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Original Article

Zingiber Officinale-supplemented diet reversed lead-induced oxidative stress and cerebral cortex injuries in adult female Wistar rats

[1]Ojo F.O., [1]Hassan L.A., [1]Olaniyi O.S., [2]Adetoro E.K., [3]Lawal R.T., [1]Lawal M.B.

ABSTRACT

Background and aim: Ginger (*Zingiber officinale*), a widely recognized medicinal plant popularly used as spice has attracted attention due to its ability to boost the immune system and reverse conditions associated with organ toxicity via its anti-oxidative and anti-inflammatory properties. This study **assessed the effects of** *Zingiber Officinale* (ginger) on the changes in feed intake, oxidative stress markers (malondialdehyde and total antioxidant capacity) and cerebral cortex injury associated with lead treatment in rats.

Materials and methods: Twenty adult female Wistar rats, each weighing between 150 and 170g, were randomly divided into four groups of five animals each (n = 5). Groups A and B; the negative and positive controls were fed with (distilled water) orally via gavage and basic lead carbonate at 30 mg/kg respectively. Both groups A and B were fed with measured standard diet. Groups C and D received a diet supplemented with powdered ginger at compositions of 1% and 5% of their feed respectively. All the administered substances were provided daily throughout the experimental period of 28 days. On day 29, the animals were euthanized by cervical dislocation and blood samples were collected through intra-cardiac puncture, stored in a heparinized bottle, and further processed to assess the levels of oxidative markers (Malondialdehyde and Anti-oxidant status). The brain tissues were extracted, visually examined, weighed, fixed in 10% neutral buffered formalin, processed for paraffin embedding, cut to a thickness of 5µm, and stained with Hemetoxylin and Eosin (H&E) for histological findings.

Results: Result showed that ginger reversed decreased feed intake, oxidative impairment, and cerebral cortex injury induced by lead.

Conclusion: The consumption of products supplemented with ginger and its usage as spice should be further encouraged. More findings are needed to ascertain its optimal consumption levels in humans.

Keywords:
Toxic Metal; Ginger; Lead; Cerebral Cortex; Oxidative Stress

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[1]Department of Anatomy, Faculty of Basic Medical Sciences, University of Ilesa, Ilesa, Osun State, Nigeria; [2]Department of Physiology, Faculty of Basic Medical Sciences, University of Ilesa, Ilesa, Osun State, Nigeria; [3]Department of Science Laboratory Technology, Faculty of Sciences, University of Ilesa, Ilesa, Osun State, Nigeria.

Address for Correspondence:
Hassan L.A.
Department of Anatomy, Faculty of Basic Medical Sciences, University of Ilesa, Ilesa, Osun State, Nigeria.
luqman_hassan@unilesa.edu.ng

INTRODUCTION

Lead (Pb) is a highly toxic metal popularly known in the environment, its exposure is a significant public health concern, particularly affecting children, who are most vulnerable to its toxic effects (Hauptman *et al.,* 2017; Anyanwu *et al.,* 2021). Lead poisoning occurs through its ability to induce oxidative stress and suppression of the body's ability to defend against oxidants. when lead accumulates in the body, often due to ingestion or inhalation of lead-containing materials, from lead paint-based (Patra *et al.,* 2011), contaminated soil (Smith *et al.,* 2023), Occupational exposure as seen with Construction Workers, Battery Manufacturing, and Recycling, Metal Production and Smelting, Plumbers and Pipe Fitters, Glass and Ceramic Manufacturers, Welders and Metal Fabricators (WHO, 2024). In the last few decades, research has found that lead poisoning is associated with brain injury, particularly in the cerebrum (Cao *et al.,* 2024). In this regard, findings focus on drugs, substances, or food-added supplements that can facilitate the adverse effects associated with lead poisoning.

Ginger (*Zingiber Officinale*) extracts possess 6-gingerol and 6-shogaol, active compounds that have been known to have a protective effect on the brain particularly on the regions associated with cognitive properties (Kim *et al.,* 2018) via their ability to modulate oxidative stress. While a number of research have discussed the effects of ginger extracts on different organs of the body, a few studies have examined the possible ameliorative impact of the powdered ginger in the treatment of deleterious impacts of lead on the brain, particularly the cerebral cortex. This study assessed the effects of a powered *Zingiber Officinale*-supplemented diet on the cerebral cortex.

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MATERIALS AND METHODS

Ethical Approval

Research ethical approval was obtained from the research ethical committee of the faculty of Basic Medical Sciences, University of Ilesa, Ilesa, Nigeria with approval number BMSUNILESA001/08/2024

Materials and reagents

Fresh ginger was sourced from round about market in Ilesa, Osun State, Nigeria, after which it was sliced into smaller sizes and air-dried for two months, the dried ginger was then grinded into powder using a spice grinder.

Diet Formulation

All animals were provided with commercially available standard rodent chow from weaning until the start of the study. At the beginning of the experimental phase, the animals were either given standard chow or a powdered ginger incorporated diet at the composition of 1% and 5%. The diet was administered *ad libitum* for 28 days.

Experimental Animals and Design

Healthy female Wistar rats used in this study were sourced from Igbo Sai animal breeder located in Ogbomoso, Oyo State, Nigeria. The animals were transported to the research Animal House at the University of Ilesa in Ilesa, Osun State, Nigeria where they were acclimatized for two weeks before the start of the study. They were kept in plastic cages measuring 25 × 15 × 14 inches in a temperature-controlled environment (22.5 °C ± 2.5 °C) with lights on at 7:00 a.m. The rats had unrestricted access to food and water. All procedures adhered to the approved protocols of the Faculty of Basic Medical Sciences, University of Ilesa, Ilesa, Nigeria and complied with the guidelines for animal care and use as outlined in the European Council Directive (EU2010/63).

Twenty adult female Wistar rats, each weighing between 150 and 170 g, were randomly divided into four groups of five animals each (n = 5). Groups A and B; the normal control and lead control were fed vehicle (distilled water) orally via gavage and basic lead carbonate at 30 mg/kg respectively. Both group A and B were fed with standard diet. Groups C and D received a diet supplemented with dried powdered ginger at compositions of 1% and 5% of their feed, respectively as previously reported by Eleazu *et al.* (2013). The vehicle, standard diet and the dried ginger-supplemented diet were provided daily throughout the experimental period of 28 days.

Determination of feed intake

Feed intake was measured daily, using an electronic weighing scale, as previously outlined by Onaolapo *et al.* (2023). The formula below was used individually for the animals. Subsequently, the results for all animals were calculated to determine the statistical average.

Biochemical test

Lipid Peroxidation

The level of lipid peroxidation of the blood sample was assessed by measuring the content of Malondialdehyde, following previously established methods by (Grotto *et al*., 2009).The color change was quantified using a spectrophotometer set to 532 nm.

Total Anti-oxidant Capacity

Total antioxidant capacity was assessed using enzyme-linked immunosorbent assay (ELISA) procedures to quantify the overall anti-oxidant capacity.

Animal Sacrifice and tissue collection

After the experimental period, the animals were euthanized by cervical dislocation, and blood taken for the assessment of the levels of oxidative markers (peroxidation and antioxidant status).The brain tissue was extracted, visually examined, weighed, and fixed in 10% neutral buffered formalin. The fixed sections of the cerebral cortex were then processed for paraffin embedding, cut to a thickness of 5µm, and stained with routine Hematoxylin and Eosin for histological findings.

Photomicrography

Histologically processed sections of the cerebral cortex were examined under a microscope using a Sellon-Olympus trinocular microscope (XSZ-107E, China) equipped with a Canon Powershot 2500 digital camera, and photomicrographs were captured at 400 magnification. A pathologist, unaware of the group assignments, assessed the histopathological changes.

Statistical analysis

Version 0.98 of Chris Rorden's ANOVA for Windows was used for data analysis. One-way analysis of variance (ANOVA) was employed for data analysis, and *post hoc* comparisons were conducted using the Tukey HSD test for both within-group and between-group comparisons. Results were presented as mean ± S.E.M., with a significance level set at $p < 0.05$ to indicate a statistically significant difference from the control group.

RESULTS

Figure 1 shows the effects of ginger on change in feed intake. Results show a statistically significant decrease ($p < 0.05$) in feed intake with lead treatment in group B compared to control group A while a significant increase ($p<0.05$) was seen in the groups treated with lead and fed ginger supplemented diet at composition 1% (group C) and 5% of feed (group D) respectively compared to group B.

Table 1 shows the effects of ginger on the levels of Malondialdehyde (MDA) and Total Anti-oxidant Capacity (TAC). Results show a statistically significant increase($p < 0.05$) in MDA levels with lead treatment in group B compared to control group A, a significant decrease ($p<0.05$)was seen in the groups treated

with lead and fed ginger supplemented diet at composition 1% (group C) and 5 % of feed (group D) respectively compared to group B. TAC levels decreased significantly ($p < 0.05$)with lead treatment in group B compared to control group A. Compared to group B, a significant increase ($p<0.05$) in the TAC levels was observed in the groups treated with lead and fed ginger supplemented diet at composition of 1% (group C) and 5% of feed (group D) respectively.

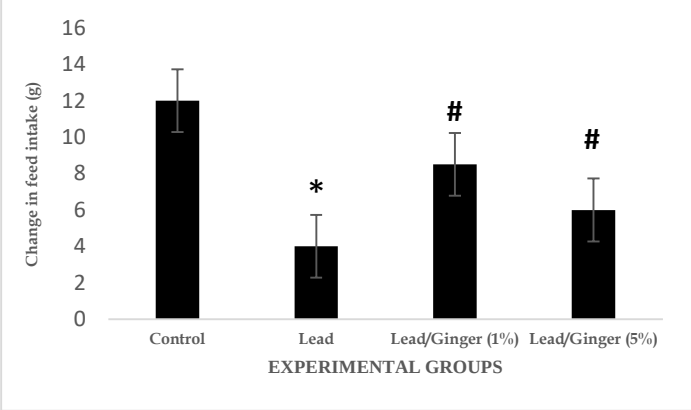

Figure 1: Effects of powdered ginger on feed intake in lead-treated rats. Each bar indicates the Mean ± Standard Error of Mean (S.E.M). Asterisks (*) denote a significant difference ($p < 0.05$) compared to the control group, while hashtags (#) indicate a significant difference ($p < 0.05$) from the lead group. The number of rats in each treatment group is 5.

Table 1: Effects of powdered ginger on the levels of Malondialdehyde (MDA) and Total Anti-oxidant Capacity (TAC) in lead-treated rats.

GROUPS	MDA (nmol/mg)	TAC (mMTE)
Control	1.20±0.14	2.22±0.44
Lead	2.31±0.15*	0.92±0.06*
Lead/Ginger (1%)	1.80±0.07*#	1.62±0.03*#
Lead/Ginger (5%)	1.79±0.09*#	1.81±0.10*#

Data presented as Mean ±Standard Error of mean (SEM), Asterisks (*) denote $p< 0.05$ vs. control, hashtags (#) denotes $p<0.05$ significant difference with Lead, each group has 10 rats. MDA: Malondialdehyde, TAC:Total Anti-oxidant Capacity,nmol/mg: Micrmole per milligram, mMTE: MillimolarTrolox Equivalents.

Histological Findings

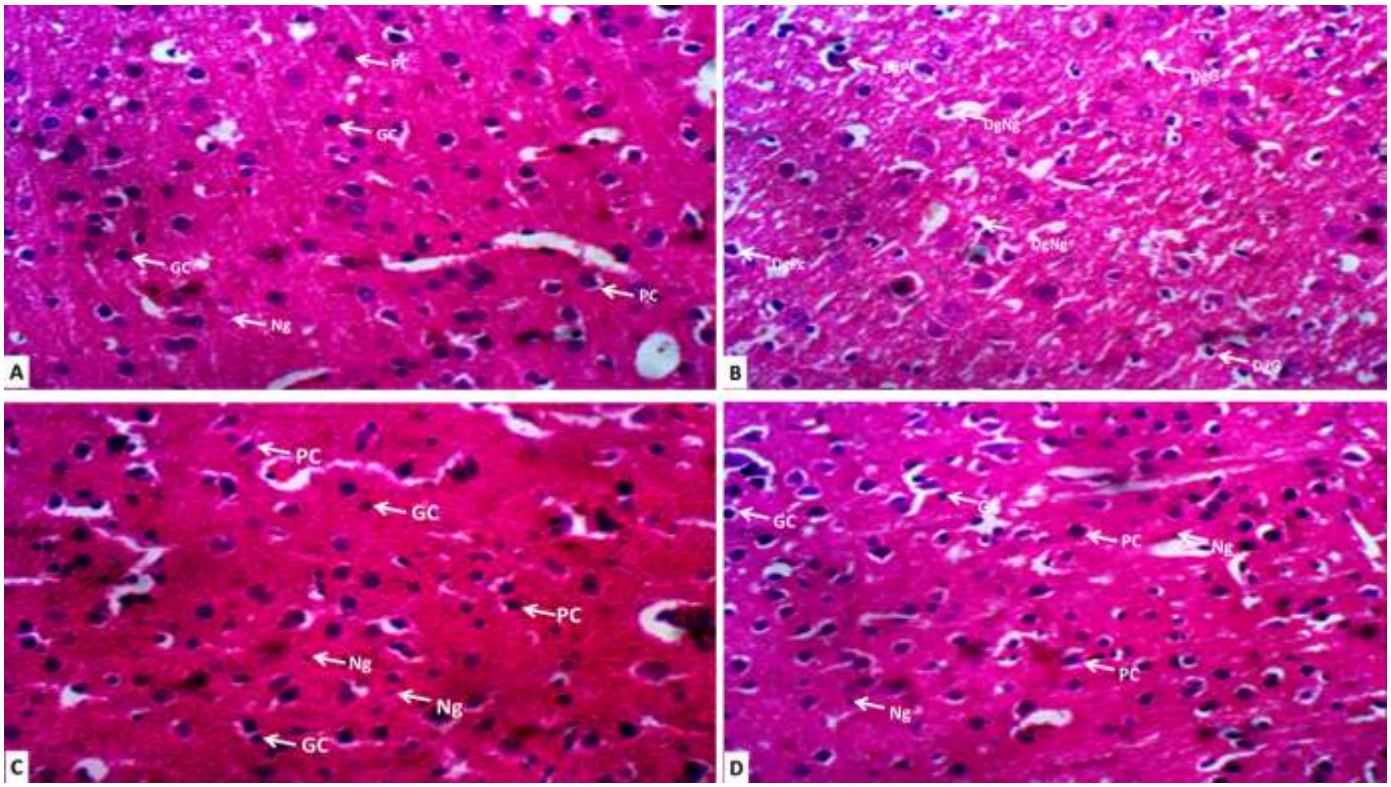

Figure 2 (a-d) shows the effects of dried ginger powered on the morphology of the cerebral cortex, (a) control, (b) Lead, (c) Lead and dried ginger supplemented diet at 1% of the feed, (d) Lead and dried ginger supplemented diet at 1% of the feed. Representative photomicrographs of sections from the rat cerebral cortex stained with hematoxylin and eosin (H&E) stained sections cerebral display pyramidal cells (Pc), neuroglia (Ng), granule cells (Gc), degenerating pyramidal cell (DgPC), degenerating granule cells (DgG). Mag. 400x.

DISCUSSION

This study explored the potential protective benefits of dried powdered ginger (*Zingiber Officinale*) on feed intake, oxidative stress and cerebral cortex injury in wholesome rats treated with lead. While several studies have examined similar effects with ginger extracts with no holistic effects, we were persuaded to examine if the administration of ginger powder would have more

ameliorative impacts than the extracts seeing that studies have shown that powdered ginger retains higher amounts of bioactive compounds (shogaols, Gingerols and Zingerone) than the extract(Mao *et al.*, 2019; Mustafa and Chin, 2023;Karangiya *et al.,* 2016).This study revealed that powdered ginger reversed the significant loss of appetite, increased oxidative stress, and cerebral cortex injury associated with lead administration.

In this study, a significant decrease in the change in feed intake was observed in both the lead-treated group and the groups co-administered lead and ginger compared to the control (Fig. 1). While powdered ginger reversed the loss of appetite associated with lead administration as observed in the groups of co-administered lead and powered ginger at one and five percent, the significant weight loss in the ginger-administered groups compared to the control group draws our attention. Several studies have enumerated the effects of ginger extracts on different organs, however, the controversies on certain factors as seen in the feed intake motivated us to examine the impacts of powdered ginger as commonly consumed by humans in Wistar rats. Our results contrast Karangiya *et al.* (2016) who in their animal study administered one percent concentration found that animals fed ginger had significantly higher feed intake than the animals in the control group, suggesting that ginger enhances digestive enzyme activity, leading to improved nutrient absorption in animals fed ginger-supplemented diets. Conversely, another study done by Eleazu *et al.* (2013) reported no significant differences in feed intake among various dietary treatment groups that included different levels of ginger (0%, 2%, 4%, and 6%). Interestingly, the feed intake result from our study is in corroboration with another study reported by Eltazi (2014) who revealed the addition of ginger powder at higher levels of ginger (above two percent) resulted in decreased feed intake compared to control, suggesting a potential threshold beyond which ginger may negatively impact consumption, as seen in our results where a decrease feed intake in the group fed five percent of powdered ginger when compared to the groups fed powder ginger at one percent and Lead was observed. In tandem with the stated factor, a study by Holt *et al.* (2012) suggests that ginger may enhance the thermic effect of food and modulate appetite-regulating hormones, contributing to a feeling of fullness and satiety. Neural mechanisms have shown that parts of the cerebral cortex particularly the left striate and extrastriate cortex are involved in hunger and satiety, moreover, disruption of the histological features of the cerebral cortex as seen in this study agrees with why the feed intake would decrease with the ginger administered group when compared to the control.

The oxidative stress markers (Malondiadehyde and Total Anti-oxidant Capacity) as shown in this study are in agreement with several studies that show an increase in levels of Malondiadehyde with lead, a well-known marker for oxidative stress, particularly resulting from lipid peroxidation of polyunsaturated fatty acids and decrease levels of Total anti-oxidant Capacity associated with lead. However, consistent with another study by Morvaridzadeh *et al.,* (2021) is the ameliorative impact of powder ginger in the groups administered one and five percent.

Also in this study, the neuroprotective effect of ginger was observed in histoarchitecture of the cerebral cortex, its neuroprotective effects are associated with its ability to impede malondialdehyde formation and Rummage the free radicals. The photomicrographs of the cerebral cortex from this study showed the degenerating pyramidal cells, granule cells, and neuroglia in agreement with Yibala *et al*. (2018) who reported the same effects on the ginger extract. However, the degenerating cells of the cerebral cortex with lead administration was fairly preserved in the groups administered lead and varying concentration of ginger at 1% and 5% in feed respectively.

CONCLUSION

In essence, the result of this study showed the ameliorative effects of powder ginger in lead-induced decrease in feed intake, oxidative stress, and cerebral cortex injury. The consumption of products supplemented with ginger and the usage of powdered ginger as spice should be further encouraged. However, while the consumption of ginger should be further enhanced, its excessive consumption should be cautioned in other to avoid adverse conditions that are associated with loss of appetite with its high intake as observed in this study.

Contributions of the authors

L.A. Hassan, F.O. Ojo and E.K. Adetorodeveloped and designed the study. E.K. Adetoro, M.B. Lawal, R.T. Lawal, and O.S Olaniyiperformed the experiments and analyzed the data. F.O. Ojo and L.A. Hassan drafted the manuscript. All authors reviewed and approved the final version of the manuscript.

Declaration of conflictof interest

The authors have no conflict of interest.

Data availability

The datasets generated during this study are available from the corresponding author if requested.

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