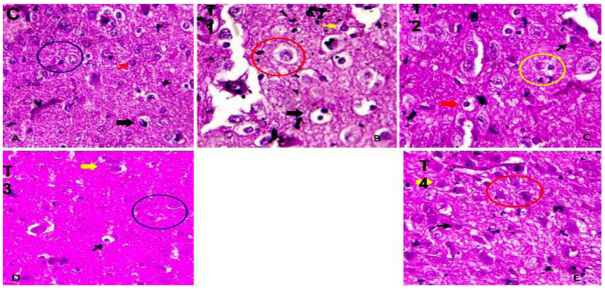


**Fig. 3.** Photomicrograph of hypothalamic tissue sections stained with Hematoxylin and Eosin (H&E) in aluminium chloride-induced rats. Groups: C (physiological saline), T1 (Aluminium Chloride), T2 (soursop extract), T3 (combination T1+T2), T4 (T1 + Donepezil). Magnification: 400×.

### 3.4. Photomicrograph and morphometric analysis of hypothalamic tissue sections stained with Cresyl violet in aluminium chloride-induced rats.

Group C: The control group demonstrates normal neuronal morphology with abundant Nissl substance. Black circles indicate healthy neurons with intensely stained Nissl bodies throughout the cytoplasm. Red arrows point to neurons with clear, pale nuclei surrounded by basophilic cytoplasm. Yellow arrows show well-preserved neuronal architecture with no degenerative changes.

Group T1: This group exhibits severe neurodegenerative changes. The red circle highlights a neuron with marked chromatolysis and loss of Nissl substance. Red arrows point to ghost neurons with severely depleted basophilic staining, indicating advanced neuronal degeneration. The overall neuronal population shows reduced Nissl staining intensity and increased pallor.

Group T2: The histological features closely resemble the control group. Red arrows indicate neurons with preserved Nissl substance and intense basophilic staining. Purple circles highlight healthy neurons with abundant Nissl granules. No evidence of chromatolysis or neuronal degeneration is observed.

Group T3: This group demonstrates significant neuroprotective effects. Black arrows point to

neurons with restored Nissl substance and improved basophilic staining. Red arrows indicate recovery of cytoplasmic Nissl granules. The neuronal population shows markedly improved staining intensity compared to T1.

Group T4: Similar neuroprotective features are evident. Green arrows indicate neurons with preserved Nissl bodies. Yellow arrows point to areas with restored basophilic staining. Black circles highlight neurons with improved cytoplasmic integrity and reduced chromatolytic changes compared to the Alzheimer model group.

**A** - Quantitative morphometric analysis of hypothalamic neurons in aluminium chloride-induced rats using Cresyl violet staining. (A) Cell density (cells/mm$^2$). It demonstrate $AlCl_3$ exposure led to severe neuronal loss in the hypothalamus. Rats in the Alzheimer model group (T1) showed significantly reduced cell density compared to the control and all other groups. Treatment with A. muricata seed extract (T3) and Donepezil (T4) both significantly preserved neuronal populations relative to T1. Rats receiving the extract alone (T2) maintained cell density comparable to the control group.

**B** - Quantitative morphometric analysis of hypothalamic neurons in aluminium chloride-induced rats using Cresyl violet staining. (A) Cell density (cells/mm$^2$), (B) Nissl intensity index (arbitrary units) $AlCl_3$ exposure resulted in marked chromatolysis with severe depletion of Nissl substance. Rats in the Alzheimer model group (T1) exhibited significantly reduced Nissl staining intensity compared to the control and all other groups. Both A. muricata seed extract (T3) and Donepezil (T4) treatment significantly restored Nissl intensity relative to T1, Rats receiving the extract alone (T2) displayed Nissl intensity comparable to the control group.

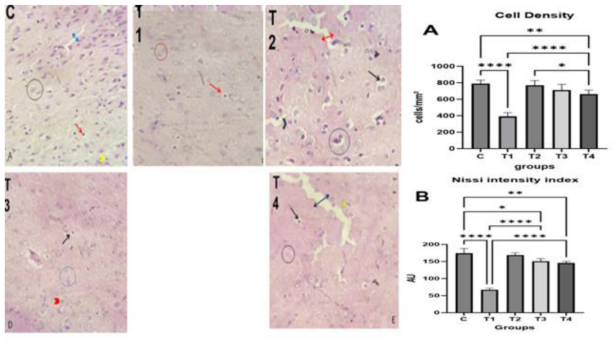


**Fig. 4.** Photomicrograph of hypothalamic tissue sections stained with Cresyl violet in aluminium chloride-induced rats. Groups: C (physiological saline), T1 (Aluminium Chloride), T2 (soursop extract), T3 (combination T1+T2), T4 (T1 + Donepezil). Magnification: 200×.

## 4. Discussion

Neurodegeneration in Alzheimer's disease (AD) is increasingly recognized as a systems-level disorder that extends beyond classical hippocampal and cortical circuits to involve subcortical regulatory centers critical for homeostasis and survival [2]. Among these, the hypothalamus has emerged as a vulnerable yet underexplored target of AD-related pathology, with accumulating evidence linking hypothalamic dysfunction to early disturbances in cognition, circadian rhythm, feeding behavior, and neuroendocrine regulation [2, 26]. In this context, the present study provides novel experimental evidence that aluminium chloride ($AlCl_3$)-induced neurotoxicity extends to the hypothalamus and that aqueous *Annona muricata* seed extract confers marked neuroprotective effects at behavioral, biochemical, and histomorphological levels.

Chronic $AlCl_3$ exposure in the present study resulted in pronounced spatial learning and reference memory deficits, as evidenced by impaired Morris Water Maze performance (Fig. 1). These findings are consistent with previous reports demonstrating that aluminium disrupts synaptic plasticity, induces oxidative stress, and interferes with neurotransmission in brain regions involved in learning and memory [1, 3]. While cognitive deficits in aluminium models are often attributed primarily to hippocampal injury, emerging data suggest that hypothalamic degeneration may indirectly exacerbate cognitive decline by disrupting neuromodulatory and metabolic signaling pathways that support cortical and hippocampal function [2].

The observed reduction in brain weight following $AlCl_3$ exposure further supports widespread neurodegeneration and neuronal loss (Fig. 1), a phenomenon reported in aluminium-based AD models and associated with oxidative damage, mitochondrial dysfunction, and neuronal apoptosis [3]. Importantly, SSE treatment significantly restored brain weight and improved behavioral outcomes, suggesting attenuation of aluminium-induced neurodegenerative processes.

A key finding of this study is the pronounced oxidative imbalance observed in the hypothalamus following $AlCl_3$ exposure, characterized by decreased antioxidant enzyme activities (SOD, catalase, and GSH) and elevated lipid peroxidation (MDA) (Fig. 2). Aluminium is known to promote redox cycling, impair mitochondrial electron transport, and generate reactive oxygen species (ROS), thereby overwhelming endogenous antioxidant defenses and triggering neuronal injury [3, 21]. The hypothalamus may be particularly susceptible to oxidative injury due to its

high metabolic activity and dense vascularization, which facilitate aluminium accumulation and ROS generation [3]. Restoration of antioxidant defenses following *A. muricata* administration strongly indicates that the extract mitigates aluminium-induced oxidative stress, likely through direct free-radical scavenging and/or upregulation of endogenous antioxidant systems. Similar antioxidant-restorative effects of *A. muricata* extracts have been reported in other models of neurotoxicity and oxidative injury [5, 6].

Neuroinflammation is a defining feature of aluminium-induced neurodegeneration and AD pathology, driven by microglial activation and excessive production of pro-inflammatory cytokines such as TNF-$\alpha$ and IL-1$\beta$ [27]. The significant elevation of hypothalamic TNF-$\alpha$ and IL-1$\beta$ observed in $AlCl_3$-treated rats in this study aligns with these established mechanisms (Fig. 2). Notably, SSE treatment markedly reduced hypothalamic pro-inflammatory cytokine levels, comparable to the effects of donepezil. This anti-inflammatory action may reflect the presence of bioactive flavonoids, alkaloids, and acetogenins in *A. muricata* [6]. Attenuation of neuroinflammation is particularly relevant in the hypothalamus, where chronic inflammatory signaling can disrupt neuroendocrine regulation and exacerbate systemic metabolic dysfunction [2].

Histological and morphometric analyses provide structural evidence supporting the biochemical and behavioral findings. $AlCl_3$ exposure produced severe hypothalamic neuronal degeneration, including chromatolysis, cytoplasmic vacuolation, spongiosis, neuronal dropout, and depletion of Nissl substance (Figs. 3 and 4). These features are characteristic of oxidative and inflammatory neuronal injury and have been described in aluminium-induced AD models affecting other brain regions [28].

Treatment with *A. muricata* significantly preserved hypothalamic cytoarchitecture, restored neuronal density, and improved Nissl staining intensity, indicating protection of protein synthesis machinery and neuronal viability. The recovery of Nissl substance suggests improved ribosomal integrity and cellular metabolic function, which are critical for neuronal survival and synaptic maintenance [29]. Importantly, these histological improvements paralleled those observed with donepezil, reinforcing the therapeutic relevance of *A. muricata*.

## 5. Conclusion

Aluminium chloride induced cognitive deficits, oxidative stress, neuroinflammation, and structural degeneration within the hypothalamus of Wistar rats. Aqueous Annona muricata seed extract attenuated these alterations, restoring antioxidant balance, reducing pro-inflammatory cytokines, and preserving neuronal integrity. These findings indicate region-specific neuroprotection in an oxidative Alzheimer-like neurodegeneration model.

## Acknowledgment

The department of anatomy, Olabisi Onabanjo Uinveristy for providing a conducive research environment and equipment for the conduction of this research.

## Conflict of interest

The authors declared no conflict of interest.

## Ethical Approval

This study received approval from Ethical Review Committee (UERC), Olabisi Onabanjo University, Ago Iwoye (OOU/SCIENG/EC/241084) and conducted in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals.

## Data availability

The authors confirm that the data supporting the findings of this study are available within the article.

## Funding statement

This research received no external funding.

## Author contribution

Opeyemi Bamgbose conceptualized the study; Omotosho Akanji collected data; Dorcas Taiwoola conducted experiments; Ponle Fakunle provided critical revisions; Olukayode Odubela performed statistical analyses; Adeseye Olayemi contributed to the literature review; Boluwatife Akanbi managed data; David assisted with project coordination and manuscript review.

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