Original Research Article

Therapeutic Potential of Ginger-Supplemented Diet in Reversing Lead-Induced Nephrotoxicity

ABSTRACT

Background: The flowering plant ginger, scientifically known as *Zingiberofficinale* offers numerous health benefits, including immune support. Its bioactive compounds such as shogaols and gingerols, contribute to its antioxidant and anti-inflammatory properties.

Objective: To access ginger (*Zingiberofficinale*) as a protective agent against Nephrotoxicity induced by Lead by accessing the levels of inflammatory markers (Interleukin -6, Tumor Necrosis Factor), kidney function (Creatinine), and general kidney morphology.

Methods: Twenty-four (24) female Wistar rats weighing 150-170g were carefully divided into four groups (6 per group) and housed in plastic cages. The groups were Groups A (Control), B (the Lead), C [Lead and ginger (1%)], and D [Lead and ginger (5%)]. The rats were treated for 28 days, the control and the Lead groups were fed with normal rat diets and distilled water, while the Lead and ginger group was fed with ginger supplemented diet.

On day 29, the rats were sacrificed using cervical dislocation following animal ethical guidelines. Blood samples were collected from the apex of the heart (intracardiac puncture), stored in a heparinized bottle, and centrifuged to undergo further analysis (creatinine, interleukin

6, and Tumor Necrosis Factor). The kidney was removed and fixed in 10% neutral buffered formalin. The organ was then processed for histological analysis.

Results: The results showed a statistically significant increase ($P<0.05$) in the levels of creatinine,Tumour Necrotic Factor Alpha **(**TNF-alpha), and Interleukin-6 (IL-6) in group B compared to group A. While a statistically significant decrease ($P<0.05$) was observed in groups C and D compared to group B. Histomorphological distortion was observed in group B compared to group A, while the lesion was reversed in groups C and D.

Conclusion: This study found that ginger has substantial health benefits for kidney tissues, particularly in nephrotoxicity caused by lead. Its ability to preserve kidney tissue, decrease inflammation, and improve kidney function highlights its significance as a treatment option for preventing or lessening kidney harm associated with toxic substances or underlying health issues. Further investigations are necessary to explore the possible adverse effects or contraindications that could be associated with ginger supplements or ginger-supplemented diets in humans.

Keywords: Lead, Nephrotoxicity, Kidney, Ginger, Anti-Inflammatory, Hazardous element.

INTRODUCTION

Ingestion of lead (Pb) can accumulate this potentially hazardous element in the blood, bones, liver, kidneys, brain, and skin (Boskabady*et al.*, 2021). Due to the body's inability to effectively eliminate Pb, its adverse health impacts can manifest in immediate and prolonged ways. Lead harms the human body's immunological, gastrointestinal, endocrine, hepatic, and reproductive systems(Krzywy*et al.*, 2010). Lead (Pb) can have severe health effects on animals, plants, and

humans through various routes of exposure such as the air, soil, food, water, and airborne particles (Chen *et al* .,2023). Lead can be ingested or inhaled through multiple routes. While it's also absorbed through the digestive system, the main pathway for lead and its compounds in the workplace is through the respiratory system (Spivey, 2007; Giel-Pietraszuk*et al*., 2012; Drop *et al*., 2018).Initial symptoms of exposure to inorganic lead include anemia, lethargy, irritability, weight reduction, loss of appetite, and occasional vomiting (Mehana*et al*., 2012).Moreover, exposure to high levels of lead is responsible for anemia, hypertension, kidney damage, behavioral alterations, and harm to the reproductive system (Kakar and Jeffery, 2005). Zhang *et al*. (2024) reported that lead (Pb) possesses nephrotoxic properties, potentially leading to a quicker onset of renal damage. Exposure to lead can occur through contact with lead-based paints, fertilizers, vehicles, batteries, etc. (Dewanjee*et al*., 2013).Exposure to lead also plays a major role in nephrotoxicity and research (Sataru*get al*.,2020) has shown that ginger has an ameliorative impact on the adverse effects of lead.

Ginger, classified as *Zingiber officinale* Roscoe within the Zingiberaceae family, shares a common family of plants with turmeric and cardamom. The pungent scent of ginger is primarily attributed to the presence of ketones, especially gingerols, which are the key components of ginger examined in the majority of health-related scientific studies(Ann and Zingang, 2011; Koh*et al*., 2011; Ali *et al*., 2023). The edible portion of ginger is the rhizome, which is the horizontal stem where roots emerge. The current name of the spice originates from the Middle English word gingivae, however, the Sanskrit word ingavera, which signifies "horn root," is earlier by over 3,000 years (Ann andZingang, 2011).The plant is primarily examined for its antibacterial, anticancer, antioxidant, antidiabetic, nephroprotective, hepato-protective, larvicidal, analgesic, anti-inflammatory, and immunomodulatory properties(Ayse*et al* .,2008; Al-Tahtawy*et*

al., 2011; OmoyaandAkharaiy 2011). The mechanism by which ginger exerts its anti-nausea effects, despite blocking serotonin receptors and having anti-vomiting effects in both the digestive and central nervous systems, remains unclear (Der Marderosian and Beutler, 2006)Studies conducted on human synoviocytes in vitro have shown that ginger extract can prevent the activation of tumor necrosis factor α and the production of cyclooxygenase-2, indicating that it has potential anti-inflammatory properties (Frondoza*et al*., 2004). Ginger adverse effects are uncommon, but they may also cause mild to moderate gastrointestinal issues, including heartburn, diarrhea, and mouth irritation (Altman and Marcussen, 2001). In addition to its beneficial inotropic effects in animal models, ginger has been linked to arrhythmia cases (Brett, 2007).In a study done by Ogunleye*et al* (2018), essential oils derived from ginger was associated with an ameliorative effects on kidney injuries observed in cadmium-treated rats. However, the current study evaluates the effects of ginger supplemented diet on nephrotoxicity associated with lead administration.

MATERIALS AND METHODS

Materials and reagents

Powdered ginger, distilled water, and normal saline.Fresh ginger was procured from a market in Osogbo, Osun state, Nigeria, after which it was cut into smaller sizes and oven-dried. The dried ginger was then ground into powder using a Rico mixer grinder.

Animals

Wistar rats used in this study were sourced from an animal facility situated in the Igbo Sai area of Ogbomoso, Oyo State, Nigeria, and were all healthy females. Animals were relocated to the Animal Research Facility at the University of Ilesa in Ilesa, Osun State, Nigeria, and allowed to

acclimate for fourteen days before the start of the study. The animals were confined to plastic enclosures measuring 25 × 15 × 14 inches within a temperature-regulated setting, maintained at a consistent temperature of 22.5 ℃ with a tolerance of ± 2.5 ℃, and were exposed to light at 7:00 a.m. The rats were provided with unrestricted access to both food and water. All procedures were conducted by the approved protocols of the Faculty of Basic Medical Sciences at the University of Ilesa and conformed to the guidelines for animal care and use, as specified in the European Council Directive (EU2010/63).

Diet

Laboratory rats were offered a commercially available rat pellet diet, which was specifically formulated to meet their nutritional needs. The pellets consisted of a composition that included: calcium, fat, protein, and carbohydrate. Grounded ginger is used as a supplementary diet with 1% representing a low dose and 5% representing a high dose. The grounded ginger was mixed into the pellets to ensure uniformity and palatability. This diet was administered *ad libitum* for 28 days.

Experimental methodology

Twenty-four (24) female Wistar rats, with weights of 150-170g, were allocated into four distinct groups, each comprising six (6) rats, and were then placed in cages for housing. The groups consisted of Group A (the Control group), Group B (the Lead group), Group C (comprising the Lead and ginger groups at 1% ginger concentration), and Group D (comprising the Lead and ginger groups at 5% ginger concentration). The rodents were given treatment for 28 days. The control and Lead groups received standard rat diets and distilled water, whereas the Lead and ginger group consumed rat diets supplemented with ginger.

On the 29th day, the rats were euthanized via cervical dislocation, adhering to established animal welfare protocols as documented by AVMA Guidelines for the Euthanasia of Animals (2020). Blood samples were taken via an intracardiac puncture at the heart's tip, placed in a heparinized container, and then spun in a centrifuge to prepare them for additional tests, including creatinine, interleukin 6, and Tumor Necrosis Factor measurements. The kidney was excised and preserved in 10% neutral buffered formalin. The organ was then subjected to histological examination procedures.

Biochemical Assays

Kidney Function Test

Creatinine is a biochemical indicator for assessing kidney function and overall metabolic health and its uses have been established by previous studies (Chernozub*et al*.,2020).High levels may indicate impaired kidney function, while normal levels suggest normal renal activity.

Level of Inflammation

Tumor Necrosis Factor (TNF-alpha), a pro-inflammatory cytokine, was assayed to monitor inflammation and immune responses in the kidney cells, as previously examined by Sethi and Hotamisligil (2021). Interleukin 6 (IL-6) is a multifunctional cytokine that plays a vital role in monitoring immune responses and inflammation of tissues.

Photomicrograph

Processed and sectioned kidney tissue was examined under the microscope and photomicrographs were captured.

Data Analysis

Data were analyzed using ezANOVA for Windows. 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. ANOVA was preferred in this study due to its ability to compare the means of all the groups simultaneously which helps in reduction of the risk associated with statistical errors.

RESULTS

Table 1 shows the effects of powdered ginger on the levels of creatinine, Tumor Necrosis Factor (TNF-alpha), and interleukin 6 (IL-6) lead-administered rats.

Groups	**Creatinine (mg/dl)**	**TNF-alpha (pg/ml)**	**IL-6 (pg/ml)**
Group A	1.65 + 0.38	132.30 + 0.58	20.75 + 0.88
Group B	3.85 + 0.66[a]	151.0 + 0.73a	25.82 + 0.90[a]
Group C	2.65 + 0.95[ab]	144.80 + 0.10[ab]	22.48 + 0.11[ab]
Group D	2.25 + 0.72[ab]	146.75 + 0.11[ab]	21.56 + 0.41[ab]

Data presented as Mean ± Standard Error of the mean (SEM), ([a]) denotes $p< 0.001$ vs. control, ([b]) represents $p<0.001$ significant difference with Lead, each group has 6 rats. TNF -alpha: Tumor Necrotic Factor, IL-6: Interluking-6.

Group A (control), Group B (Lead group), Group C (Lead and 1% ginger), and Group D (Lead and 5% ginger).

HISTOLOGICAL FINDINGS

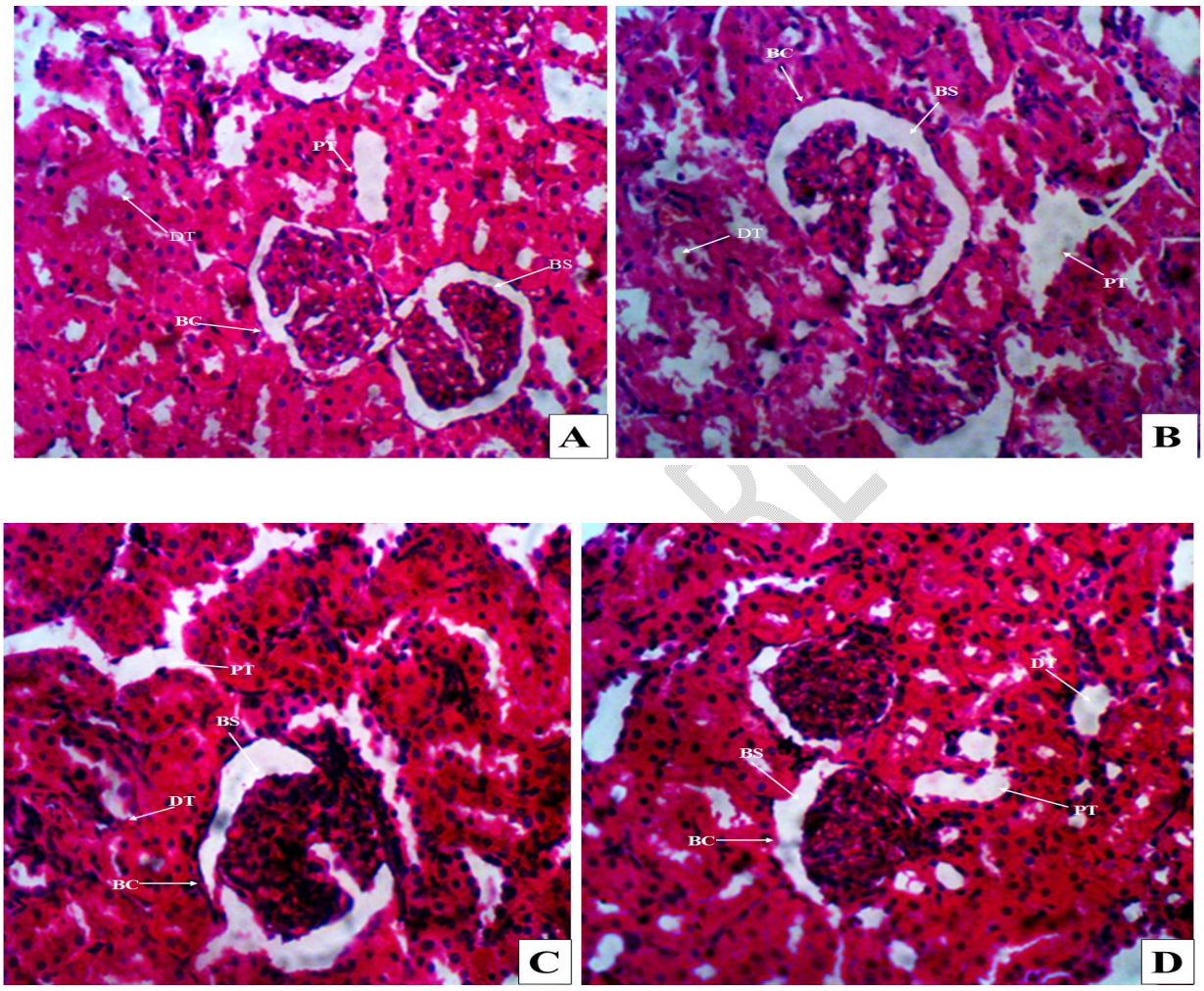

Figure 1 (a-d) shows the effects of dried ginger powered on the morphology of the kidney (a) control, (b) Lead, (c) Lead and 1% of dry ginger, (d) Lead and 5% of dry ginger. Representative photomicrographs of sections from the rat kidney stained with hematoxylin and eosin (HandE) stained sections of the kidney display bowman space (BS), bowman capsule(BC), proximal tubule (PC), distal tubule (DT).

DISCUSSIONS

This study examined the potential health benefits of ginger (*Zingiber officinale*) as a preventative measure on the general morphology of the kidney, kidney function, and its anti-inflammatory effects associated with lead administration in rats. Several studies have proven that lead exposure is linked to various structural and functional alterations in numerous organs,particularly the kidney (Reddy *et al.,* 2014; Nakhaee*et al.,* 2018; Bhasin*et al.,* 2023). This study also backs the theory of the effectiveness of powdered ginger over-extracted ginger as reported by the survey conducted by Mustafa *et al*.,2019.

In this study, a significant decrease in the level of the pro-inflammatory markers (TNF-alpha and Interleukin 6) was observed with ginger administration when compared to the lead-fed groups. This corroborates the reports by Pratap *et al*., 2017 on the ameliorative effects of ginger administration on the level of inflammation in the system.Generally, serum creatinine levels are critical indicators of kidney function,the administration of ginger in this study resulted in a marked decrease in serum creatinine levels, indicating improved renal function as previously discussed by Okutu*etal*., 2019. The bioactive compounds, including flavonoids and gingerols found in ginger,are suggested to play a crucial role in its ability to counteract inflammation, improve kidney function, and safeguard kidney cells from injury via its anti-inflammatory properties in tandem with the study done byOkutu*et al*., 2019.

Furthermore, this study also explores the possible changes in the histomorphology of the kidney. The nephroprotective effects of ginger were revealed in the ginger-fed groups. The photomicrographs of the H&E stained section of the kidney tissue from this study (Fig. 1B)

showed that administration of lead was associated with alteration of the bowman space due to the widening of the bowman space, degeneration of the glomerular structures and damage of the tubules both proximal and distal tubules such as cloudy swelling of Proximal Tubule agrees with the study conducted by Nisar *et al*., (2012).The anti-inflammatory properties of ginger as seen in TNF alpha and Interleukin 6 as earlier mentionedare said to be a contributing factor in reversing the impaired histoarchitecture of the kidney tissue in Fig. 1C and 1D followed by lead administration. Humans exposed to heavy metals such as lead are prone to develop kidney-related issues(Zhang*et al.,* 2025).However, the results of this study corroborate a study done by Zheng*et al.,* (2023) on the beneficial impacts of ginger on health conditions. This information would help the regulatory bodies in making policies that embrace the use of ginger supplements in mitigating adverse effects caused by lead, especially in environments inevitably exposed to lead toxicity.

CONCLUSION

This study found that ginger has substantial health benefits for kidney tissues, particularly in the context of nephrotoxicity caused by lead. Its ability to preserve kidney tissue structure, decrease inflammation,and improve kidney function metrics highlights its value as a treatment option for preventing or lessening kidney injuries resulting from toxic substances or underlying health issues. Further investigations are necessary to explore the possible adverse effects or contraindications that could be associated with ginger supplements or ginger-supplemented diets in humans.

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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