

Curcumin-Enriched *Curcuma longa* Extract in Aluminum-Induced Neurotoxicity: Impact on Oxidative Stress, Inflammatory Response, and Neural Health

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ABSTRACT

Aluminum exposure is linked to neurodegeneration due to oxidative stress and neuroinflammation, impacting cognitive health. *Curcuma longa*, containing the polyphenol curcumin, is recognized for its antioxidant and anti-inflammatory properties and shows potential in counteracting metal-induced neurotoxicity. This study investigates the neuroprotective effects of curcumin-enriched *Curcuma longa* extract against aluminum-induced neurotoxicity, focusing on oxidative stress, inflammation, and neural health indicators. Mice were assigned to six groups, receiving normal saline, various doses of *Curcuma longa* extract, aluminum chloride (AlCl₃), or a combination of AlCl₃ and *Curcuma longa* extract for 14 days. Oxidative stress markers (SOD, MDA), inflammatory cytokines (IL-1, IL-6), behavioral assessments, and histopathology were evaluated. Mice exposed to AlCl₃ exhibited increased oxidative stress (reduced SOD, elevated MDA) and inflammation (higher IL-1, IL-6), along with impaired cognitive performance. *Curcuma longa* extract, particularly at higher doses, mitigated these effects, with decreased oxidative and inflammatory markers, improved behavior, and reduced neural tissue damage. Curcumin-enriched *Curcuma longa* extract demonstrates neuroprotective potential by reducing aluminum-induced oxidative stress and inflammation, suggesting its promise in addressing neurotoxicity. Optimal dosing enhances its efficacy, with implications for therapeutic applications in neurodegenerative conditions.


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Introduction

The cerebrum, or telencephalon, is the largest part of the brain, divided into two hemispheres and liver's vulnerability stems from its exposure to responsible for processing sensory information, motor control, and higher cognitive functions [1]. Neurotoxins, such as aluminum, pose significant threats to cerebral health. Aluminum, a lightweight yet toxic metal found widely across the environment, has no known biological function and exhibits neurotoxic effects, particularly through the generation of oxidative stress, which contributes to the pathology of neurodegenerative diseases [2, 3].

Chronic exposure to aluminum compounds, including aluminum chloride (AlCl_3), leads to progressive neurodegenerative changes, with aluminum ions crossing the blood-brain barrier and accumulating in neural tissues like the hippocampus, cortex, and corpus callosum [4] [5]. High aluminum levels have been associated with neuroinflammatory responses and cognitive decline, contributing to diseases such as Alzheimer's and Parkinson's [6, 7].

Given the risks posed by aluminum exposure, there is increasing interest in plant-derived compounds with neuroprotective properties. *Curcuma longa*, commonly known as turmeric, contains the polyphenolic compound curcumin, which is known for its antioxidant and anti-inflammatory effects [8]. Epidemiological evidence suggests a positive correlation between *Curcuma longa* consumption and cognitive function, with studies indicating that curcumin binds redox-active metals, reducing oxidative stress and offering neuroprotective effects [9]. However, curcumin's therapeutic potential is limited by its poor water solubility and bioavailability, requiring combination with enhancers like piperine to improve brain uptake [10, 11].

This study evaluates the efficacy of a curcumin-enriched *Curcuma longa* extract in an aluminum-induced neurotoxicity model, examining its impact on oxidative stress, inflammation, and neural health. The findings could inform therapeutic strategies for neurodegenerative diseases linked to metal toxicity.

Materials and Methods

Ethical approval for Study

All experimental procedure was carried out in accordance with the ethical guidelines as stipulated by the Research Ethics Committee of the College of Health Sciences, Benue State University, Makurdi. A copy of the research proposal was submitted to the committee for ethical approval.

Animal procurement, housing, and acclimatization

Thirty male mice (30–45 g) were obtained from a certified breeder and housed in six plastic cages (30 cm x 20 cm), with five mice per cage. Animals were maintained under controlled conditions ($25 \pm 1^\circ\text{C}$, 12-hour light/dark cycle) and provided ad libitum access to standard pellet feed and water. All procedures followed guidelines approved by the Institutional Animal Care and Use Committee (IACUC) [12].

Plant procurement and extract preparation

Fresh *Curcuma longa* rhizomes were sourced from Wurukum Market, Benue State, Nigeria. The rhizomes were washed to remove debris, cut into small pieces, and air-dried at room temperature. The dried material was ground into a fine powder, and 306.1 g of the powder was macerated in 2000 ml of distilled water for 48 hours. The aqueous extract was filtered, and the filtrate was lyophilized to obtain a powdered extract, which was stored in airtight containers at 4°C until use. The extract was freshly prepared in distilled water each day prior to administration [13].

Other materials

The following materials were used: gloves, sterile containers, syringes, needles, dissecting board and kit, fixative (10% formal saline), hematoxylin and eosin (H&E) stain, cover slips, glass slides, microscope, microtome, centrifuge, distilled water, feeding plates, and water bottles.

Experimental design

The mice were randomly divided into six groups ($n=5$ per group) and acclimated for 10 days before treatments. Baseline weights were recorded following acclimatization. Treatments were administered once daily for 14 days as follows:

Group 1 (Control Group): 5 ml/kg body weight of Normal Saline once daily for 14 days

Group 2: 250 mg/kg per body weight of *Curcuma longa* Extract once daily for 14 days

Group 3: 500 mg/kg per body weight of *Curcuma longa* Extract once daily for 14 days

Group 4: 100mg/kg per body weight of AlCl_3 once daily for 14 days

Group 5: 250 mg/kg body weight of *Curcuma longa* + 100mg/kg of AlCl_3 for 14 days (Low - Dose Combination Group)

Group 6: 500 mg/kg body weight of *Curcuma longa* + 100mg/kg of AlCl_3 for 14 days (High - Dose Combination Group)

Animal sacrifice and sample collection

At the end of the 14-day treatment, the mice were fasted overnight and euthanized via chloroform inhalation. Blood samples were collected in sterile

containers for biochemical assays. Brain tissues (cerebrum) were harvested and fixed in 10% formal saline for histological processing and analysis.

Behavioral studies: morris water maze test

Spatial learning and memory were assessed using the Morris Water Maze. The test was conducted in a basin filled with water (25°C) to a depth of 20 cm and colored with gentian violet for contrast. A stone platform was placed at the center. During training trials over three consecutive days, each mouse was introduced to the maze twice daily and given up to 90 seconds per trial to locate the platform, with a 30-second rest period between trials. In the test phase, each mouse was placed in the maze with its head facing the wall and allowed to locate the platform. If the mouse failed within 90 seconds, it was gently placed on the platform to rest for an equivalent time. The escape latency, or time to locate the platform, was recorded to evaluate learning and memory [14].

Determination of pro-inflammatory cytokines (IL-6, IL-1 β) and oxidative stress

Brain tissue homogenates (10%) were centrifuged at 4000xg for 15 minutes. The supernatant was analyzed for pro-inflammatory cytokines (IL-6) and IL-1 β using enzyme-linked immunosorbent assay (ELISA) kits, following the manufacturer's instructions. Cytokine levels were expressed in pg/ml.

Lipid peroxidation was measured by determining malondialdehyde (MDA) levels in brain tissue homogenates using a thiobarbituric acid (TBA) reaction. Tissue homogenates were prepared in a buffer containing Tris-HCl, EDTA, and butylated hydroxytoluene. Homogenates were incubated with TBA reagents and heated in a water bath at 95°C for 1 hour. Following the addition of a butanol/pyridine mixture, samples were centrifuged at 10,000xg for 10 minutes, and absorbance was read at 532 nm. MDA concentration was calculated using a standard curve and expressed as nmol TBARS/mg protein.

Superoxide dismutase activity was determined following the method by Winterbourn et al. [15] and Rukmini et al. [16], which measures SOD's inhibition of nitro-blue tetrazolium (NBT) reduction. The reaction mixture contained phosphate buffer (0.067M, pH 7.8), riboflavin, methionine, NBT, and the enzyme sample. The mixture was illuminated under a 15W fluorescent lamp for 10 minutes, and absorbance was read at 560 nm. One unit of SOD activity was defined as the enzyme quantity required to inhibit NBT reduction by 50%, and results were expressed as units/mg protein.

Histological analysis

Cerebral tissue was sectioned, fixed in 10% formalin, and processed for paraffin embedding. Sections of 5 μ m thickness were stained with hematoxylin and eosin for histopathological examination. Standard dehydration through graded ethanol series, clearing in xylene, and embedding in paraffin wax were followed. After mounting on slides, sections were dried, dewaxed, rehydrated through decreasing ethanol concentrations, and rinsed. Micrographs were obtained using a Canon PowerShot A80 camera.

Data analysis

Data was subjected to statistical analysis using IBM SPSS version 25. Mean differences between groups was analyzed using Analysis of Variance (ANOVA) and comparison between the means by Tukey HSD post hoc test. P - Values less than 0.05 ($p < 0.05$) were considered statistically significant.

Results

Physical observations: body weight

The body weight data for all groups were analyzed, with results presented as mean \pm standard error of the mean (S.E.M) as shown in figure 1. Statistical comparisons between the control and treatment groups were performed using a one-way analysis of variance (ANOVA) followed by Duncan's multiple range test, with a significance level set at $p < 0.05$.

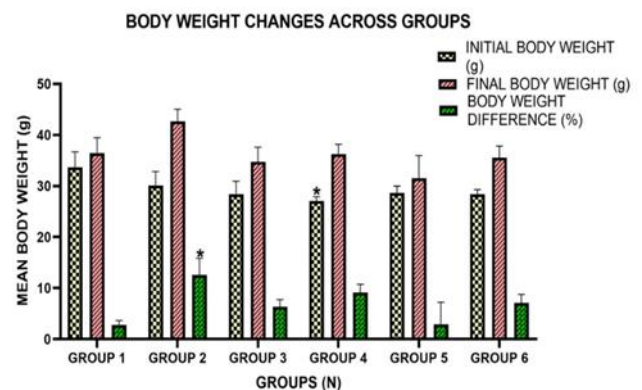


Figure 1: Simple Bar Chart showing the Mean Body Weight Changes across Groups Compared on One - Way ANOVA. N = 5, * = statistically significant difference in mean at $p < 0.05$ compared to the control group (group1).

For initial body weight, Group 4 showed a statistically significant increase compared to the control group (Group 1). At the final body weight measurement, no statistically significant differences were observed between the treatment and control

groups. However, when evaluating the body weight difference (final minus initial weight), Group 2 showed a statistically significant difference relative to the control group (* $p < 0.05$).

Anti-inflammatory markers and oxidative stress: interleukins 1 and 6, superoxide dismutase (SOD) and malondialdehyde (MDA)

The levels of interleukin-1 (IL-1), interleukin-6 (IL-6) superoxide dismutase (SOD) and malondialdehyde (MDA) were assessed across all groups, and the results shown in figures 2 and 3. One-way ANOVA analysis indicated statistically significant increases in both IL-1 and IL-6 levels for Groups 2 - 6 compared to the control group (Group 1), indicating an inflammatory response across these treatment groups (* $p < 0.05$). For SOD activity, Groups 2 - 6 demonstrated statistically significant reductions in comparison to the control group (Group 1), reflecting elevated oxidative stress in these groups (* $p < 0.05$). In contrast, for MDA levels, only Group 2 showed a statistically significant increase compared to the control group (* $p < 0.05$).

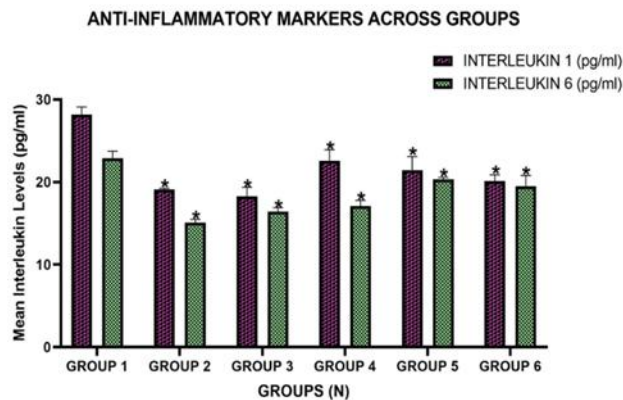


Figure 2: Simple Bar Chart showing the Mean Anti-inflammatory Markers Levels across Groups Compared on One - Way ANOVA. N = 5, * = statistically significant difference in mean at $p < 0.05$ compared to the control group (group1).

Behavioral studies

Behavioral assessments were conducted over multiple days as presented in figure 4, with escape time measured as an indicator of neural function. On the first day, Groups 2 - 6 displayed a statistically significant increase in escape time compared to the control group, indicating possible cognitive impairment (* $p < 0.05$). By day two, only Group 6 showed a significant difference in escape time relative to the control group. On the fourth day of testing, a statistically significant difference was observed solely in Group 5 compared to the control group (* $p < 0.05$).

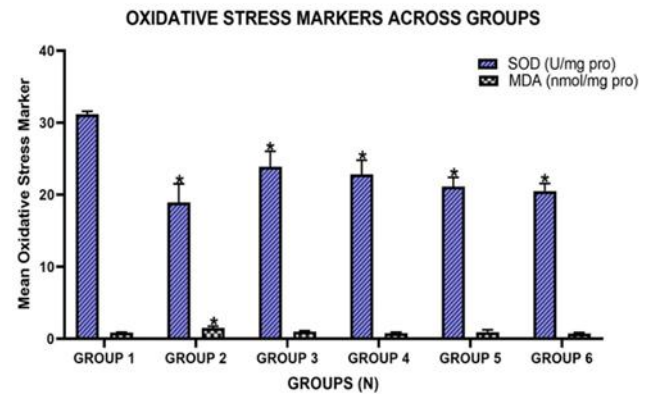


Figure 3: Simple Bar Chart showing the Mean Oxidative Stress Markers Levels across Groups Compared on One - Way ANOVA. N = 5, * = statistically significant difference in mean at $p < 0.05$ compared to the control group (group1)

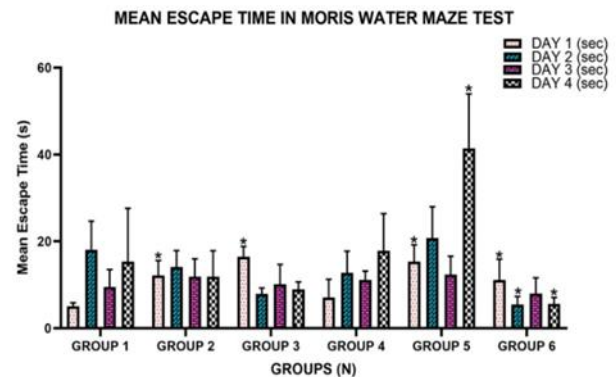


Figure 4: Simple Bar Chart showing the Mean Escape Time in Morris Water Maze Test across Groups Compared on One - Way ANOVA. N = 5, * = statistically significant difference in mean at $p < 0.05$ compared to the control group (group1).

Histological profile

Hematoxylin and Eosin (H & E) sections of the control group (group 1) showed normal cerebral histo-morphology, with intact layers, prominent glial cells and pyramidal neurons. Sections from group 2 mice also showed similar histological features to those of the control group, with intact cell layers and densely packed glial cells and pyramidal neurons. Cerebral histological sections of group 3 mice showed intact cerebral cell layers with hyperchromic glial cell nuclei and pyramidal neurons. Sections from group 4 mice showed marked pathological changes in the cerebrum including disorganization of cell layers, extensive neuropil vacuolization and loss of nerve cells. Pyramidal cells of the cerebral cortex showed irregular shapes, hyperchromic, pyknotic nuclei, surrounded by vacuoles. Sections from group 5 showed marked cellular disorganization, vacuolization and necrotic tissues. These alterations of marked pathological changes in

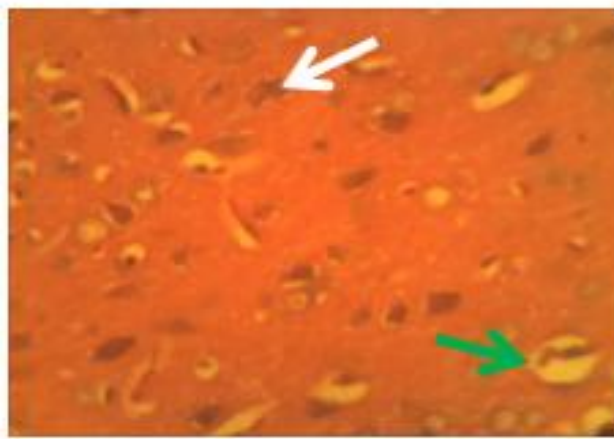
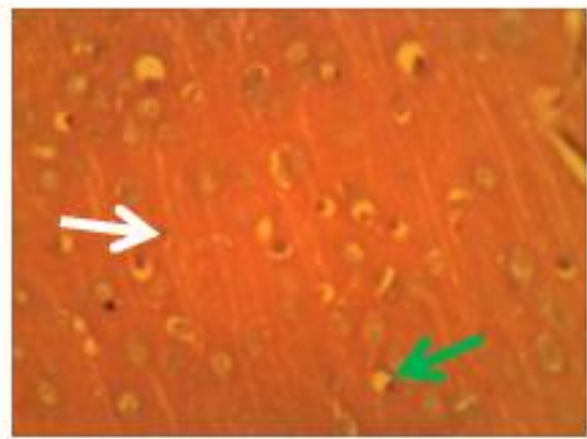
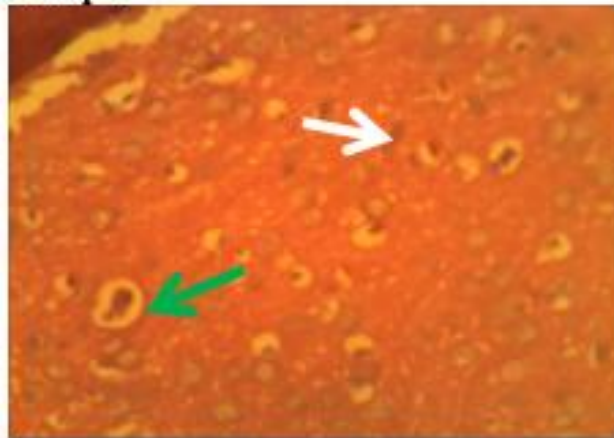
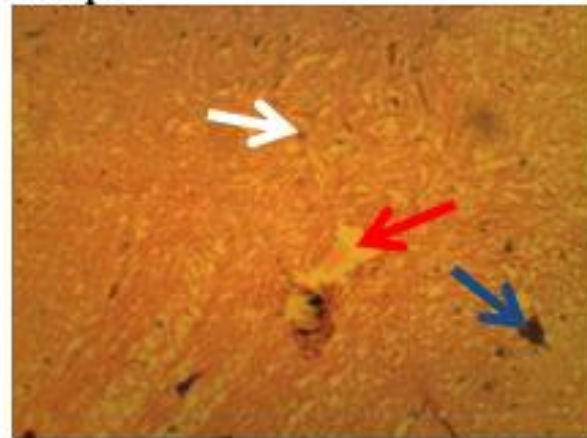
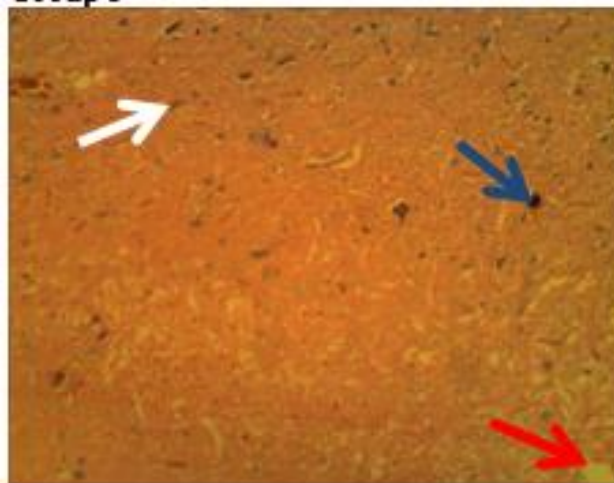
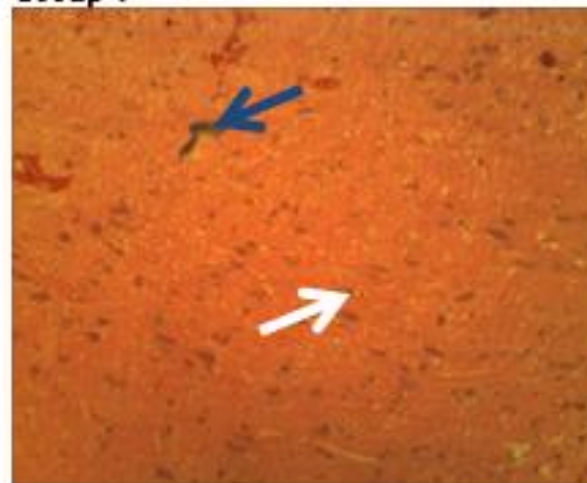
**Group 1****Group 2****Group 3****Group 4****Group 5****Group 6**

Figure 5: Photomicrographs of groups 1 - 6 showing glial cells (white arrows), pyramidal neurons (green arrows), necrotic cellular debris (blue arrows) and vacuolation (red arrows) (H&E x40). Group 1: showing intact cell layers, prominent glial cells and pyramidal neurons (H&E x40). Group 2: showing intact cell layers, densely - packed glial cells and pyramidal neurons (H&E x40). Group 3: showing intact cell layers, densely - packed glial cells with hyperchromic nuclei and pyramidal neurons (H&E x40). Group 4: sections show vacuolation, glial cells with pyknotic nuclei, and necrotic cellular debris, indicating extensive damage (H&E x40). Group 5: sections show vacuolation, glial cells with pyknotic nuclei, and necrotic cellular debris, indicating extensive damage (H&E x40). Group 6: showing intact cell layers, reduced vacuolar changes and less necrotic tissue (H&E x40).

layers, extensive neuropil vacuolization and loss of nerve cells. Notably, in Group 4 and Group 5; Histological sections showed vacuolation, glial cells with pyknotic nuclei, and necrotic cellular debris, indicating extensive damage. Differences in severity were negligible between these groups (H&E x40). In group 6, there was notable decrease in the incidence of neuropathological lesions. There was less disorganization of the cell layers; reduced vacuolar changes and fewer damaged neurons compared to the groups 4 and 5.

Discussion

The findings from this study suggest a protective role of *Curcuma longa* extract against aluminum-induced neurotoxicity, evident in body weight, inflammatory markers, oxidative stress markers, behavioral performance, and cerebral histopathology.

Body weight measurements provide a primary indicator of general health and response to toxic exposure and treatment. Changes in body weight serve as a general indicator of systemic health under toxic exposure and treatment. In this study, the significant weight gain in Group 4 (AlCl₃-only) may reflect initial metabolic dysregulation, possibly due to aluminum-induced alterations in appetite or metabolism. Interestingly, Group 2 (250 mg/kg *Curcuma longa* alone) exhibited a significant body weight change relative to the control, suggesting a dose-dependent metabolic modulation by *Curcuma longa*. This aligns with studies highlighting curcumin's role in regulating lipid and glucose metabolism via pathways such as AMPK activation and suppression of adipogenesis [17]. However, the lack of significant differences in final body weights across most groups indicates that neither AlCl₃ exposure nor *Curcuma longa* supplementation caused pronounced metabolic disturbances, suggesting the extract's safety at tested doses.

The marked increase in IL-1 and IL-6 levels across Groups 2 to 6 reflects a systemic inflammatory response induced by AlCl₃, consistent with previous reports on aluminum's inflammatory effects in neural tissues [18]. The Elevated IL-1 and IL-6 levels in Groups 2 through 6 confirm aluminum-induced systemic inflammation, consistent with aluminum's activation of pro-inflammatory pathways via NF-κB signaling and microglial activation [18]. While these markers were notably higher in AlCl₃-treated groups, the gradual reduction in Groups 5 and 6 with *Curcuma longa* supplementation suggests its dual-phase action, initially enhancing immune response but subsequently attenuating inflammation by downregulating cytokine production [19]. This modulatory role reflects curcumin's ability to regulate inflammatory

mediators such as COX-2, TNF-α, and IL-6, underscoring its potential to counteract neuroinflammation.

SOD activity significantly declined in all treatment groups compared to the control, suggesting that aluminum exposure induced oxidative stress, even with *Curcuma longa* supplementation. This aligns with findings where AlCl₃ exposure impairs the antioxidant defense system by depleting SOD levels [20]. Interestingly, MDA levels were notably elevated only in Group 2, suggesting that while lower doses of *Curcuma longa* may exhibit antioxidant properties, they may not sufficiently counteract aluminum's lipid peroxidative effects at higher oxidative stress levels, as shown in recent studies on curcumin's dose-dependent antioxidative effects [21]. AlCl₃ exposure significantly impaired antioxidant defenses, as indicated by reduced SOD activity in all treatment groups. This aligns with evidence that aluminum disrupts redox homeostasis by generating reactive oxygen species and depleting endogenous antioxidants [20]. Elevated MDA levels, particularly in Group 2, highlight insufficient lipid peroxidation mitigation at lower doses of *Curcuma longa*. These findings emphasize the need for dose optimization to balance the extract's antioxidant efficacy, as supported by studies demonstrating curcumin's dose-dependent attenuation of oxidative damage via upregulation of Nrf2-mediated antioxidant pathways [21].

The protective effects of *Curcuma longa*, particularly at 500 mg/kg (Group 6), suggest dose-dependent efficacy. While Group 4 (AlCl₃ only) exhibited severe neuroinflammation and oxidative stress, Group 6 demonstrated reduced IL-1, IL-6, and MDA levels, alongside improved cognitive performance. These findings align with prior research emphasizing curcumin's dual role as an anti-inflammatory and antioxidant agent [19, 22]. However, the elevated oxidative stress markers in Group 2 highlight the need for dose optimization to achieve maximal neuroprotective benefits.

Behavioral analysis revealed significant cognitive impairment in Groups 2 to 6, evidenced by increased escape times in the water maze test. However, Groups 3 (500 mg/kg *Curcuma longa*) and 6 (AlCl₃ + 500 mg/kg *Curcuma longa*) exhibited progressive improvement over time, suggesting partial cognitive recovery mediated by the neuroprotective effects of curcumin. Curcumin's role in enhancing synaptic plasticity and reducing neuroinflammation likely underpins these outcomes, consistent with prior studies showing its ability to ameliorate neurotoxic damage and restore cognitive function [22, 23].

Cerebral histology demonstrated substantial neuroprotection in Group 6, with reduced neuronal disorganization, hyperchromatic nuclei, and vacuolar changes compared to AlCl₃-only groups. These observations align with reports of curcumin preserving neuronal structure, mitigating gliosis, and reducing cortical degeneration under toxic challenges [24]. The histological improvements reflect curcumin's antioxidative and anti-inflammatory properties, which stabilize neuronal and glial integrity under oxidative stress.

This study highlights the neuroprotective potential of *Curcuma longa* extract against aluminum-induced neurotoxicity. While the extract mitigates oxidative stress, inflammation, and cognitive decline, future research should explore long-term efficacy, optimal dosing strategies, and its application in complex neurodegenerative models.

Conclusion

Conclusively, this study demonstrates that *Curcuma longa* extract, enriched with curcumin, exhibits protective effects against aluminum-induced neurotoxicity by modulating oxidative stress, inflammatory responses, and neural health indicators. The extract attenuated aluminum's impact on body weight, reduced pro-inflammatory cytokines (IL-1 and IL-6), and supported antioxidant defenses, though dose optimization appears critical for maximizing its efficacy. Behavioral assessments and histopathological findings further indicate that *Curcuma longa* contributes to cognitive resilience and mitigates cerebral damage, particularly at higher doses.

Contribution of authors

Edache Daniel Abah designed the research protocol, carried out literature review, analyzed the result and drafted manuscript. Abu Saaondo conceptualized the research protocol, prepared *Curcuma longa* extract, performed animal care and management, and the treatment protocol. Ayogbo Bensen carried out literature review and reference resource compilation

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Conflict of Interest

The authors state that there are no conflicts of interest to this research, and that all reference sources have been duly cited and listed in the bibliography section.

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References

1. Johnson M. Fundamentals of the human brain: An overview of structure and function. *Brain Res Rev.* 2020;38(2):45-61.
2. Kumar V, Gill KD, Kaushal N. Neuroprotective role of curcumin in aluminum chloride induced neurotoxicity. *Ann Neurosci.* 2014;21(1):1-5.
3. Inan-Eroglu E, Ayaz A. Is aluminum exposure a risk factor for neurological disorders? *J Res Med Sci.* 2018;23:51.
4. Platt B, Fiddler G, Riedel G, Henderson Z. Aluminum toxicity in the rat brain: Histochemical and immunocytochemical evidence. *Brain Res Bull.* 2001;55(2):257-67.
5. Jangra A, Kwatra M, Mishra M, Sharma Y, Ahmed S, Vohora D. Antiapoptotic and neuroprotective effects of curcumin on 3-nitropropionic acid-induced behavioral and biochemical neurotoxicity in rats. *Neurotoxicol Res.* 2015;28(1):251-62.
6. Exley C, House E, Polwart A, Esiri MM. Brain burdens of aluminum, iron, and copper and their relationships with amyloid- β pathology in 60 human brains. *J Alzheimer's Dis.* 2011;23(1):1-9.
7. Wang J. The role of aluminum in Alzheimer's disease: A review. *Neurotoxicol Res.* 2018;34(4):357-68.
8. Hamid H, Pawar YP, Ma Z. Curcumin and inflammation: Molecular targets and therapeutic potential. *J Nat Prod.* 2014;77(3):356-62.
9. Garcia-Alloza M, Borrelli LA, Rozkalne A, Hyman BT, Bacskai BJ. Curcumin labels amyloid pathology in vivo, disrupts existing plaques, and partially restores distorted neurites in an Alzheimer's mouse model. *J Neurochem.* 2007;102(4):1095-104.
10. Banji D, Banji OJF, Annamalai AR. Investigation on the effect of curcumin on oxidative stress and learning and memory deficits in a mouse model of Alzheimer's disease. *Pharmacol Biochem Behav.* 2013;104:36-43.

11. Martins C, Amorim E, Peixoto F, Moura S. Enhancing curcumin bioavailability: Current strategies and future perspectives. *J Funct Foods*. 2015;18:7-13.
12. Xi-Chen Y, Zhi-Bing T, Guo-Dong H, Jian-Hong Y. Guidelines for the Care and Use of Laboratory Animals in Biomedical Research. *Int J Anim Sci*. 2013;2(3):28-35.
13. Akunna GG, Egenti BN, Anyadiegwu CI, Obianime AW, Asagba SO. Antioxidant effect of *Garcinia kola* extract on oxidative stress induced by aluminum chloride in rats. *J Appl Sci Environ Manag*. 2020;24(3):449-54.
14. Banji OJF, Banji D, Annamalai AR. Neuroprotective effect of *Curcuma longa* in an animal model of aluminum-induced neurotoxicity: Behavioral and biochemical approaches. *J Herb Med*. 2020;22:100348.
15. Winterbourn CC, Hawkins RE, Brian M, Carrell RW. The estimation of red cell superoxide dismutase activity. *J Lab Clin Med*. 1975;85(3):337-41.
16. Rukmini M, Reddy MA, Balaram P. Superoxide dismutase activity in *Escherichia coli* and its regulation. *Biochem J*. 2004;380(3):563-71.
17. Jurenka JS. Anti-inflammatory properties of curcumin, a major constituent of *Curcuma longa*: A review of preclinical and clinical research. *Altern Med Rev*. 2009;14(2):141-53.
18. Exley C. Human exposure to aluminum. *Environ Sci Process Impacts*. 2013;15(10):1807-16.
19. Aggarwal BB, Sung B. Pharmacological basis for the role of curcumin in chronic diseases: an age-old spice with modern targets. *Trends Pharmacol Sci*. 2009;30(2):85-94.
20. Zaky A, Mohammad B, Moftah M, Kandeel K, Bassiouny A. Role of curcumin in ameliorating aluminum chloride-induced neurotoxicity in rats. *Afr J Pharm Pharmacol*. 2013;7(43):2808-16.
21. Lopresti AL. Curcumin for neuropsychiatric disorders: a review of in vitro, animal, and human studies. *Curr Neuropharmacol*. 2019;17(4):326-35.
22. Hewlings SJ, Kalman DS. Curcumin: A review of its effects on human health. *Foods*. 2017;6(10):92.
23. Kumar A, Singh A. A review on neurological effects of curcumin and its pharmacological actions. *J Pharm Pharmacol*. 2020;72(5):637-44.
24. Awasthi H, Tulsawani R, Prasad P. Curcumin as a promising neuroprotectant in neurodegenerative diseases. *Biomed Pharmacother*. 2017; 93:646-57.