ORIGINAL ARTICLE

ABUTH Pharma Journal

The Official Journal of the Department of Pharmaceutical Services, Ahmadu Bello University Teaching Hospital Zaria, Nigeria.
Journal Homepage: https://abuthpharmajournal.com/

Pharmacological Evaluation of the Neuroprotective Effects of *Momordica foetida* Schumach (Cucurbitaceae) in Aluminum Chloride-Induced Alzheimer's Model in Wistar Rats

Saliu K. Abdulazeez[1], Abdulrahman Adamu[1], Abdulmumin Z. Abubakar[1], and Aishatu Shehu[2]

[1] *Department of Pharmacognosy and Drug Development, Ahmadu Bello University, Zaria, Nigeria*
[2] *Department of Pharmacology and Therapeutics, Ahmadu Bello University, Zaria, Nigeria*

Corresponding Author: *Saliu K. Abdulazeez* ***Email:*** *abdulazeezkhidiru1996@gmail.com* ***Phone:*** *+2347033818413*

How to Cite: Abdulazeez *et. al.* (2026).Pharmacological Evaluation of the Neuroprotective Effects of Momordica foetida Schumach (Cucurbitaceae) in Aluminum Chloride-Induced Alzheimer's Model in Wistar Rats. *ABUTH Pharma Journal.* Vol. 2(1) 1-9

Editor-in-Chief: Olurishe Comfort (Ph.D, FPCPharm) Department of Pharm. Services, A.B.U.T.H, Shika, Zaria.

Funding: No funding was received for this study.

Conflict of Interest: The authors declare they have no conflicts of interest that are directly or indirectly related to the research.

ABSTRACT

Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline, memory loss, and neuronal dysfunction associated with oxidative stress and acetylcholinesterase (AChE) hyperactivity. Despite existing therapies, effective neuroprotective agents with fewer adverse effects remain limited. *Momordica foetida* (Cucurbitaceae), widely used in African traditional medicine, possesses antioxidant and antidepressant properties that may confer neuroprotection.

Objectives: This study investigated the neuroprotective effects of *Momordica foetida* ethanol leaf extract against aluminum chloride ($AlCl_3$) induced Alzheimer's like neurodegeneration in Wistar rats.

Methods: The ethanol leaf extract of Momordica foetida was prepared using maceration method. Thirty Wistar rats were divided into six groups: control (Normal saline), $AlCl_3$ (untreated), standard (Donepezil 1 mg/kg), and extract-treated groups (250, 500, and 1000 mg/kg). AD was induced with $AlCl_3$ (17 mg/kg/day) for four weeks, followed by behavioral (Y-maze), biochemical (AChE activity, oxidative stress biomarkers), and histopathological evaluations.

Results: The extract significantly ($p < 0.05$) improved memory indices, reduced MDA levels, restored SOD, CAT, and GSH activities, and lowered hippocampal AChE activity compared to the $AlCl_3$ group. Histopathological analysis revealed neuronal preservation in extract-treated rats.

Conclusion: *Momordica foetida* demonstrated significant neuroprotective potential against $AlCl_3$ induced Alzheimer's-like neurodegeneration, supporting its ethnomedicinal use and providing a foundation for future drug development.

Key Words: *Momordica foetida*; Alzheimer's disease; Neuroprotection; Antioxidant; Acetylcholinesterase, Wistar rats

INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by irreversible cognitive decline, behavioral changes, and neuronal loss, primarily in the hippocampus and cortex. The disease, first described by Alois Alzheimer in 1906, remains the leading cause of dementia globally, affecting more than 50 million individuals[1,2]. Its pathology involves extracellular accumulation of β-amyloid plaques and intracellular neurofibrillary tangles composed of hyperphosphorylated tau protein, oxidative stress, and cholinergic dysfunction.[3,4] These changes disrupt synaptic communication and neuronal viability, leading to cognitive deficits. [5]

Current pharmacotherapy for AD, including cholinesterase inhibitors (donepezil, rivastigmine) and N-Methyl-D-Aspartate (NMDA) antagonists (memantine), provide only symptomatic relief and do not halt disease progression. Moreover, these agents are often associated with adverse effects such as; insomnia, muscle cramps, confusion, hallucination etc., and limited accessibility in low-resource settings.[6] Thus, there is an urgent need to identify natural neuroprotective agents that are safer, cost-effective, and capable of modulating multiple pathogenic pathways.

Momordica foetida Schumach. (Cucurbitaceae) is an indigenous African medicinal plant traditionally used to manage headaches, malaria, diabetes, and stomach disorders. [7,8] Phytochemical studies of *Momordica foetida* have identified a range of bioactive constituents, including alkaloids, flavonoids, tannins, saponins, terpenoids, and phenolic compounds. [9,10,11] This chemical profile, rich in antioxidants and anti-inflammatory agents, correlates with the plant's demonstrated antidepressant-like and radical scavenging activities, as reported in the same body of work, pointing to its potential neuroprotective effects.

Aluminum chloride ($AlCl_3$) is widely used to induce AD-like neuropathology in animal models because it promotes oxidative stress, neuro-inflammation, and acetyl cholinesterase (AChE) hyperactivity in biochemical and behavioral alterations similar to those seen in AD.[2] This model provides a reliable platform for evaluating plant-based neuroprotective interventions.

Consequently, this study was designed to assess the therapeutic potential of *Momordica foetida* ethanol leaf extract, specifically its neuroprotective effects, in a Wistar rat model of Alzheimer's disease induced by aluminum chloride ($AlCl_3$).

MATERIALS AND METHODS

Chemicals and drug

Donepezil Hydrochloride Tablets USP 5 mg (Vega Biotech Pvt. Ltd., GUJ/DRUGS/G/25/2242), aluminum chloride ($AlCl_3$), ethanol, distilled water, phosphate buffer (pH 7.4), Ellman's reagent (5,5′-dithiobis (2-nitro benzoic acid, DTNB), 10% buffered formalin, xylene, paraffin wax and hematoxylin and eosin (H&E).

Animals

The animals consisted of 30 rats of the Wistar strain aged three (3) weeks and weighing between 90 and 130 g. Animals were raised in the animal house of the Department of Pharmacology and Therapeutics of Ahmadu Bello University Zaria, housed in standard cages and maintained under standard laboratory conditions (temperature 24-25°C, relative humidity and a 12 h/12 h light-dark cycle). They had free access to food and water. Institutional guidelines and ethical principles of Veterinary/Pharmacology laboratory (Ahmadu Bello university Zaria) were followed.

Plant

The plant material is composed of fresh leaves of *Momordica foetida* collected in August 2025 from Division of Agricultural College (DAC) Ahmadu Bello University, Zaria, Kaduna State, Nigeria. A plant specimen was identified and authenticated with the assistance of Botanists at the Herbarium Unit of the Department of Botany, Ahmadu Bello

University (Voucher No. ABUHO1683). The leaves were then washed, dried under shade at 20°C for one week, and then powdered.

Preparation of *Momordica foetida* ethanol leaf extract

Five hundred grams of the powdered leaf were macerated in a volume of 4 L of an ethanol-distilled water mixture (70:30, v/v) for 72 hour with intermittent manual shaking. The macerate obtained was filtered and evaporated under vacuum at 45°C using a rotary evaporator. The evaporated extract was lyophilized to obtain a dry extract stored in the desiccator until use.

Experimental design

Aluminum chloride was employed to induce AD in Wistar rats as described by Krasovski[13] and Zaher[14]. Thirty Wistar rats were randomly divided into six groups of five animals each. The first group was treated with normal saline (1 ml/kg) via oral gavage and serve as the vehicle control. The other groups (2,3,4,5 & 6) were pretreated with $AlCl_3$ (17 mg/kg/day) administered orally for four weeks to experimentally develop AD-like symptoms. The AD-like state was confirmed through cognitive deficits observed in the Y-maze test via impairments in spatial recognition and working memory. Group 2 was left untreated while group 3 received Donepezil (1 mg/kg/day) with groups 4, 5 and 6 administered 250, 500 and 1000 mg/kg dose of the plant extract respectively. All treatments were given orally over a period of four weeks following $AlCl_3$-induced AD-like state. Acute toxicity testing followed OECD guidelines (Test No. 425).

Behavioural study

The behavioural evaluation was determined by exploration time using Y-maze test as previously described by Chen.[15] The maze was made of painted wood (to minimize spatial orientation visual signals) and contain three identical arms, each 40 cm long, 35 cm high, and 12 cm broad, positioned at equal angles and labelled A (Start arm), B (Other arm), and C (Novel arm). The test consists of two phases, the trial phase and the test phase. For the trial phase, the rats were placed at the end of arm A and allowed to freely move through the other arm for 3 minutes while the novel arm remained closed. After a short trial interval, the rats were reintroduced into the maze and all three arms were opened, the rats were again allowed to explore for another 3 minutes, time spent in each arm was recorded to assess memory performance. Memory was evaluated based on time spent in the novel arm.

Measurement of oxidative stress parameters in hippocampal tissue

Oxidative stress biomarkers, including malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH), were evaluated in hippocampal tissue. The hippocampus was excised and homogenized in ice-cold 0.1 M phosphate buffer (pH 7.4) using a probe homogenizer. MDA levels were determined following the method described by Ohkawa.[16] SOD activity was measured according to Paoletti[17], catalase activity was assessed using the method of Luck [18], and GSH levels were estimated using Ellman's method. [19]

Measurement of Acetylcholinesterase activity in hippocampal tissue

Acetylcholinesterase (AChE) activity in the hippocampus was determined using an Acetylcholinesterase Inhibitor Screening Kit (MAK324), based on an improved Ellman method. The assay involved the reaction of thiocholine, produced by acetylcholinesterase activity, with 5,5′-dithiobis (2-nitrobenzoic acid) (DTNB) to form a yellow chromogen, which was measured spectrophotometrically at 412 nm. [20]

Histopathological examination of the hippocampus

Histopathological evaluation of the hippocampus was performed using hematoxylin and eosin (H&E) staining. Brain tissues were fixed in 10% buffered formalin, washed, and dehydrated through graded alcohol concentrations. The tissues were cleared in xylene

and embedded in paraffin. Sections of 4 µm thickness were prepared using a microtome, deparaffinized, stained with H&E, and examined under a light microscope for histological alterations. [20]

RESULTS

Limit dose showed no signs, symptoms and no death of acute toxicity in the ethanol leaf extract of *M. foetida* at 5000 mg/kg body weight.

Exploration time in the novel arm during the Y-maze test showed that $AlCl_3$ significantly decreased exploration time compared to normal control, indicating memory impairment. Treatment with *Momordica foetida* extract (especially at 500 and 1000 mg/kg) significantly improved alternation exploration time, comparable to Donepezil as indicated in table 1.

Biochemical results demonstrated that $AlCl_3$ exposure elevated MDA levels and AChE activity while reducing SOD, CAT, and GSH activities. Extract-treated rats dose-dependently ameliorated these biochemical parameters, confirming antioxidant and anticholinesterase effects. Histopathological examination revealed marked neuronal degeneration in the $AlCl_3$ group, whereas extract-treated brains showed preserved hippocampal neurons and reduced gliosis as indicated in table 2 and plate 1.

Table 1: Effects of *Momordica foetida* Leaf Extract on Novel Arm Exploration Time in Aluminium Chloride-Induced Alzheimer's Disease in Wistar Rats

Group	Dose (mg/kg)	Pre-induction (mins)	Post-induction (mins)	Post-treatment (mins)
Normal saline	1 ml/kg	2.40 ± 0.07	2.33 ± 0.07	2.40 ± 0.06
$AlCl_3$ only	17	2.64 ± 0.15	0.82 ± 0.18$^{\#}$	0.54 ± 0.10$^{\#}$
Donepezil	1	2.32 ± 0.83	0.70 ± 0.21$^{\#}$	2.85 ± 0.11*
ELMF	250	2.35 ± 012	0.63 ± 0.30$^{\#}$	2.30 ± 0.24*
ELMF	500	2.60 ± 017	0.57 ± 0.23$^{\#}$	2.52 ± 0.11*
ELMF	1000	2.21 ± 0.03	0.71 ± 0.24$^{\#}$	2.70 ± 0.12*

Data are expressed as mean ± SEM; n= 5; $^{\#}p < 0.05$ when compared with normal control, $^{*}p < 0.05$, when compared with disease control group and pre-induction phase. Repeated measures ANOVA followed by Dunnett's post hoc test. ELMF= Ethanol leaf extract of *Momordica foetida*, $AlCl_3$ = Aluminium Chloride

Table 2: Effect of *Momordica foetida* Leaf Extract on Hippocampal Oxidative Stress Markers in Aluminium Chloride-Induced Alzheimer's Disease in Wistar Rats

Group (mg/kg)	MDA (nmol/mg)	SOD (μmol/mg)	CAT (nmol)	GSH (μmol/mg)	AChE (μg/min/mg)
Normal control	7.70 ± 0.50	8.56 ± 0.47	9.68 ± 0.62	11.34 ± 0.71	1.20 ± 0.10
$AlCl_3$ only	13.58±0.34$^{\#}$	4.83 ± 0.27$^{\#}$	3.69 ± 0.76$^{\#}$	5.09 ± 0.25$^{\#}$	3.90 ± 0.20$^{\#}$
Donepezil (1)	8.10±0.31*	7.90±0.52*	8.80±0.52*	9.80±0.60*	1.40 ± 0.12*
ELMF (250)	9.20±0.50*	6.63±0.52*	6.03±0.55*	6.41±0.82*	2.50±0.18*
ELMF (500)	8.80±0.41*	7.08±0.57*	7.14±0.20*	8.20±0.82*	2.10±0.15*
ELMF (1000)	8.40±0.27*	7.54±0.70*	7.70±0.30*	9.00±0.83*	1.80±0.14*

Data are expressed as mean ± SEM (n = 5), $^{\#}p < 0.05$ when compared with normal control, $^{*}p < 0.05$ when compared with disease control, One-way Anova was used followed by Dunnett's post hoc test. SEM: Standard Error of Mean; ELMF= Ethanol Leaf Extract of *Momordica foetida*. MDA = Malondialdehyde, SOD = Superoxide Dismutase, CAT = Catalase, GSH = Glutathione, AChE = Acetylcholinesterase

DISCUSSION

The neuroprotective evaluation of *Momordica foetida* ethanol leaf extract demonstrated significant protection against aluminium chloride ($AlCl_3$) induced neurotoxicity in wistar rats. Aluminium exposure caused pronounced cognitive impairment and oxidative stress, evidenced by reduced Y-maze alternation performance, increased malondialdehyde (MDA) concentration, and decreased activities of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH). These outcomes reflect the established neuro-pathological patterns of aluminium-induced oxidative stress and neuronal damage.[4,21]

Treatment with *M. foetida* extract significantly improved spatial memory performance and reversed oxidative stress biomarkers. The extract restored antioxidant enzyme levels and reduced MDA concentration in a dose-dependent manner, demonstrating potent antioxidative and neuroprotective effects. Similarly, it was found that natural antioxidants mitigate aluminium-induced hippocampal injury by upregulating SOD and CAT activities, mirroring the biochemical improvements observed in this study.[5]

The observed antioxidative effects can be attributed to the rich presence of flavonoids, phenolics, and saponins in *M. foetida*, which are known to scavenge free radicals, enhance endogenous antioxidant defense, and stabilize cellular redox balance. [10,11] The ability of the extract to modulate oxidative biomarkers supports its potential in mitigating oxidative stress-mediated neurodegeneration, a central feature of Alzheimer's disease (AD) pathology.

The extract's dose-dependent inhibition of acetylcholinesterase (AChE) enzyme in aluminium chloride-pretreated rats indicates a cholinergic mechanism contributing to its neuroprotective effects. Unlike previous reports that primarily described in vitro activity or effects in other *Momordica* species,

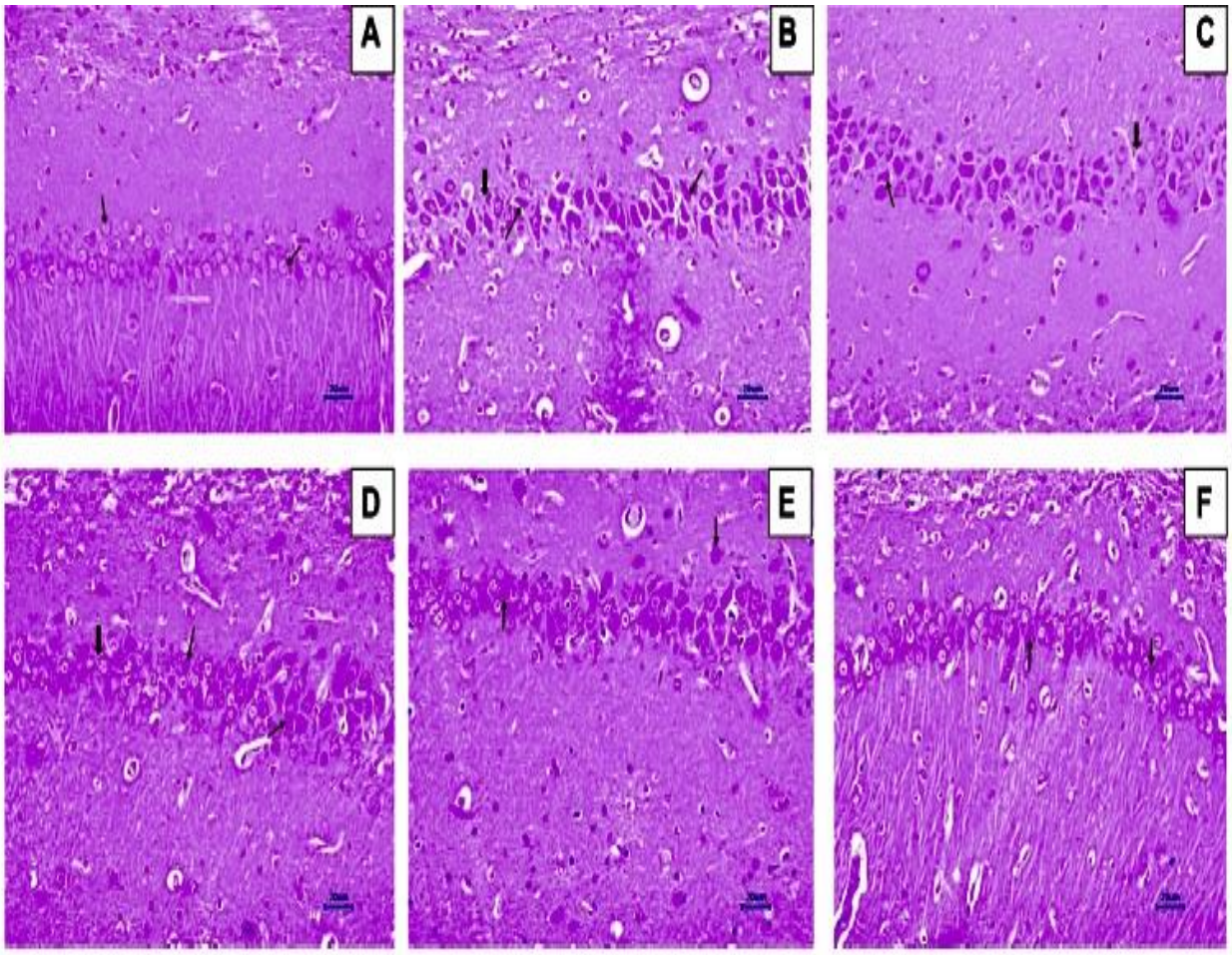

Plate I: Effects of *Momordica foetida* on H&E-Stained Hippocampus Tissue of Aluminium Chloride-Induced Alzheimers Diseased Wistar Rats (H&E Stained, Magnification X400)

(A) Normal control: showing normal histology and normal neuronal cells in the hippocampus (small arrow)
(B) Disease control: hippocampus neuronal degeneration with pyknotic nuclei (small arrow), hippocampus neuronal cell layer reduction (large arrow)
(C) Donepezil (1 mg/kg): reduced hippocampus neuronal degeneration with pyknotic nuclei (small arrow), improved hippocampus neuronal cell layer integrity (large arrow)
(D) Extract (250 mg/kg): reduced hippocampus neuronal degeneration with pyknotic nuclei (small arrow), improved hippocampus neuronal cell layer integrity (large arrow)
(E) Extract (500 mg/kg): reduced hippocampus neuronal degeneration with pyknotic nuclei (small arrow) improved hippocampus neuronal cell layer integrity
(F) Extract (1000 mg/kg): improved hippocampus neuronal degeneration with pyknotic nuclei and improved hippocampus neuronal cell layer integrity (small arrow)

this study provides in vivo evidence that *M. foetida* can prevent AChE hyperactivity induced by aluminium toxicity, supporting its potential to enhance cholinergic neurotransmission in Alzheimer neurodegeneration.

Histopathological changes in the hippocampal sections substantiated the biochemical and behavioral outcomes. Aluminium exposure resulted in neuronal loss, vacuolation, and disorganization of pyramidal cells hallmarks of hippocampal neurodegeneration. In contrast, hippocampal sections from *M. foetida*–treated groups exhibited relatively preserved neuronal architecture, reduced vacuolation, and higher pyramidal cell density, with more pronounced features observed at higher doses. These findings are consistent with reports from Ashikaa who reported that plant-derived antioxidants preserved neuronal architecture in rodent models of AD.[20] Similarly, Jadhav and Kulkarni observed preservation of hippocampal cytoarchitecture following antioxidant therapy in aluminium-exposed rats. [22] The preservation of neuronal integrity observed here underscores the extract's ability to prevent oxidative and excitotoxic damage, thereby supporting its neuroprotective efficacy.

The mechanisms underlying the neuroprotective effects of *M. foetida* appear to involve the synergistic actions of its phytoconstituents. Flavonoids and phenolics act as free-radical scavengers and metal chelators, saponins contribute to membrane stabilization, and terpenoids may modulate neuronal signaling pathways and the presence of these phytochemicals were previously reported.[9,10] This multimodal action supports the concept of phytochemical synergy, which is often more effective in complex disorders like AD than single compound therapy.

Behavioral improvements observed in the Y-maze further confirmed the extract's neuro functional benefits. Rats treated with *M. foetida* displayed increased exploration time percentages, indicative of enhanced working memory and cognitive flexibility. These behavioural outcomes are consistent with biochemical recovery patterns and parallel findings also reported similar cognitive enhancements following treatment with antioxidant-rich plant extracts.[5,23] The consistency of these effects across different experimental parameters behavioral, biochemical, and histological validates the robustness of the neuroprotective actions of *M. foetida*.

Importantly, the present findings corroborate earlier evidence from related species such as *M. charantia*, *M. cymbalaria*, and *M. balsamina*, which have demonstrated neuroprotective and antioxidant potentials in diverse models of neurotoxicity.[10,11,13] The present study demonstrates that *Momordica foetida* exerts neuroprotective effects in an aluminium chloride-induced model of neurodegeneration. This is supported by improvements in behavioral performance, improvement of antioxidant and anti-lipid peroxidative status, inhibition of cholinesterase activity, and preservation of hippocampal neuronal integrity. These findings collectively validate the plant's traditional use in managing neurological disorders and provide a basis for further mechanistic investigations. Future studies should focus on elucidating the molecular pathways underlying these effects, optimizing dosing regimens, assessing long-term safety, and evaluating pharmacokinetics, as human dose extrapolation and clinical relevance remain to be established.

CONCLUSION

Momordica foetida ethanol leaf extract demonstrated protective effects against aluminium chloride–induced neurotoxicity, supporting its traditional use and suggesting its potential relevance in Alzheimer's disease–related neurodegeneration.

ACKNOWLEDGEMENTS

The authors acknowledge the Department of Pharmacognosy and Drug Development and Department of Pharmacology, Faculty of Pharmaceutical Sciences, Ahmadu Bello University, Zaria, for providing the opportunity

and laboratory facilities. No specific grant was received for this research. The authors declare no conflicts of interest.

REFERENCES

1. Chen X, Zhang Y, Li R, Zhao Y (2021). Advances in the pathogenesis and therapeutic strategies for Alzhei- mer's disease. *Front Neurosci* 15:789–812.
2. World Health Organization (2024). Dementia fact sheet. Geneva: WHO Press.
3. Breijyeh Z, Karaman R (2020). Comprehensive review on Alzheimer's disease: Causes and treatment molecule 25(24):5789.
4. Gadhave K, Gadhave R, Dhabarde D (2024). Mechanistic insights into oxidative stress and tau pathology in Alzheimer's disease. Neurochem Int. 182:106519.
5. Lamptey R, Ofori E, Ntim M (2022). Antioxidant-rich plant extracts ameliorate aluminium induced neuro-toxicity in rats. J Ethnopharmacol 292:115229.
6. Ogunniyi A (2024). Challenges in Alzheimer's disease management in sub-Saharan Africa: Therapeutic access and care gaps. Afr J Neurol Sci 43(1): 12–19.
7. Getachew A (2015). Ethnobotanical study of medicinal plants used by local communities in Ethiopia. J Med Plants Res 9(27):722–734.
8. Mukaila YA, Lawal B, Sulaimon AA (2023). Ethnopharmacological survey of Momordica species in West Africa. Afr J Tradit Complement Altern Med 20(2):45–57.
9. Adia MM (2016). Phytochemical screening and biological activities of *Momordica foetida* Schumach. Int J Pharm Sci Res. 7(3):1276–1283.
10. Kada SM, Bello MA, Musa H (2022). Phytochemical constituents and pharmacological potentials of *Momordica foetida* Schumach. Heliyon 8(11):117 93.
11. Bibiane TC, Ndukwe IG, Obasi CU (2025)Antioxidant and neuroprotective effects of *Momordica foetida* extracts in experimental models. J Nat Prod Res 39(4):455–466.
12. Castillo-Rangel I, García-García M, Muñoz L (2023). Aluminium chloride-induced neurotoxicity as a model for Alzheimer's disease: Behavioral and biochemical insights. Brain Res Bull 199:44–53.
13. Krasovski GN, Vasukovich LY, Chariev OG (1979). Experimental study of biological effects of aluminium compounds. Environ Health Perspect. 30:17–25.
14. Zaher MAF, Bendary MA, Aly AS (2020). Effect of thymoquinone against aluminum chloride-induced Alzheimer -like model in rats: a neurophysiological and behavioral study. Med J Cairo Univ. 88(1):355–365.
15. Chen F, et al (2023). Assessment of spatial working memory using the Y-maze test in rodents. Behav Brain Res 439: 114199.
16. Ohkawa H, Ohishi N, Yagi K. (1979). Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal Biochem 95(2):351–358.
17. Paoletti F, Aldinucci D, Mocali A, Caparrini A (1986). A sensitive spectro photometric method for the determination of superoxide dismutase activity. Anal Biochem 154(2):536–541.
18. Luck H. Catalase. In: Bergmeyer HU, editor. Methods of Enzymatic Analysis. New York: Academic Press; 1971. p. 885–893.
19. Ellman GL (1959). Tissue sulfhydryl groups. Arch Biochem Biophys 82(1): 70–77.
20. Ashikaa T, Kumar D, Rajesh K (2023). Protective effect of plant-derived antioxidants on hippocampal morphology in Alzheimer's rat models. Neurochem Res 48(7): 1678–1688.
21. Kumar V, Singh P, Sharma R (2015). Aluminium-induced neurotoxicity: role

of oxidative stress and apoptosis. Neurotoxicology 51:158–166.

22. Jadhav VR, Kulkarni SK (2023). Neuroprotective mechanisms of antioxidants against aluminium-induced hippocampal damage. J Neurosci Res 101(8):2224–2236.
23. Eze CN, Uzoegwu PN, Okeke CE (2021). Neurobehavioral and biochemical effects of antioxidant-rich plant extracts in aluminium-exposed rats. J Basic Clin Physiol Pharmacol 32(5): 871–882.