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Research Article

Ameliorative Effect of Dietary *Zingiber officinale* (Ginger) on Lead-Induced Gastrointestinal Damage in Wistar Rats

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ABSTRACT
This study investigated the protective effects of a *Zingiber officinale* (ginger)-supplemented diet against lead (Pb)-induced gastrointestinal damage in female Wistar rats. We assigned twenty-four rats to four groups for 28 days: Control, Lead-Only (30 mg/kg), Lead + 5% Ginger diet, and Lead + 10% Ginger diet. Serum biomarkers for oxidative stress (MDA, TAC) and inflammation (TNF-α, IL-6) were assessed alongside gastric and intestinal histopathology. Lead exposure significantly ($p < 0.05$) increased serum MDA, TNF-α, and IL-6 and depleted TAC, causing severe gastric necrosis and intestinal villous atrophy. Both 5% and 10% ginger diets dose-dependently reversed these biochemical changes and promoted significant histological repair. Notably, the 10% ginger diet normalized IL-6 levels and nearly restored the intestinal villous architecture. In conclusion, dietary ginger confers potent, dose-dependent protection against lead-induced gastrointestinal toxicity by combating systemic oxidative stress and inflammation. These findings support its use as a functional food for chemoprevention against heavy metal toxicity.
Keywords: Gastrointestinal damage; Inflammation; Lead-Induced toxicity, Oxidative stress; Wistar rats; *Zingiber officinale*

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INTRODUCTION

Heavy metals are pervasive environmental toxicants, with lead (Pb) being of particular concern due to its toxicity even at minute concentrations (Aglan *et al*., 2020). Widespread environmental contamination from anthropogenic activities has led to its presence in the air, water, and food chain, prompting regulatory bodies to establish maximum permissible limits in food products (Raj *et al*., 2023; Zhou *et al*., 2020).

Upon ingestion, lead is absorbed and distributed throughout the body, with over 95% sequestered in bone tissue where it can persist for decades, leading to chronic toxicity long after exposure has ceased (Wang *et al*., 2018; de Souza *et al*., 2018). Chronic lead exposure exerts multisystemic damage to the hematological, neurological, renal, and reproductive systems. In the gastrointestinal tract, it induces significant disturbances, such as abdominal pain and gastric irritation, primarily through mechanisms of

oxidative stress and inflammation (El-Tantawy, 2016; Aglan *et al*., 2020).

In the search for effective mitigation strategies, natural phytotherapeutics like *Zingiber officinale* (ginger) have gained considerable attention. Used for centuries in traditional medicine, ginger's therapeutic effects are attributed to its rich composition of phenolic compounds, such as gingerols and shogaols, which confer potent antioxidant and anti-inflammatory benefits (Mao *et al*., 2019; Strzelec *et al*., 2023). These properties are linked to the activation of the Nrf2 antioxidant pathway and the inhibition of the pro-inflammatory Akt/NF-κB signaling cascade (Ayustaningwarno *et al*., 2024; Ojo *et al*., 2025).

While the toxic effects of lead and the therapeutic potential of ginger are independently established, the specific ameliorative capacity of ginger against lead-induced gastrointestinal damage requires further investigation. This study, therefore, aims to investigate the protective effect of a *Zingiber officinale*-supplemented diet against lead-induced gastric and intestinal damage in an albino Wistar rat model.

MATERIALS AND METHODS

Ethical Approval

All experimental procedures involving animals were conducted in strict accordance with the guidelines for animal experimentation. The study protocol was reviewed and approved by the Institutional Animal Ethics Committee of the University of Ilesa, Osun State, Nigeria.

Plant Material and Diet Preparation

Fresh rhizomes of ginger (*Zingiber officinale*) were procured from a local market (Oja Odo Ori, Iwo, Osun State). The plant material was identified based on its distinct morphological and organoleptic characteristics, and as it is a widely available commercial food product. The rhizomes were washed, cut into small pieces, and air-dried at room temperature (25±2°C) for 3 weeks until a constant weight was achieved to ensure complete dehydration. The dried ginger was then pulverized into a fine powder using an industrial blender (automatic ginger production line).

A standard commercial growers mash (Top Feed Grower Mash Feed) served as the basal diet. Two experimental diets were prepared by thoroughly mixing the ginger powder with the standard mash to achieve final concentrations of 5% (w/w) and 10% (w/w). The diets were mixed in a commercial feed blender for 20 minutes to ensure homogeneity. The diets were stored in airtight containers until use.

Experimental Animals and Housing

Twenty-four (24) healthy female Wistar albino rats, with an initial body weight of 150–200g, were procured from Jumorak Farms (Iwo, Osun State). The animals were housed in polypropylene cages in the animal facility at the Faculty of Basic Medical Sciences, University of Ilesa. They were acclimatized for two weeks under standard laboratory conditions: a controlled temperature of 25±2°C, a 12-hour light/dark cycle, and adequate ventilation. Standard growers mash and clean drinking water were provided *ad libitum*. The estrous cycle of each rat was monitored, and animals in the same cycle phase were selected for the experiment to ensure hormonal consistency.

Experimental Design and Treatment Protocol

Following acclimatization, the 24 rats were randomly allocated into four groups (n=6 per group). The treatment was carried out for 28 consecutive days.

- **Group 1 (Control):** Received the standard diet and distilled water *ad libitum*, plus a daily oral gavage of distilled water (vehicle).
- **Group 2 (Lead-Only):** Received the standard diet *ad libitum* and was administered 30 mg/kg body weight of lead acetate (Pb $(CH_3COO)_2$) dissolved in distilled water daily via oral gavage.
- **Group 3 (Lead + 5% Ginger):** Received the 5% ginger-supplemented diet *ad libitum* and was administered 30 mg/kg body weight of lead acetate daily via oral gavage.
- **Group 4 (Lead + 10% Ginger):** Received the 10% ginger-supplemented diet *ad libitum* and was administered 30 mg/kg body weight of lead acetate daily via oral gavage.

Sample Collection and Processing

Twenty-four hours after the final administration on day 28, the rats were euthanized by cervical dislocation. Whole blood was collected via cardiac puncture into heparinized tubes. The blood samples were then centrifuged at 3000 rpm for 15 minutes to separate the plasma, which was stored at -20°C for subsequent biochemical analysis. Immediately following blood collection, the abdomen was opened,

and the stomach and a segment of the small intestine were excised, rinsed with normal saline, and fixed in 10% neutral buffered formalin for histopathological examination.

Histopathological Analysis

Specimens of the stomach and intestine were fixed in 10% neutral buffered formalin for at least 48 hours. The tissues were then dehydrated through an ascending series of ethanol concentrations (70%, 80%, 95%, and 100%), cleared in xylene, and embedded in paraffin wax. Sections of 5 µm thickness were cut using a rotary microtome and stained with **Hematoxylin and Eosin (H&E)** following standard protocols (Nasr *et al*., 2017). The stained sections were examined under a light microscope, and photomicrographs were captured at ×400 magnification.

Biochemical Assays

Lipid peroxidation (Malondialdehyde - MDA) assay

The level of lipid peroxidation in the plasma was quantified by measuring malondialdehyde (MDA) concentration using the thiobarbituric acid reactive substances (TBARS) method described by Buege and Aust (1978), with minor modifications (Dare *et al*., 2024). Briefly, 1.0 mL of plasma was mixed with 2.0 mL of a TCA-TBA-HCl reagent (15% w/v trichloroacetic acid; 0.375% w/v thiobarbituric acid; 0.25 N hydrochloric acid). The mixture was vortexed and heated in a boiling water bath for 15 minutes. After cooling, the mixture was centrifuged at 3000 rpm for 10 minutes. The absorbance of the resulting pink supernatant was measured at 532 nm against a reagent blank.

Total antioxidant capacity (TAC) assay

The total antioxidant capacity (TAC) of serum was determined through the ferric reducing antioxidant power (FRAP) assay. This approach measures TAC by evaluating the conversion of the ferric tripyridyltriazine (Fe^{3+}-TPTZ) complex into its ferrous (Fe^{2+}) form, with $FeSO_4 \cdot 7H_2O$ solution (0.1–1 mmol/L) serving as the calibration standard (Benzie & Strain, 1996).

Tumor necrosis factor-alpha (TNF-A) and interleukin-6 (IL-6) assay

The concentration of the pro-inflammatory cytokine TNF-alpha and IL-6 in the plasma was determined using a commercial Enzyme-Linked Immunosorbent Assay (ELISA) kit (Abcam, Cambridge, UK), following the manufacturer's provided protocol.

Data Analysis

All data were analyzed using GraphPad Prism software (Version 6.01). Results were expressed as the mean ± Standard Error of the Mean (SEM). Statistical comparisons between the groups were performed using a one-way Analysis of Variance (ANOVA), followed by Tukey's post-hoc test for multiple comparisons. A p-value of less than 0.05 ($p < 0.05$) was considered statistically significant.

RESULTS

The effects of lead exposure and ginger supplementation on key serum biomarkers are summarized in Table 1. Exposure to lead acetate (Group 2) induced a state of significant oxidative stress and inflammation when compared to the control group (Group 1). This was evidenced by a significant ($p < 0.05$) increase in the lipid peroxidation marker, malondialdehyde (MDA), from 1.351 ± 0.072 µM/L to 2.223 ± 0.106 µM/L. Concurrently, the total antioxidant capacity (TAC) was significantly ($p < 0.05$) depleted, decreasing from 2.377 ± 0.150 mmol/l in the control group to 1.076 ± 0.086 mmol/l in the lead-only group. Furthermore, the pro-inflammatory cytokines, TNF-α and IL-6, were significantly ($p < 0.05$) elevated in the lead-only group.

Dietary supplementation with *Zingiber officinale* effectively counteracted these changes in a dose-dependent manner. Both the 5% and 10% ginger-supplemented groups (Groups 3 and 4) showed a significant ($p < 0.05$) reduction in MDA levels and a significant ($p < 0.05$) restoration of TAC compared to the lead-only group. Similarly, both ginger diets led to a significant ($p < 0.05$) attenuation of TNF-α and IL-6 levels. Notably, the 10% ginger diet demonstrated superior efficacy, reducing IL-6 levels to 20.82 ± 0.3629 pg/mL, a level not significantly different from the healthy control group.

The histopathological examination of the stomach revealed the protective effects of ginger at the tissue level (Plate 1). The control group (Plate 1C) displayed a normal gastric mucosal architecture with well-organized glands. In sharp contrast, the lead-only group (Plate 1B) exhibited severe histopathological damage, characterized by widespread necrosis of glandular cells and extensive cytoplasmic vacuolation. The ginger-supplemented group (Plate 1D) showed a marked improvement, with a significant

reduction in necrosis and clear evidence of tissue regeneration.

Similarly, lead exposure caused catastrophic damage to the intestinal lining (Plate 2). The control group (Plate 2A) presented a healthy mucosal structure with long, intact villi and deep crypts. The lead-only group (Plate 2B) suffered from severe villous atrophy, with blunted, fused villi and widespread sloughing of the surface epithelium. Ginger supplementation induced a remarkable, dose-dependent recovery. While the 5% ginger group (Plate 2C) showed partial healing, the 10% ginger group (Plate 2D) displayed a near-complete regeneration of the villous architecture, which closely resembled the healthy structure of the control group.

Table 1. Effects of *Zingiber officinale* (Ginger) Supplementation on Serum Biomarkers of Oxidative Stress and Inflammation in Lead-Exposed Female Wistar Rats

	MDA (µM/L)	TAC (mmol/l)	TNF-alpha (pg/mL)	IL-6 (pg/mL)
Group 1 (Control):	1.351 ± 0.072	2.377 ± 0.150	123.3 ± 3.349	17.48 ± 1.027
Group 2 (Lead-Only):	2.223 ± 0.106 α	1.076 ± 0.086 α	176.5 ± 3.209 α	25.69 ± 1.244 α
Group 3 (Lead + 5% Ginger)	1.903 ± 0.003 αβ	1.788 ± 0.065 β	150.9 ± 5.232 αβ	24.79 ± 0.4502 αβ
Group 4 (Lead + 10% Ginger	1.670 ± 0.038 αβ	1.869 ± 0.275 β	144.6 ± 2.839 αβ	20.82 ± 0.3629 β

Data presented as mean ± SEM. α represents a significant difference ($p < 0.05$) compared to the Control Group. β represents a significant difference ($p < 0.05$) compared to the Lead-Only Group.

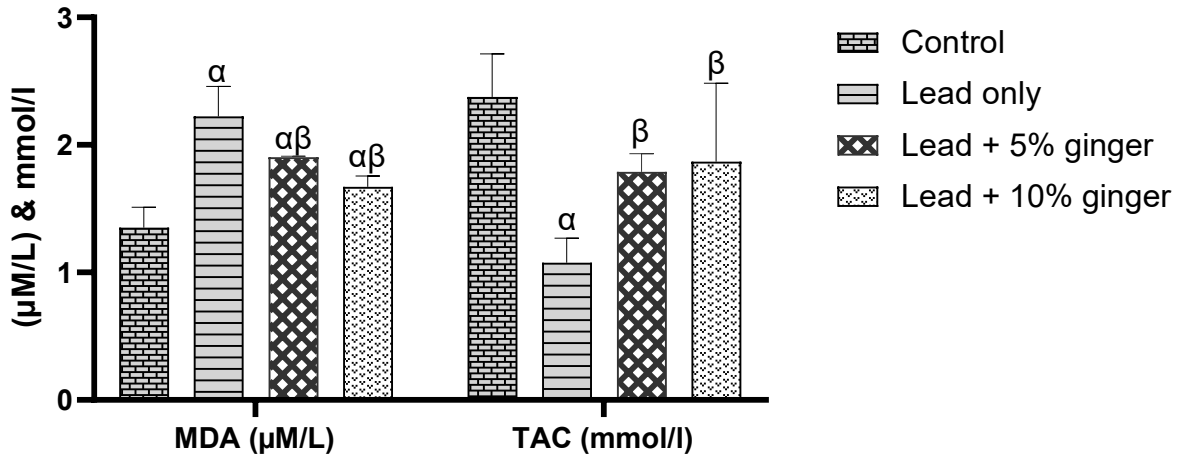

Figure 1. Effects of Ginger supplementation on Serum Malondialdehyde (MDA) and Total Antioxidant Capacity (TAC) in lead-exposed Wistar rats

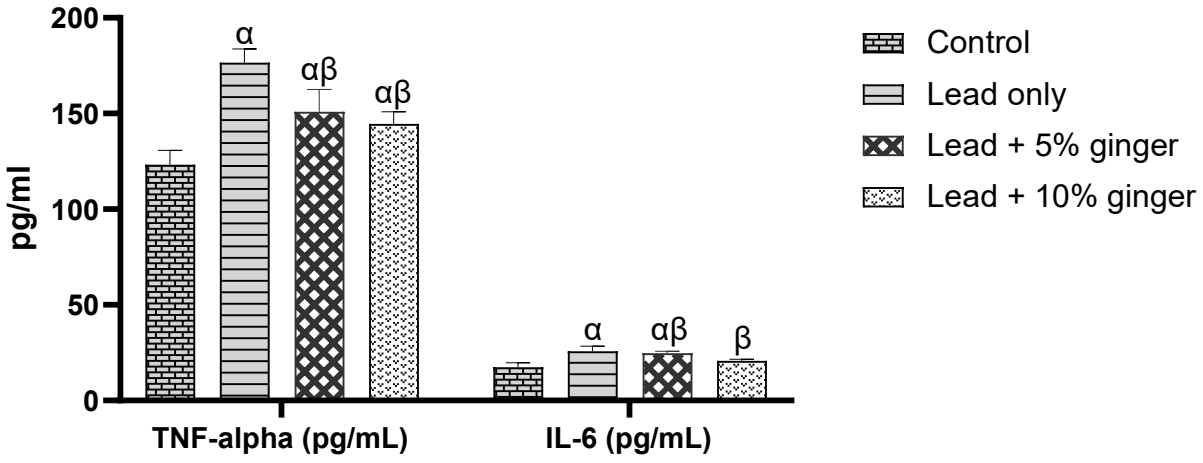

Figure 2. Effects of Ginger supplementation on Serum Tumor Necrosis Factor-alpha (TNF-α) and Interleukin-6 (IL-6) in lead-exposed Wistar rats

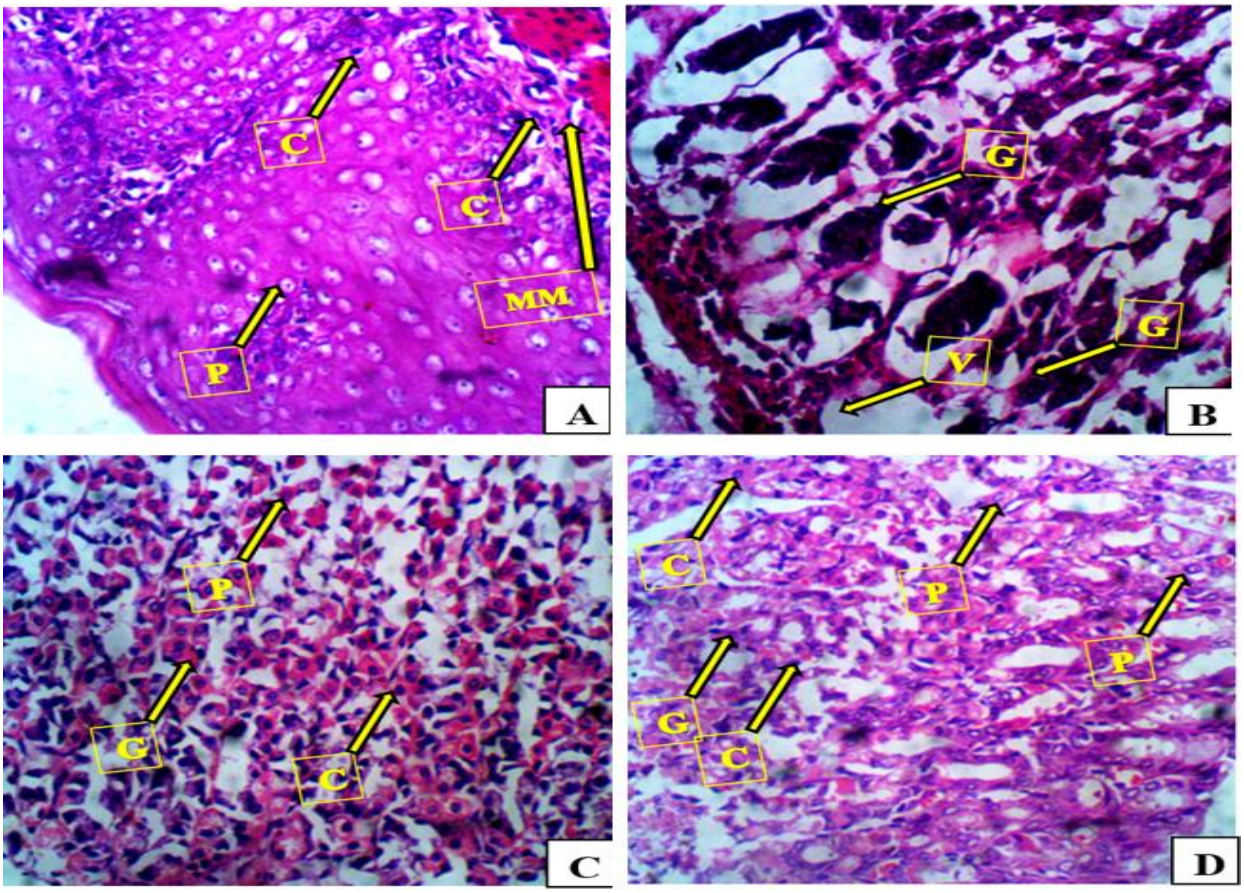

Plate 1. Protective effect of ginger on lead-induced gastric histopathology (H&E, 400x)

(**A**) Control group, showing normal gastric glands (G) with parietal (P) and chief (C) cells. (**B**) Lead-Only group, exhibiting severe necrosis and cytoplasmic vacuolation (V). (**D**) Lead + 10% Ginger group, showing marked regeneration of gastric glands

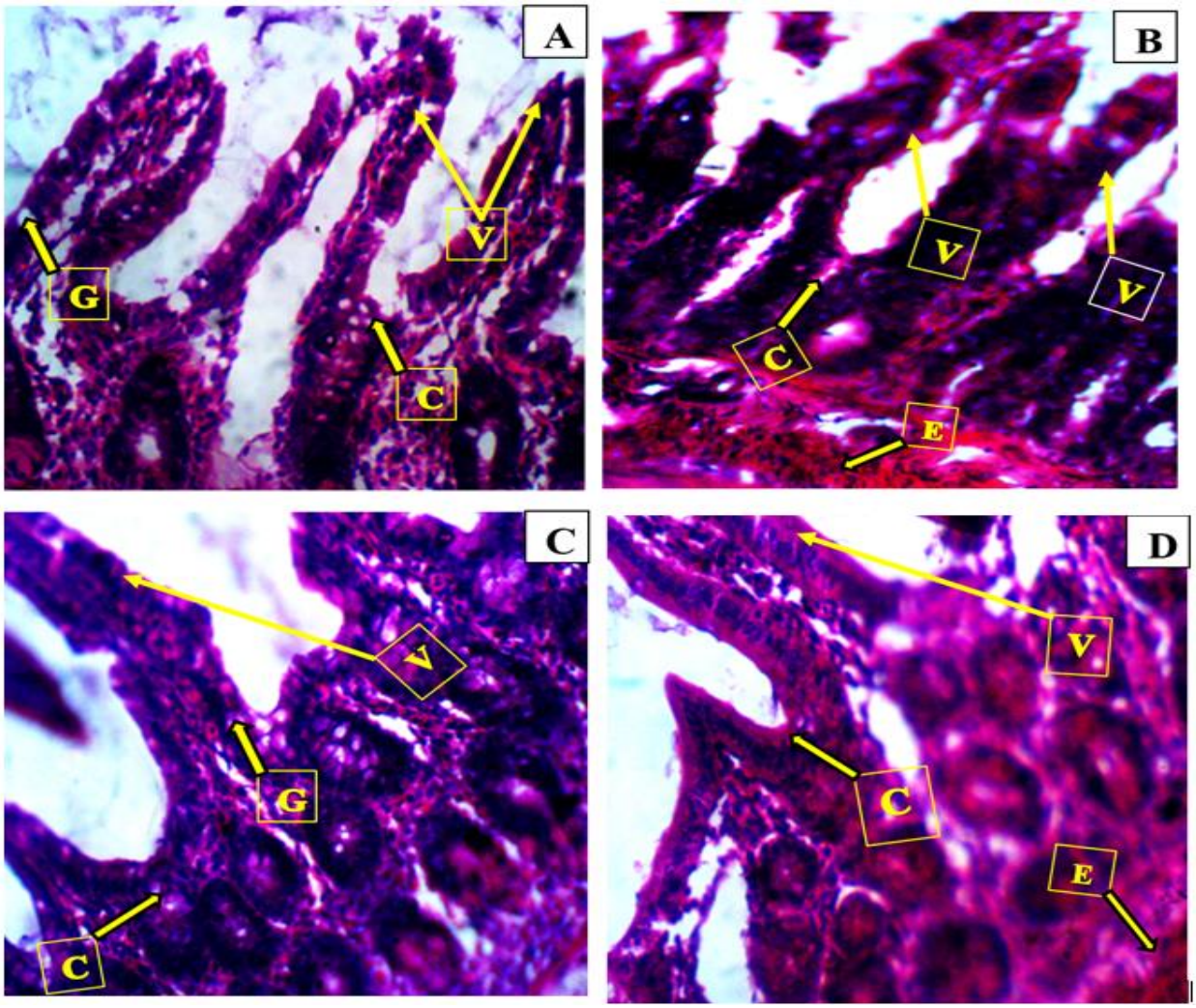

Plate 2. Ameliorative effect of ginger on lead-induced intestinal histopathology (H&E, 400x).
(**A**) Control group, with long, intact villi (V) and deep crypts (C). (**B**) Lead-Only group, showing severe villous atrophy and epithelial sloughing (E). (**C**) Lead + 5% Ginger and (**D**) Lead + 10% Ginger groups, demonstrating dose-dependent restoration of villous architecture.

DISCUSSION

Lead (Pb) is a major health concern, damaging the gastrointestinal (GI) tract through oxidative stress and inflammation (Asiwe *et al*., 2022). Ginger (*Zingiber officinale*), rich in antioxidant and anti-inflammatory compounds (Mao *et al*., 2019; Mashhadi *et al*., 2013), may offer protection, but its dose-dependent effects on Pb-induced GI damage are unclear. This study shows that ginger-supplemented diets provide dose-dependent protection against lead-induced stomach and intestinal injury in female Wistar rats.

This study results reinforce the well-established mechanism of lead-induced toxicity, as lead exposure in Lead-Only group (Group 2), significantly increased plasma malondialdehyde (MDA), a key marker of lipid peroxidation driven by excessive reactive oxygen species (ROS) (Virgolini & Aschner 2021; Lopes *et al*., 2016) as seen in Table 1 and Figure 1. This biochemical injury was clearly visible in the present study as marked histopathological alterations, including necrosis and cytoplasmic vacuolation in the stomach (Plate 1B), and villous atrophy with epithelial shedding in the intestine (Plate 2B). Such pathological changes are well known to impair digestive and absorptive capacity, as previously documented in other models of lead toxicity (Wani *et al*., 2015).

The novelty of this work lies in demonstrating that a simple dietary strategy can mitigate such damage.

Both 5% and 10% ginger-supplemented diets reduced MDA levels significantly compared to the Lead-Only group. The 10% ginger diet (Group 4) was especially potent, reducing MDA concentrations significantly relative to the Lead-Only group, effectively restoring them to values not statistically different from healthy controls. This antioxidant effect can be attributed to bioactive compounds in ginger, particularly 6-gingerol, which is known to neutralize free radicals directly while also enhancing endogenous antioxidant enzymes such as superoxide dismutase and catalase (Alsahli *et al*., 2021). By scavenging ROS and stabilizing membranes, ginger prevented the extensive lipid peroxidation and necrotic cell death evident in untreated, lead-exposed rats.

Lead exposure significantly reduced Total Antioxidant Capacity (TAC) from 2.377 ± 0.150 mmol/L in the healthy control group to 1.076 ± 0.086 mmol/L. This decline indicates significant oxidative stress, a state where lead-induced reactive oxygen species deplete the body's natural antioxidant reserves. Conversely, dietary ginger partially restored these levels, demonstrating a protective effect. The groups receiving 5% and 10% ginger supplementation showed significantly improved TAC values of 1.788 ± 0.065 mmol/L and 1.869 ± 0.275 mmol/L, respectively. While not fully returning to control levels, these results confirm that ginger enhanced the overall antioxidant defense capacity in a dose-dependent manner against lead-induced toxicity.

The interplay between oxidative stress and inflammation is central to understanding these results. ROS not only damage cellular structures directly but also activate redox-sensitive transcription factors such as Nuclear Factor-kappa B (NF-κB). NF-κB is a key regulator of inflammation, controlling the expression of pro-inflammatory cytokines including Tumor Necrosis Factor-alpha (TNF-α) and Interleukin-6 (IL-6) (Lawrence, 2009). Activation of this pathway creates a self-perpetuating inflammatory cycle that amplifies tissue injury (Harshitha *et al*., 2024). This findings strongly support this mechanism. In the Lead-Only group, plasma TNF-α and IL-6 were significantly elevated (Table 1), indicating a systemic inflammatory state that directly contributed to the mucosal lesions observed.

The supplemented ginger diet was able to suppress these cytokines highlighting its anti-inflammatory efficacy. The 10% ginger diet significantly reduced both TNF-α and IL-6, and most notably restored IL-6 to levels indistinguishable from the control group. This aligns with mechanistic studies demonstrating that gingerols and shogaols inhibit NF-κB activation, thereby reducing the transcription of pro-inflammatory mediators (Ballester *et al*., 2022). By interrupting this inflammatory loop, ginger created a biological environment more favorable for tissue healing.

This biochemical stabilization provided the foundation for the structural recovery observed in histological sections. In the stomach, necrosis and vacuolation evident in the Lead-Only group were replaced by regenerating gastric glands in ginger-supplemented groups (Plate 1D). The protective effect was even more striking in the intestine. Severe villous atrophy and epithelial loss in lead-exposed rats were restored in a dose-dependent manner, with the 10% ginger group (Plate 2D) showing nearly complete regeneration of villous architecture. The well-formed, elongated villi and intact epithelial lining closely resembled those of the control group, indicating restoration of both absorptive and barrier functions. This structural recovery suggests not only morphological repair but also functional preservation of the gastrointestinal system, which is essential for maintaining overall health under toxic stress.

This protection is closely linked to the antioxidant and anti-inflammatory activities of ginger, which helped counteract systemic biochemical disturbances and preserved the structure of gastrointestinal mucosa. Among the tested groups, a 10% ginger-supplemented diet was particularly effective, as it normalized oxidative and inflammatory biomarkers to levels comparable with healthy controls and supported significant regeneration of damaged gastric and intestinal tissues.

While these findings are from an animal model, they hold potential translational implications for human health. Given that ginger (*Zingiber officinale*) is a widely consumed food spice with a high safety profile, its role as a functional food for mitigating heavy metal toxicity warrants consideration. Lead exposure remains a global public health issue, particularly in developing nations, and accessible, affordable nutritional strategies could serve as a valuable protective tool. These results suggest that dietary ginger could complement conventional therapies or act as a primary preventive measure in populations at

high risk, although clinical trials are necessary to validate these protective effects in humans.

While this study provides compelling evidence for the protective effects of dietary ginger, several limitations should be acknowledged. Firstly, this research was conducted using an animal model. Although Wistar rats are a well-established model for toxicological studies, direct extrapolation of these findings, particularly the dosage, to human populations must be done with caution. Secondly, the intervention period was 28 days, representing sub-chronic exposure. The efficacy of ginger against chronic, low-dose lead exposure, which is a more common human exposure scenario, warrants further investigation. Thirdly, our biochemical analyses were performed on plasma, reflecting systemic changes. A more nuanced understanding could be achieved by performing tissue-specific assays for oxidative stress and inflammatory markers directly within the gastric and intestinal mucosa. Finally, while we demonstrated a functional outcome (tissue protection), we did not delve into the deeper molecular mechanisms, such as the direct quantification of NF-κB activation or the expression levels of endogenous antioxidant enzymes (e.g., SOD, CAT, GPx).

Furthermore, this study did not include a 'Ginger-Only' control group. While our primary objective was to assess the protective effects of ginger against lead-induced damage, this additional group would have allowed for a clearer understanding of ginger's baseline effects on the measured gastrointestinal and biochemical parameters in healthy, non-exposed rats.

CONCLUSION

In conclusion, this study provides definitive evidence that dietary supplementation with *Zingiber officinale* confers significant, dose-dependent protection against lead-induced gastric and intestinal damage. By potently attenuating systemic oxidative stress and inflammation, ginger preserves the histological integrity and promotes the regeneration of the gastrointestinal mucosa. These findings strongly support the use of ginger as a functional food and underscore the immense potential of chemopreventive nutritional strategies in combating the pervasive toxicity of environmental heavy metals like lead. This research paves the way for further exploration of whole foods as a safe, accessible, and effective means to enhance physiological resilience against environmental toxicants.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this study.

Authors' Contributions

Olamide Samuel Olayemi and Luqman Adepoju Hassan conceived and designed the research. while Oluwabukola Margaret Oladele, and Oluwafemi Samuel Olaniyi contributed to data collection and experimental procedures. Kolade Pelumi Folorunso assisted in data analysis. The manuscript was drafted by Olamide Samuel Olayemi and revised critically for intellectual content by all authors, who also approved the final version.

REFERENCES

Alsahli, M. A., Almatroodi, S. A., Almatroudi, A., Khan, A. A., Anwar, S., Almutary, A. G., Alrumaihi, F., & Rahmani, A. H. (2021). 6-Gingerol, a major ingredient of ginger attenuates diethylnitrosamine-induced liver injury in rats through the modulation of oxidative stress and anti-inflammatory activity. *Mediators Inflamm.*, *2021*, 6661937. https://doi.org/10.1155/2021/6661937

Angon, P. B., Islam, M. S., Kc, S., Das, A., Anjum, N., Poudel, A., & Suchi, S. A. (2024). Sources, effects and present perspectives of heavy metals contamination: Soil, plants and human food chain. *Heliyon*, *10*(7), e28357. https://doi.org/10.1016/j.heliyon.2024.e28357

Asiwe, J. N., Daubry, T. M. E., & Okon, I. A. (2022). Ginkgo biloba supplement reverses lead (II) acetate–induced haematological imbalances, hepatic and renal dysfunctions in male Wistar rat. *Biol. Trace Elem. Res.*, *200*(11), 5134–5144. https://doi.org/10.1007/s12011-022-03098-6

Ayustaningwarno, F., Anjani, G., Ayu, A. M., & Fogliano, V. (2024). A critical review of Ginger's (Zingiber officinale) antioxidant, anti-inflammatory, and immunomodulatory activities. *Front. Nutr.*, *11*, 1364836. https://doi.org/10.3389/fnut.2024.1364836

Ballester, P., Cerdá, B., Arcusa, R., Marhuenda, J., Yamedjeu, K., & Zafrilla, P. (2022). Effect of ginger on inflammatory diseases. *Molecules*, *27*(21), 7223. https://doi.org/10.3390/molecules27217223

Benzie, I. F., & Strain, J. J. (1996). The ferric reducing ability of plasma (FRAP) as a measure of "antioxidant power": the FRAP assay. *Anal. Biochem.*, *239*(1), 70–76. https://doi.org/10.1006/abio.1996.0292

Buege, J. A., & Aust, S. D. (1978). Microsomal lipid peroxidation. *Methods Enzymol.*, *52*, 302-310.

de Souza, I. D., de Andrade, A. S., & Dalmolin, R. J. S. (2018). Lead-interacting proteins and their implication in lead poisoning. *Crit. Rev. Toxicol.*, *48*(5), 375–386. https://doi.org/10.1080/10408444.2018.1429387

El-Tantawy, W. H. (2016). Antioxidant effects of Spirulina supplement against lead acetate-induced hepatic injury in rats. *J. Tradit. Complement. Med.*, *6*(4), 327–331. https://doi.org/10.1016/j.jtcme.2015.02.001

Flora, G., Gupta, D., & Tiwari, A. (2012). Toxicity of lead: A review with recent updates. *Interdiscip. Toxicol.*, *5*(2), 47–58. https://doi.org/10.2478/v10102-012-0009-2

Harshitha, P., Bose, K., & Dsouza, H. S. (2024). Influence of lead-induced toxicity on the inflammatory cytokines. *Toxicology*, *503*, 153771. https://doi.org/10.1016/j.tox.2024.153771

Ilesanmi, O. B., Adeogun, E. F., Odewale, T. T., & Chikere, B. (2022). Lead exposure-induced changes in hematology and biomarkers of hepatic injury: Protective role of TrévoTM supplement. *Environ. Anal. Health Toxicol.*, *37*(2), e2022007. https://doi.org/10.5620/eaht.2022007

Lawrence, T. (2009). The nuclear factor NF-kappaB pathway in inflammation. *Cold Spring Harb. Perspect. Biol.*, *1*(6), a001651. https://doi.org/10.1101/cshperspect.a001651

Lopes, A. C., Peixe, T. S., Mesas, A. E., & Paoliello, M. M. (2016). Lead exposure and oxidative stress: A systematic review. *Rev. Environ. Contam. Toxicol.*, *236*, 193–238. https://doi.org/10.1007/978-3-319-20013-2_3

Mao, Q. Q., Xu, X. Y., Cao, S. Y., Gan, R. Y., Corke, H., Beta, T., & Li, H. B. (2019). Bioactive compounds and bioactivities of ginger (Zingiber officinale Roscoe). *Foods*, *8*(6), 185. https://doi.org/10.3390/foods8060185

Mashhadi, N. S., Ghiasvand, R., Askari, G., Hariri, M., Darvishi, L., & Mofid, M. R. (203). Anti-oxidative and anti-inflammatory effects of ginger in health and physical activity: Review of current evidence. *Int. J. Prev. Med.*, *4*(Suppl. 1), S36–S42.

Nasr, M., Abdel-Naser, S., El-Naqib, M. H., & Omar, G. (2017). Multimodal deep learning for multimodal image analysis of PD-L1, immunotherapy response, and overall survival in clear cell renal cell carcinoma. *Sci. Rep.*, *7*(1), 10703. https://doi.org/10.1038/s41598-017-11209-2

Ojo F.O., Hassan L.A., Olaniyi O.S., Adetoro E.K., Lawal R.T. and Lawal M.B. (2025). Zingiber Officinalesupplemented diet reversed lead-induced oxidative stress and cerebral cortex injuries in adult female Wistar rats. *J. Exp. Clin. Anat.*, *22*(1), 22-26.

Patra, R. C., Rautray, A. K., & Swarup, D. (2011). Oxidative stress in lead and cadmium toxicity and its amelioration. *Vet. Med. Int.*, *2011*, 457327. https://doi.org/10.4061/2011/457327

Raj, K., & Das, A. P. (2023). Lead pollution: Impact on environment and human health and approach for a sustainable solution. *Environ. Chem. Ecotoxicol.*, *5*, 79–85. https://doi.org/10.1016/j.enceco.2023.02.001

Strzelec, M., Detka, J., Mieszczak, P., Sobocińska, M. K., & Majka, M. (2023). Immunomodulation—a general review of the current state-of-the-art and new therapeutic strategies for targeting the immune system. *Front. Immunol.*, *14*, 1127704. https://doi.org/10.3389/fimmu.2023.1127704

Virgolini, M. B., & Aschner, M. (2021). Molecular mechanisms of lead neurotoxicity. *Adv. Neurotoxicol.*, *5*, 159–213. https://doi.org/10.1016/bs.ant.2020.11.002

Wang, Z., Hasegawa, J., Wang, X., Matsuda, A., Tokuda, T., Miura, N., & Watanabe, T. (2011). Protective effects of ginger against aspirin-induced gastric ulcers in rats. *Yonago Acta Med.*, *54*(1), 11–19.

Wani, A. L., Ara, A., & Usmani, J. A. (2015). Lead toxicity: A review. *Interdiscip. Toxicol.*, *8*(2), 55–64. https://doi.org/10.1515/intox-2015-0009

Zhou, F., Yin, G., Gao, Y., Ouyang, L., Liu, S., & Jia, Q. (2020). Insights into cognitive deficits caused by low-dose toxic heavy metal mixtures and their remediation through a postnatal enriched environment in rats. *J. Hazard. Mater.*, *388*, 122081. https://doi.org/10.1016/j.jhazmat.2019.122081