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Neuroprotective Effect of Aqueous Extract of *Garcinia kola* on Monosodium Glutamate - Induced Cerebellar Cortical Damage in Adult Wistar Rats

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Authors' contributions

This work was carried out in collaboration between all authors. Authors AAJ and FPB designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors KBD and ONO managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Aims: This study assessed the neuroprotective effect of the aqueous extract of *Garcinia kola* on monosodium glutamate- induced toxicity in the cerebellar cortex of adult Wistar rats.
Study Design: Twenty-five adult Wistar rats were randomly assigned into five groups (n=5): A, B, C, D, and E. Group A served as the control while the other groups served as the treated groups. Animals in group A were given feed and water liberally.
Place and Duration of Study: This study was carried out in the Animal Holdings of the Department of Anatomy, Ladoke Akintola University of Technology Ogbomoso, Nigeria between September 2011 and December, 2011.
Methodology: Animals in group B received 2.5 g/kg of monosodium glutamate orally for 14 days,

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group C received 200 mg/kg of *Garcinia kola* extract orally for 14 days, group D received 2.5 g/kg of monosodium glutamate and 200 mg/kg of *Garcinia kola* extract orally for 14 days and group E was pretreated with 200 mg/kg of *Gracinia kola* extracts orally for 14 days prior to the administration of 2.5 g/kg of monosodium glutamate for 14 days. The brain was excised and weighed before fixing in 10 % formal saline for histological processing.

Results: The results reveal intact cerebellar neurons in group A, C and D. Group B reveals some cellular degeneration of cortical layers compared with other groups. Preservation of cerebellar tissue was observed in group B. Group E which was pretreated with *Garcinia kola* shows an appreciable preserved cerebellar tissue.

Conclusion: This study concluded that *Garcinia kola* has protective effects on monosodium glutamate-induced cerebellar damage in adult Wistar rats.

Keywords: Neuroprotective; Garcinia kola; monosodium glutamate; cerebellar cortex.

1. INTRODUCTION

The brain is particularly sensitive to oxidative stress injury because it has high rate of oxidative metabolic activity, high content of polyunsaturated fatty acids and relatively low antioxidant capacity compared to other tissues [1]. The brain cells are damaged and destroyed by oxidized compounds called free radicals that are generated in the body by stress, exercise, oxidation of food and other chemical reactions that occur in the cell [2]. Neurodegenerative diseases such as Alzheimer's Parkinson's, Huntington's and stroke are usually a consequence of excessive production of these free radicals from the oxidative stress [3]. Reactive oxygen species (ROS) are generated spontaneously in cells during metabolism and have been implicated in the aetiology of different degenerative diseases, such as heart diseases, stroke rheumatoid arthritis and cancer [4]. Lipid peroxidation is a crucial step in the pathogenesis of several disease states in adult and infant patients [5]. There is a globally increasing concern on the burden of neurological disorders in both the developed and developing countries. The oxygen radicals produced from oxidative stress are scavenged by antioxidants [6], which are produced endogenously or from nutritional supplements.

There is a great deal of interest in edible plants that contain antioxidants and health – promoting phytochemicals as potential therapeutic agents. One of such plant is *Garcinia Kola* which is generally known as bitter kola in Nigeria that belongs to the family of tropical plant known as *Guttiferae. Garcinia kola* (Bitter kola) (*G. kola*) and its relatives are found in Nigeria and also in the humid lowland plain of West Africa extending from Sierra Leone to Zaire [7]. Bitter cola, False Kola, *Garcinia* or male kola are other common English names [5]. Investigators have carried out various studies on the extract of various components of the plant as a result of its wide spread consumption in different parts of Nigeria. The photochemical studies shown that *Garcinia kola* Nut (GKN) contains phenolic compounds, steroids, xanthines, benzophenones [8,9], tannis, guttiferins and saponins [8]. *Garcinia kola* seeds contain energy-yielding nutrients and minute quantities of kolaviron [10]. The seeds of *Garcinia kola* are chewed as a masticatory substance to stimulate the flow of saliva and widely consumed as snacks [11]. Furthermore, reports from studies have indicated that *Garcinia kola* consists of a complex mixture of alkaloid, phenols and tannins [12]. The plant is referred to as a wonder plant because every part of this plant has been found to be of medicinal significance [13].

The extracts possess anti-inflammatory [14], and antioxidant properties [15]. Antioxidants in the body protect brain cells and perform numerous important functions that improve health antioxidants terminate chain reactions in lipid peroxidation by removing free radical intermediates and inhibit other oxidation reactions [5]. The body internal production of antioxidants is not enough to neutralize all the free radicals and the production of antioxidants in the body declines with increasing age, consequently, supplementation from nutritional sources by increasing dietary intake of antioxidants help to boost the body's antioxidant system with the hope of maintaining health and preventing diseases [5].

The cerebellum is a region of the brain that plays an important role in motor control. It may also be involved in some cognitive functions such as attention and language and in regulating fear and pleasure responses [16]. The cerebellum does

not initiate movement, but it contributes to coordination, precision and accurate timing. It receives input from sensory systems and from other parts of the brain and spiral cord and integrates these inputs to fine time motor activity [17]. The cerebellar cortex is divided into three layers. At the bottom lies the thick granular layer densely packed with granule cells, along with interneurons mainly the Golgi cells. In the middle lies the Purkinje layer that contains only the cell bodies of Purkinje cells. At the top lies the molecular layer which contains the flattened dendritic trees of Purkinje cells along with the huge array of parallel fibers penetrating the Purkinje cell dendritic trees at right angles. This outermost layer of the cerebellar cortex also contains two types of inhibitory interneurous, stellate and basket cells. Both stellate and basket cells form GABAergic synapse onto Purkinje cell dendrites [18]. Two types of neuron play dominant roles in the cerebellar circuit: Purkinje cells and granule cells. Three types of axons also play dominant roles: Mossy fibers and climbing fibers and parallel fibers. There are two main pathways through the cerebellar circuit; originating from Mossy and climbing fibers both eventually terminating in the deep cerebellar nuclei [18]. The Mossy fiber and climbing fiber inputs each carry fiber-specific information; the cerebellum also receives dopaminergic; serotonergic, noradrenergic and cholinergic inputs that presumably perform global modulation [19].

Monosodium glutamate (MSG) is commonly used as a flavour enhancer [20], which increases palatability and food selection in a meal [21].Glutamate is the main excitatory neurotransmitter in rat brain [22]. Glutamate in high doses produce neuro-endocrine abnormalities and neuronal degeneration [23] and oxidative damage in different organs [20,23].

The consumption of MSG may have some deleterious effects on the cerebellum of adult Wistar rats at higher doses [24]. In view of the previous reports on the effects of MSG on the brain, this study examines the neuroprotective effect of *Garcinia kola* on monosodium glutamate-induced cerebellar damage in Wistar rats.

2. MATERIALS AND METHODS

Twenty five adult Wistar rats of both sexes weighting 150-270g were procured from Olatunde Farm Osogbo, Nigeria. The rats were acclimatized for four weeks due to their smaller weights at the Animal Holdings of the Department of Anatomy, Ladoke Akintola University of Technology Ogbomoso, Nigeria under 12hr light/dank cycle before the commencement of the experiment. The rats were maintained under standard laboratory conditions. The rats had free access to water and standard feed (Bovayay feeds, Ogbomoso, Nigeria). The animals were given adequate care in accordance with the Principle of Laboratory and Animal Care prepared by the National Academy of Sciences and published by the National Institute of Health [25]. All the rats were carefully assessed and screened at the end of the acclimatization period. The investigation was conducted in accordance with the principles and guidelines for animal research.

2.1 Plant Materials and Extraction

The nuts of *Garcinia kola* were purchased from a local market in Ogbomoso. The seeds were authenticated to be *Garcinia kola* in the Department of Pure and Applied Biology, Ladoke Akintola University. The seeds were chopped to smaller pieces after the outer coats were removed. They were washed and air- dried before they were finally ground to a fine powder using a mechanical blender. The aqueous extract was prepared by maceration following the method of one of the previous investigator [26].

2.2 Chemicals

A brand of monosodium glutamate (99.9% MSG) marketed by West African Seasoning Company Limited was bought from open market at Ogbomoso, Nigeria. Other chemicals were of certified analytical grade and were used without further purification.

2.3 Experimental Design

The twenty five Wistar rats were randomized into five groups of five rats each and they were subjected to the following treatment schedule.

Group A: received only distilled water
Group B: (MGS – treated group) received 2.5 g/kg orally
Group C: (*Garcinia kola*-treated group) received 200 mg/kg orally.
Group D: (*Garcinia kola* + MSG-treated group) received orally both treatments from B and C concurrently.
Group E: (Group pretreated with *Garcinia kola* + MSG) received 200 mg/kg of *Garcinia kola* extract orally prior to 2.5 -MSG exposure.

The selection of the working close of *Garcinia kola* in this study was based on previous report [35]. The dose of MSG used in this study was selected based on the reports from previous investigators [27,28,29].

2.4 Administration of Monosodium Glutamate and *Garcinia kola* Extract

Group A: Received only distilled water for 14 days.

Group B: Received 2.5 g/kg of MSG orally for a period of 14 days.

Group C: Received aqueous extract of *Garcinia kola* (200 mg/kg) orally for 14 days. Group D received 2.5 gkg of MSG aqueous extract of *Garcinia kola* for 14 days.

Group E: Received pretreatment of aqueous extract and 2.5 g/kg of MSG was administered orally for another 14 days. The rats were sacrificed by cervical dislocation on day 15 of the experiment. The brain of each rat was excised and weighed before fixing in 10% formal saline for tissue processing.

Histological study was carried out using the method of Carleton [30]. The techniques involved dehydration of the cerebellar tissues with graded ethanol concentrations (50%, 70%, 90% and 100% respectively), clearing in xylene, followed by infiltration in paraffin wax for 2hr at 56ºC and embedding in paraffin wax for 48hr.

Sectioning of the embedded tissue was done using a rotary microtome at 5 µm thick, before the sections were subjected to haematoxylin and eosin (H & E) staining procedure and examination of the slides was done under a light microscope. Permanent photomicrographs of the observations made were taken using a trinocular microscope with a digital camera attached to one of the eye pieces.

The data obtained were analyzed using Analysis of Variance (ANOVA) and tested for significance using the student's t test and $P<0.05$ was considered to be significant.

3. RESULTS

Table 1 below indicates the changes in the body weights of Wistar rats before and after the treatment. All the groups except MSG –treated group B, generally show a slight decrease in the body weights during the period of study. While MSG –treated group B reveals ant increase in the body weight. However, no significance difference ($p>0.05$) in body weights between the control and treated groups Table 1. The body weights increased significantly (($P<0.05$) from week 0 to week 3 in group B. Conversely, the body weights decreased significantly ($P<0.05$) from week 0 to week 3 in group C, D and E Table 1.

Fig. 1 below shows the total brain weights in various groups following MSG exposure. The brain weight decreased significantly ($P<0.05$) in group B (MSG –treated) rats compared with control. Similarly, the brain weights slightly increased in the other treated groups compared with MSG –treated group in group B Fig. 1.

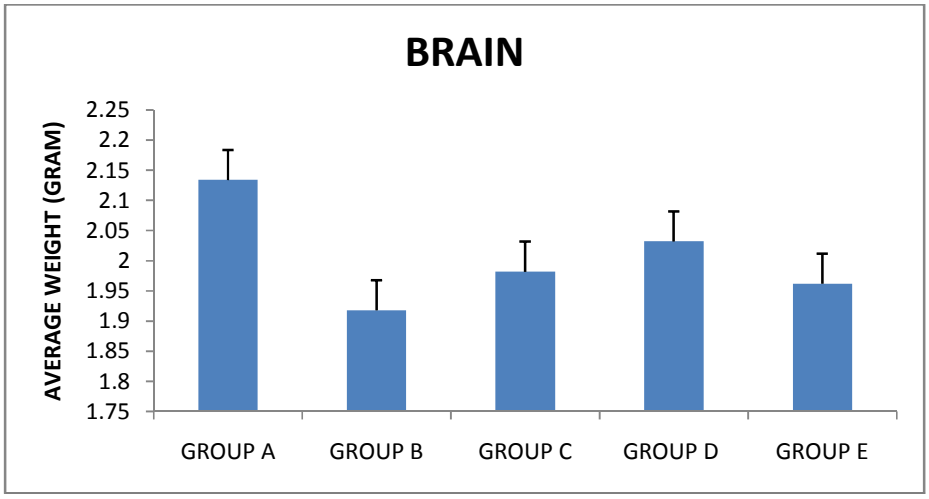


Fig. 1. Effects of *Garcinia kola* extract on MSG- induced cerebellar damage in Wistar rats. Each bar indicates Mean ± S.E.M *(P<0.05)*. Values in treated groups are significantly different from corresponding control (*p<0.05)

Table 1. Effects of *Garcinia kola* and MSG on the body weights of Wistar rats during the period of study

Period (Weeks)	Group A	Group B	Group C	Group D	Group E
WEEK 0	212±12.7	182±9.0	200±7.0	234±11.2	235±3.15
WEEK 1	204±12.0	184±9.7	191±12.2	236±8.6	237±6.2
WEEK 2	205±16.2	182±8.7	182±13.1	223±8.5	204±5.98
WEEK 3	205±13.1	187±9.6	171±17.4	223±10.6	186±3.97

Values are mean ± S.E.M., n=5

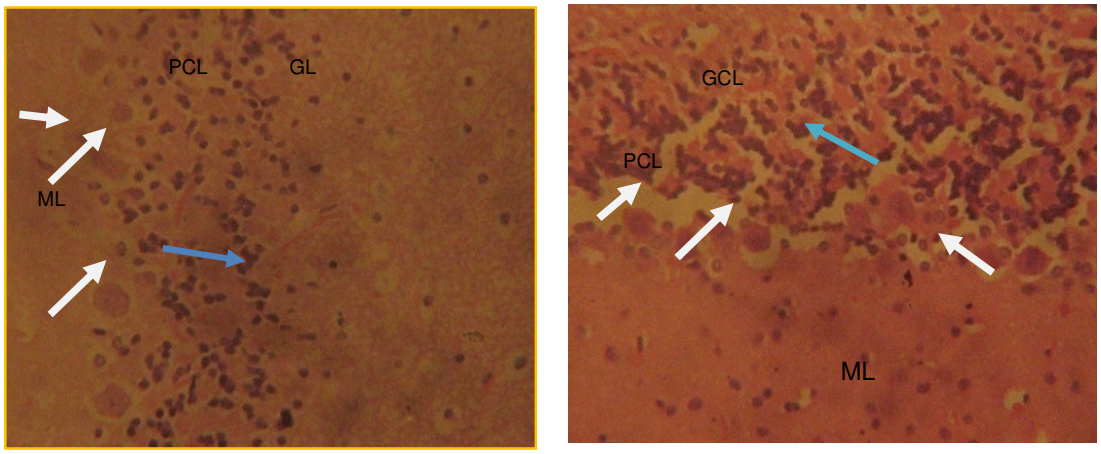
Control Group A: This section shows H & E stained cross sections of the cerebellar cortex with intact cortical layers. The three cortical layers appeared normal. The outer molecular layer, inner granular layer and a monolayer of flask shaped Purkinje cells in the Purkinje cell layer sandwiched between the inner granular and external molecular layers (Plate 1a).

Treated Group B: This section shows H & E stained cross sections of the MSG-treated cerebellar cortex. This section reveals partial loss of the cortical neurons particular the Purkinje cells in the middle layer. The cortical layers appeared distorted with loss of some cellular components of the cortical layers (Plates 1b, 2b, 3b and 4b).

Treated Group C: The cross section of the cerebellar cortical layers of the *Garcinia-kola*-treated group shows intact cortical layers. The three layers appeared normal (Plate 2a).

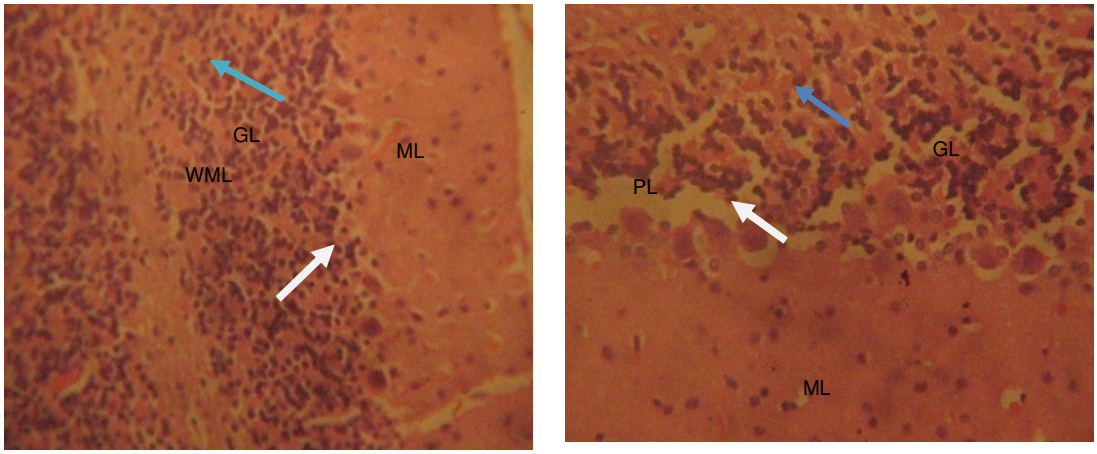
Treated Group D: The cross section of the cerebellar cortical layers of the rats concurrently treated with MSG and *Garcinia kola* showing intact cortical layers. All the three cortical layers appeared normal and comparable with the control section and comparable with the control section. The cortical layers appear to have been preserved from distortion and loss of cortical neurons observed in Group B MSG – treated group (Plate 3a).

Treated Group E: The cross section of the cerebellar cortical layers of the rats that were pretreated first with *Garcinia kola* before subsequent administration of MSG. This section similarly shows intact cortical layers. The preservation of the cortical layers from distortion and neuronal loss in the cortical layers in this group appeared to be less compared with the treated Group D rats (Plate 4a).



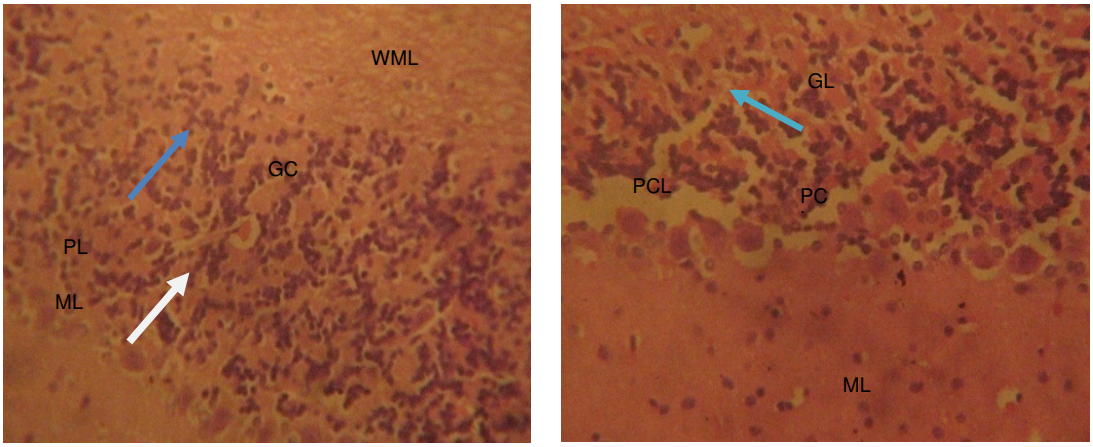
A B

Plate 1a. Cross section of the cerebellar cortical layers of the rats in control group A. Section shows intact layers. Molecular layer (ML), purkinje cell layer (PCL), Granular layer (GL), Purkinje cell (white arrow), granule cell (blue arrow) X 400. Plate 1b. Cross section of the cerebellar cortical layers of the rats in MSG-treated group (B). Section shows distorted layers and the punkinje cells become degenerated. Molecular layer (ML), purkinje cell layer (PCL), Granular layer (GL), Purkinje cell (white arrow), granule cell (blue arrow) X 400



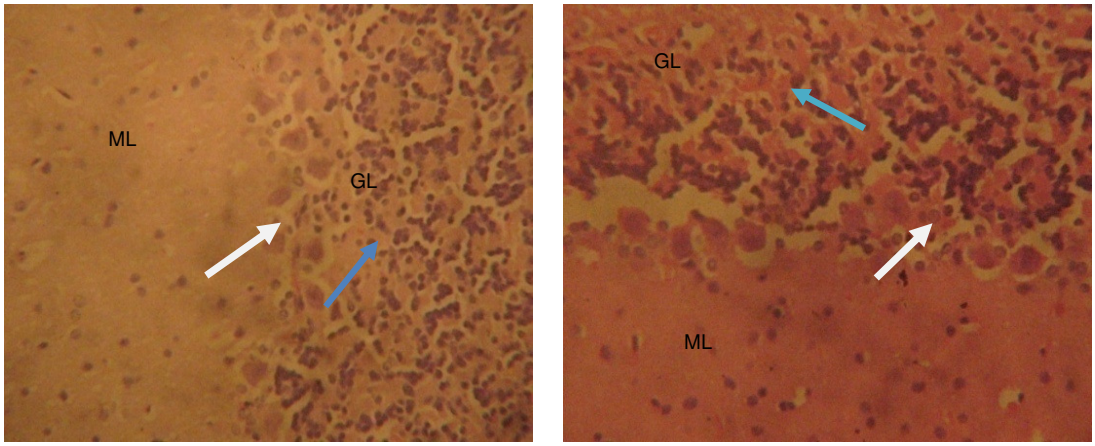
A B

Plate 2a. Cross section of the cerebellar cortical layers of the rats in *Garcinia kola* treated (group C). Section shows intact cortical layers. Molecular layer (ML), purkinje cell layer (PCL), Granular layer (GL), Purkinje cell (white arrow), granule cell (blue arrow X 400. Plate 2b. Cross section of the cerebellar cortical layers of the rats in MSG -treated group (B). Section shows distorted layers and the punkinje cells become degenerated. Molecular layer (ML), purkinje cell layer (PCL), Granular layer (GL), Purkinje cell (white arrow), granule cell (blue arrow) X 400



A B

Plate 3a. Cross section of the cerebellar cortical layers of the rats in *Garcinia kola* and MSG (simultaneously) treated group (D). Section shows intact cortical layers. Molecular layer (ML), purkinje cell layer (PCL), Granular layer (GL), Purkinje cell (blue arrow), granule cell (white arrow), white matter layer (WML) X 400. Plate 3b. Cross section of the cerebellar cortical layers of the rats in MSG -treated group (B). Section shows distorted layers and the punkinje cells become degenerated. Molecular layer (ML), purkinje cell layer (PCL), Granular layer (GL), Purkinje cell (white arrow), granule cell (blue arrow) X 400



A **B**

Plate 4a. Cross section of the cerebellar cortical layers of the rats in *Garcinia kola*- Pretreated and MSG - treated group (E). Section shows numerous purkinje cells. Molecular layer (ML), purkinje cell layer (PCL), Granular layer (GL), Purkinje cell (white arrow), granule cell (blue arrow), white matter layer (WML) X 400. Plate 4b. Cross section of the cerebellar cortical layers of the rats in MSG -treated group (B). Section shows distorted layers and the punkinje cells become degenerated. Molecular layer (ML), purkinje cell layer (PCL), Granular layer (GL), Purkinje cell (white arrow), granule cell (blue arrow) X 400

4. DISCUSSION

The nervous system is the major communication network in the human body. Its normal functioning is strongly dependent on the maintenance of its structural integrity and many complex metabolic processes. However, the processes that disrupt normal structure or metabolism, or both are capable of producing neurological disease. The degenerative diseases of the central nervous system (CNS) encompass a hetereogenous group of disorders characterized by spontaneous progressive degeneration of neurons in specific regions of the brain, spinal cord, or both.

Glutamate is the main excitatory neurotransmitter in rat brain [22]. High doses of glutamate produce neuro-endocrine abnormalities and neuronal degeneration [23]. Extensive cell death in the central nervous system is associated with all neuro-degenerative diseases. The prime factor for inducing the massive cell destruction observed in neuro-degeneration are neurotoxins [31].

Apoptotic and necrotic cell death which differ morphologically and biochemically have been described by previous investigators [27,32]. Accidental cell death is known as necrotic which could result from extrinsic insults to the cells such as toxic, thermal, osmotic and traumatic factors [33]. Conversely, pathological cell death is known as apoptotic and is an organized programmed cell death (PCD) that is mediated by intrinsic and active mechanism.

Neuronal deterioration and loss in the cerebellar cortex in MSG – treated rats in this study might be due to cell death occasioned by neurotoxic effect of MSG which was ameliorated or/ mitigated in rats that were treated with aqueous extract of *Garcinia kola*. Consumption of high doses of MSG may adversely affect the cerebellar cortex in wistar rats which consequently may result in tremor, unstable and uncoordinated movement, ataxia and loss of some cerebellar functions [27].

Similarly, some neurodegenerative changes in the frontal lobe of the cerebral cortex of wistar rats after MSG exposure have been reported [34]. It has been shown by dietary and epidemiological studies that flavonoid consumption from vegetables, fruits and plant derived beverages is particularly important for maintenance of neuronal health [35]. The present study has shown preservation of the cerebellar tissue from toxic effect of MSG as morphological damage has been prevented in rats that were exposure concurrently to extract of *Garcinia kola* and MSG. It has also been similarly reported that biflavonoids from *Garcinia kola* have anti-

inflammatory properties [36], as well as natural antioxidant potentials [37,38].

The oral administration of monosodium glutamate at a dose of 2.5 g/kg in this study has resulted in degeneration and loss of some neuronal components of the cerebellar cortex in the MSG-treated rats. Some neurons appear distorted particularly degeneration and loss of Purkinje cells in the middle layer became more prominent in group B MSG – treated rats.

The neuroprotective effect of *Garcinia kola* on the cerebellum has been reported in mice following 3-nitropropionic acid exposure [39]. Severe neurochemical damage has been reported in some brain regions of rats that were treated with MSG [40,41].

The results from this present study have shown that *Garcinia kola* has neuroprotective potentials on the cerebellar cortex of wistar rats as indicated by the preservation of the neuronal cells of the cerebellar cortex (Plates 3a and 4a) from the neurotoxic effect of the MSG which caused neuronal distortion and loss in MSG – treated rats (Plates 1b and 2b). The preservation of the cerebellar cortex architecture from neuronal degeneration and loss in group C, D and E following exposure to aqueous extract of *Garcinia kola* might be due to the previously reported anti-inflammatory and anti-oxidative properties of *Garcinia kola* which might have prevented MSG-induced oxidative damage that has been observed in MSG-treated rats in group B.

There was no significant difference between the body weights of treated rats and control (Table 1). The significant increase in body weights obtained in MSG- group in this study is consistent with the finding of previous investigator [42]. The brain weights decreased significantly in the MSG- treated rats. Fig. 1. The significant decreased in the brain weights in this group could be attributed to the toxic effects of MSG on the neuronal cells of the cerebellum of MSG- treated rats. Drug poisoning water intoxication, hypoxia and acute hyponatremia have been implicated in cell swelling [43].

This finding is indicating the protective effect of *Garcinia kola* which prevented degeneration and loss in rats that were treated with this antioxidant substance.

This study concluded that oral administration of 2.5 g/kg body weight of MSG for 14 days resulted in degeneration and loss of cortical neurons particularly the Purkinje cells. However, the co-administration of aqueous extract of *Garcinia kola* and MSG resulted in neuro-preservation of cortical neurons of the cerebellar cortex from toxic effect of MSG as seen in Group B MSG – treated rats. Further studies would be carried out particularly on antioxidant enzymes in relation to this study so as to corroborate this report.

5. CONCLUSION

This study concluded that oral administration of 2.5 g/kg body weight of MSG for 14 days resulted in degeneration and loss of cortical neurons particularly the Purkinje cells. However, the co-administration of aqueous extract of *Garcinia kola* and MSG resulted in neuro-preservation of cortical neurons of the cerebellar cortex from toxic effect of MSG as seen in Group B MSG – treated rats. Further studies would be carried out particularly on antioxidant enzymes in relation to this study so as to corroborate this report.

CONSENT

Not applicable.

ETHICAL APPROVAL

All authors hereby declare that "Principles of laboratory animal care" (NIH publication No. 85-23, revised 1985) were followed, as well as specific national laws where applicable. All experiments have been examined and approved by the appropriate ethics committee.

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Shulman RG, Rothman D, Behar KL, Hyder F. Energetic basis of brain activity.

Implications for neuroimaging. Trends Neurosci. 2004;27:275-285.
2. Anderson JK. Oxidative stress in neurodegeneration: Cause or consequence? Nature Rev Neurosci. 2005;5:18-25.
3. Butterfield DA, Hensley K, Cole P, Subramaniam R, Askenov M, Bummer PM, Haley BE, Carney JM. Oxidatively induced structural alteration of glutamine synthetase assessed by analysis of spin label incorporation kinetics: Relevance to Alzheimer's disease. J Neurochem. 1997;68(6):2451-2457.
4. Halliwell B, Gutteridge JMC, Cross CE. Free radicals, antioxidants and human disease. J Lab Clin Med. 1992;119:598-620.
5. Oloyede OI, Afolabi AM. Antioxidant potential of *Garcinia kola*. Acad Res Int. 2012;l2(2):49-54.
6. Cantuti-castelvetri I, Shukitt-Hale B, Joseph JA. Neurobehavioural aspects of antioxidants in aging. Int J Dev Neurosci. 2000;18(4-5):367-381.
7. Adefule AO, Adefule AK, Oosa BO, Onyeneva PC. Antifugal activity of *Garcinia kola* extract as an ocular bacterial isolatesin Lagos Nigeria. Nig Q J Hosp Med. 2004;14:112-114.
8. Iwu MM, Igboko O. Flavonoids of *Garcinia kola* seeds. J Nat Prod. 1985;45:650-651.
9. Iwu MM, Igboko OA, Onwuchekwu U, Okunji CO. Evaluation of the antihepatoxicity of the biflavonoids-*Garcinia kola* seeds. J Ethnopharmacol. 1987;21:127-138.
10. Adebisi AA. A case study of *Garcinia kola* nut production-to consumption system in J4 Area of Omo forest reserve, Southwest Nigeria. In: Sunderland T, Ndoye O. (eds). Forest products, livelihoods and conservation: Case studies on non-timber forest systems. Bogor Barat: Center for International Forestry Research. 2004;115-132.
11. Mackeen MM, Ali AM. Lajis NH, Kawazu K, Kikuzaki H, Nakatami N. Antifugal *Garcinia* acids esters from the fruits of *Garcinia atroviridis*. Z Naturforch. 2002;57(34):291-295.
12. Okwu DE. Phytochemical, vitamins and mineral contents of two Nigerian medicinal plants. Int J Mol Med Adv Sci. 2005;1(4):375-381.
13. Iwu MM, Igboko O. Flavonoids of *Garcinia kola* seeds. J Nat Prod. 1990;45:650-651.
14. Nwoha PU, Ojo GB, Ajayi SA, Ofusori Da, Oluwayinka OP, Odukoya SA, Falana BA. *Garcinia kola* diet provides slight protection to mice neurons against neurotoxins. J Environ Neurosci Biomed. 2007;1(2):125-136.
15. Adaramoye OA, Farombi EO, Adeyemi EO, Emerole GO. Comparative study on the antioxidant properties of flavonoids of *Garcinia kola* seeds. Parkistan J Med. 2005;21(3):1-2.
16. Wolf U, Rapoport MJ, Schweizer TA. Evaluating the affective component of the cerebell ar cognitive affective syndrome. J Neuropsychiatry Clin Neurosci. 2009;21(3):245–53.
17. Fine FJ, Ionitta CC, Lohr L. The history of the development of the cerebellar examination. Semin Neurol. 2002;22(4):375-384.
18. Linas RR, Walton KD, Lang EJ. *Cerebellum*. Ch. 7 in Shepherd GM. The synaptic organization of the brain. New York: Oxford University Press; 2004.
19. Schweighofer N, Doya K, Kuroda S. Cerebellar aminergic neromodulation towards a functional understanding. Brain Res Rev. 2004;44(2-3):103-106.
20. Farmobi EG, Onyema OO. Monosodium glutamate-induced oxidative damage and genotoxicity in the rat: Modulatory role of vitamin C, vitamin E and quercetin. Hum Exp Toxicol. 2004;25(25):1-259.
21. Bellisle F, Dalix AM, Chappius AS, Rossi F, Fiquet P. Monosodium glutamate affects mealtime food selection in diabetic patients. Appetite. 1996;26:267-276.
22. Rotta LN, Schmidt AP, Mello ST, Nogueira CW, Souza KB, Izquierdo IA, Perry ML, Souza DO. Effects of undernutrition on glutamatergic parameters in rat brain. Neurochem Res. 2003;28:1181-1186.
23. Moore KL. Congenital malformations due to environmental; Developing Humans. W.B. Saunders co. Ltd. Philadelphia 2nd ed. 2003;173-183.
24. Eweka AO, Om'Iniabohs FAE. Histological studies of the effects of monosodium glutamate on the cerebellum of adult wistar rats. The Internet Journal of Neurology. 2006;8(2).
25. National Institute of Health Guide for the Care and Use of Laboratory Animals; DHEW Publication (NIH). Revised office of science and health. Reports DRR/NIH Bethesda USA; 1985.

26. Morakinyo AO, Achema PU, Adegoke OA. Effect of *Zingiber officinale* (Ginger) on sodium arsenite- induced reproductive toxicity in male rats. Afr J Biomed Res. 2010;13:39-45.
27. Eweka AO, Om'Iniabohs FAE. Histological studies of the effects of monosodium glutamate on the lateral geniculate body of adult wistar rats. Electron J Biomed. 2007;2:14–18.
28. Narayanan SN, Kumar RS, Paval J, Nayak S. Effect of ascorbic acid on the monosodium glutamate – induced neurobehavioral changes in preadolescent rats. Experimental Study, Pratis 1 Lek Listy. 2010;111(5):247-252.
29. Ashaolu JO, Ukwenya VO, Okonoboh AB, Ghazal OK, Jimoh AAG. Effects of, monosodium glutamate on hematological parameters in wistar rats. International Journal of Medicine and Medical Sciences. 2011;3(6):219-222.
30. Carleton H. Carleton's histological technique. 4th edition Oxford University Press. Oxford. 1967;33-320.
31. Waters CM, Wakinshaw G, Moser B, Mitchell IJ. Death of neurons in the neonatal rodent globus pallidus occurs as a mechanism of apoptosis. Neuroscience. 1994;63:881-894.
32. Kamuren Z, Sanders R, Watkins JB. Low carbohydrate diet and oxidative stress in diabetic and non diabetic rats. J Biochem Mol Toxicol. 2006;20:259-269.
33. Farombi OE, Akanni OOB, Emerole GO. Antioxidant and scavenging activities of flavonoid extract (kolaviron) of *Garcinia kola* seeds. J Pharm Biol. 2002;40:107-116.
34. Alao OA, Ashaolu JO, Ghazal OK, Ukenya VO. Histological and biochemical effects of monosodium glutamate on the frontal lobe of adult wistar rats. International Journal of Biomedical and Health Sciences. 2010;(4):197-203.
35. Ofusori D, Ayoka A, Adelakun A, Falana B, Adeeyo O, Ajeigbe K, Yusuf U. Microanatomical effect of ethanolic extract of *Garcinia kola* on the lung of Swiss albino mice. Internet Journal of Pulmonary Medicine. 2007;10(1).
36. Braide VB. Anti-inflammatory effect of kolaviron, a biflavonoid of *Garcinia kola* seeds. Fitoterapia. 1990;64(5):433-436.
37. Farombi EO, Hansen M, Ravn-Haren G, Moller P, Dragsted LO. Commonly consumed and naturally occurring dietary substances affect biomarkers of oxidative stress and DNA damage in healthy rats. Food Chem Toxicol. 2004;42(8):1315-1322.
38. Terashima K, Takaya Y, Niwa M. Powerful antioxidant agents based on garcionic acid from *Garcinia kola*. Bioorg Med Chem. 2002;10(5):1619-1625.
39. Ajayi SA, Ofusori DA, Ojo GB, Ayoka CA, Abayomi TA, Tijani AA. The microstructural effects of aqueous extract of *Garcinia kola* on the hippocampus and cerebellum of malnourished mice. Asian Pac J Trop Biomed. 2011;1(4):261-265.
40. Pavlovic V, Pavlovic D, Kocic D, Sokolovic D, Jevtovic-Stoimenov J. Effect of monosodium glutamate on oxidative stress and apoptosis in rat thymus. Mol Cell Biochem. 2000;303:161-166.
41. Martin LJ, Sieber FE, Traystman RJ. Apoptosis and necrosis occur in separate neuronal populations in hippocampus and cerebellum after ischemia and are associated with differential alterations in metabotropic glutamate receptor signaling pathways. J Cereb Blood Flow Merab. 2000;20:153-167.
42. Egbuonu ACC, Obidoa O, Ezeokonkwo CA, Ejikeme PM, Ezeanyika LUS. Some biochemical effects of sub-acute oral administration of L-arginine on monosodium glutamate-fed Wistar albino rats 1: Body weight changes, serum cholesterol, creatinine, and sodium ion concentrations. Toxicol Environ Chem. 2010;92(7):1331-1337.
43. Johnanson CE. Effects of fluid in Balances. Neuroscience in Medicine. P. Michael conn, JB Lippincott Company. 1995;187-189.

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