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Research Article

Protective Effect of Aqueous Extract of *Zingiber officinale* Roscoe (Ginger) on Paracetamol-Induced Liver Damage in Albino Rats

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ABSTRACT

Paracetamol overdose is one of the leading causes of drug-induced liver injury, resulting in hepatocellular damage through the formation of the toxic metabolite N-acetyl-p-benzoquinone imine (NAPQI). *Zingiber officinale* (ginger) possesses antioxidant and anti-inflammatory phytochemicals that have been reported to exert hepatoprotective effects. This study investigated the effect of *Zingiber officinale* on paracetamol-induced liver injury. Twenty-five albino rats were randomly divided into five groups (n = 5). Group I served as normal control and received distilled water. Group II received paracetamol (1000 mg/kg) only and served as negative control. Groups III and IV received paracetamol followed by aqueous extract of *Zingiber officinale* at doses of 200 mg/kg and 400 mg/kg, respectively, while Group V received paracetamol followed by silymarin (100 mg/kg). Treatments were administered orally for five days. Body weight, liver index, and histological changes of the liver were evaluated. Data were analyzed using one-way ANOVA followed by Dunnett's multiple comparison test, with $p < 0.05$ considered statistically significant. Significant differences ($P<0.001$) were observed in body weight but not in liver index among the experimental groups. Rats treated with 400 mg/kg of *Zingiber officinale* exhibited a trend toward improved body weight gain and liver index compared with paracetamol-only group. Histological examination revealed severe centrilobular congestion, sinusoidal collapse, hemorrhage, and lymphocytic infiltration in the paracetamol-treated group. Administration of *Zingiber officinale* markedly preserved hepatic architecture, reduced inflammatory cell infiltration, maintained sinusoidal integrity, and prevented severe vascular congestion. The hepatoprotective effect was more pronounced at the 200 mg/kg dose and was comparable to that observed with silymarin treatment. *Zingiber officinale* demonstrated hepatoprotective activity against paracetamol-induced liver injury by preserving liver histoarchitecture and reducing inflammatory changes despite producing no significant effects on body weight or liver index. These findings suggest that *Zingiber officinale* may serve as a promising natural hepatoprotective agent against paracetamol-induced hepatic damage.

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1.0 INTRODUCTION

Paracetamol (acetaminophen) is an over-the-counter medication used to relieve pain and reduce fever. It is a commonly used medication to reduce fever (Toska et al., 2014). Paracetamol toxicity is a common cause of acute liver failure and affects the normal function of the liver. The toxic limit for adults is a single dose of 7.5 to 10g. The toxic dose for children is typically 150mg/kg (Ershad, 2019). Paracetamol toxicity is a significant medical concern as it is a leading cause of drug-induced liver injury globally and accounts for over 100,000 calls to poison center in the United States (El-Aziz et al., 2025). There is therefore a need for quick treatment to prevent further liver damage.

Zingiber officinale has been used in many traditional and Ayurvedic remedies to treat varied ailments and disorders including its use for nausea relief, it acts as an analgesic, has antioxidant properties and improves heart and blood health (Ahmed et al., 2021, Hamman et al., 2022). Several studies show that *Zingiber officinale* has hepatoprotective effects due to its antioxidant and anti-inflammatory phytochemical content which protect hepatocytes and the liver cytoarchitecture (Hamza et al., 2021). Silymarin is a natural compound with antioxidant properties, anti- inflammatory effects, and antifibrotic activity, has shown potential in treating liver damage caused by alcohol, NAFLD, drug-induced toxicity, and viral hepatitis as used in various studies (Saleh et al., 2025, Manye et al., 2025).

The current study investigated the use of *Zingiber officinale* in the treatment of paracetamol induced liver damage to observe its hepatoprotective role by specifically observing the weight of the rats, liver index and histology of the liver tissue.

METHODOLOGY

Materials used for the Experimental Research

Materials used includes triple beam balance, microtome, paraffin wax, refrigerator, hematoxylin, plastic cages, wire nets, feed and water containers, intubation tube, 10ml syringe, beakers, hand gloves, sample bottles, light microscope, 10% formalin, dissecting set, razor blaze, pins, microtome etc.

Procurement and Authentication of Plant Material

Dried ginger rhizome (*Zingiber officinale*) was obtained from Monday Market Maiduguri, Borno state. The rhizomes were identified and authenticated by Professor E. T. Rabo, a plant Taxonomist from the Department of Biological Science, Faculty of Science, University of Maiduguri.

Preparation of *Zingiber officinale* Extract.

The *Zingiber officinale* rhizomes were pulverized into powdery form using mortar and pestle. The powder was sieved and extracted using Soxhlet extractor. Six hundred grams (600g) of *Zingiber officinale* was extracted using 2.5 liters of distilled water. The resultant liquid filtrate was dried condensed in an oven of 65ºC until a crude extract was formed. The crude extract that was formed weighed 118g. A stock mixture of 200mg/kg and 400mg/kg were prepared from the crude extract.

Experimental Animals

Twenty-five (25) albino rats of both sexes, weighing 90-150g were obtained from the animal house of the National Veterinary Research Institute (NVRI) in Vom, Plateau state. They were housed in plastic cages and were allowed to acclimatize for a month in the animal house unit of Biochemistry, University of Maiduguri. The rats were fed with regular chow and distilled water *ad libitum*.

Drug

Paracetamol tablets (Emzor Pharmaceuticals) were obtained from Pharmacy, Shehu Laminu way, Maiduguri, Borno state. Two (2) tablets (each tablet weighing 500mg) of paracetamol were dissolved in 10ml of distilled water. This was administered to the rats to induce hepatotoxicity in the current investigation. Silymarin is a natural compound extracted from the milk thistle plant widely used for its powerful antioxidant, anti-inflammatory and cell-protecting properties. It is primarily used as a supportive therapy to protect, regenerate and detoxify the liver. In the current study, it was used as the conventional medication to alleviate the effects of paracetamol hepatotoxicity.

Experimental design

The animals were randomly distributed among the experimental groups following the acclimatization period. The rats were grouped

into five groups designated Groups I-V containing five rats each. Group I was administered distilled water and served as the control group, Group II was the negative control group and received 1000mg/kg of paracetamol, Group III were administered 200mg/kg of *Zingiber officinale* aqueous extract and 1000mg/kg of paracetamol. Group IV were administered 400mg/kg of *Zingiber officinale* aqueous extract and 1000mg/kg of paracetamol. Group V was administered 100mg/kg of Silymarin and 1000mg/kg of paracetamol. The method of administration was by orogastric intubation. The rats in Groups II, III, IV and V were administered the dosage of paracetamol and after three hours, the treatment was administered to these rats. A single acute dose of paracetamol was administered on the first day as carried out in standard preclinical hepatotoxicity studies to reliably overwhelm glutathione stores and trigger acute centrilobular liver necrosis (Abdallah et al., 2023). The study took place for a period of five days and on the sixth day all the animals were sacrificed by administration of 100mg/kg of ketamine injection to the left thigh of the rat in accordance to protocol carried out in previous studies (Hamman et al., 2022) A median incision was made on the anterior abdominal wall and the liver was excised, surrounding connective tissue was trimmed off and it was weighed to determine the liver index and it was placed immediately in a 10% formalin and underwent routine histological processing as carried out in previous studies (Dani et al., 2022). After fixing in 10% formalin, the tissues were dehydrated in graded series of alcohol, cleared in xylene, and embedded in paraffin wax (Dani et al., 2022, Manu et al., 2022). The tissues were sectioned at 4 μm with a rotary microtome and stained with Hematoxylin and Eosin (H and E). The liver tissue was then observed under the microscope and photographed under X 100 magnification to observe histological features in the tissue.

Determination of Liver Weight and Index

The rats were weighed before, during and after the experimental study, just before sacrifice to determine changes in the body weights. The weight of the liver was also determined and liver index was calculated for each group using the formula below:

Liver index = (Liver weight/Body weight) x 100%

Statistical analysis

Values were expressed as means + SE. Results were analyzed using one way analysis of variance (ANOVA) followed by Dunnett's multiple comparisons test to compare all groups. Differences were considered significant at $p<0.05$.

RESULTS

General and Physical Observation

The rats were observed for signs of weakness and loss of appetite during the experimental study. Rats in Group I showed no weakness and lack of appetite. In comparison, rats in Groups II-V were comparably weaker and had less appetite during the experimental period.

Effect of *Zingiber officinale* on body weight of the rats

Table 1 shows the weight of animals in all groups was recorded during the experimental period. There was a significant (P<0.001) change in the weight of rats in groups when compared to the control group, although there was a decrease in weight in rats in Groups II and III when compared to the control group. The groups treated with the highest dose of *Zingiber officinale* showed the highest weight difference at 6.37g (Figure 1).

Table1: Showing the effect of *Zingiber officinale* and paracetamol on the body weights of rats.

Groups	Initial Weight (g)	Final Weight (g)	Weight Difference	Weight Difference (%)	P value
I	104.30±4.24	108.50±5.22	4.20	3.87%	P<0.001
II	88.50±1.84	90.98±2.09	2.48	2.73%	P<0.001
III	137.70±18.05	139.02±16.32	1.32	0.95%	P<0.001
IV	96.78±2.11	103.15±1.47	6.37	6.18%	P<0.001
V	109.86±13.41	112.66±14.50	2.80	2.49%	P<0.001

All figures are presented as All values are expressed in Mean ± SEM, g=gram. Values share an identical P-value because the metric is derived from an overall comparison between the experimental groups rather than individual comparisons against the control

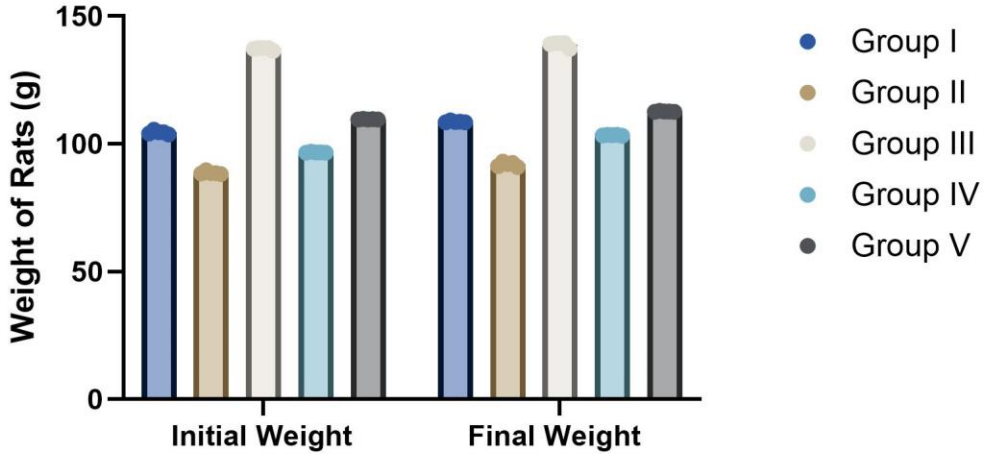

Figure1: showing the initial and final weight of rats in all groups

The Effect of *Zingiber officinale* on the Liver Index

The indices of rats in the control group were higher than rats of other groups, while indices of rats treated with paracetamol non-significantly decreased (P=0.0790, F=4.718) when compared to the control and treated groups (Figure 2).

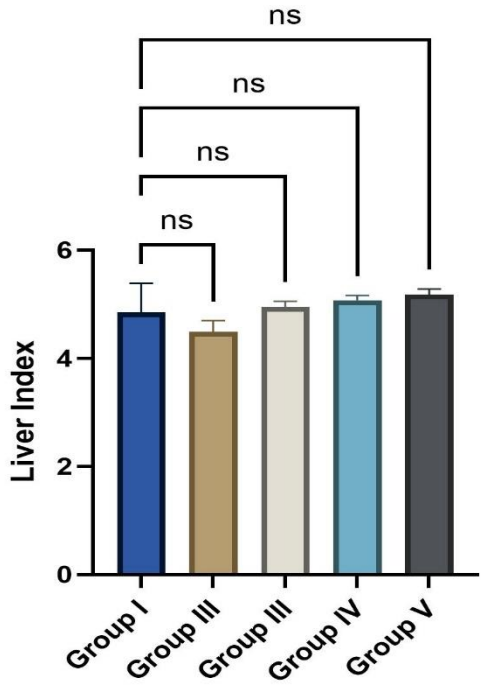

Figure 2: showing the liver index in all groups

Effect of *Zingiber officinale* on the Histology of the Liver

The liver of the rats in the control group had normal liver tissue with the hepatocytes arranged

in columns which radiate towards the central vein similar to a bicycle spoke. The sinusoidal spaces which are found between the sinusoids were clear, narrow spaces which also radiated towards the central vein. The central vein lumen contained red blood cells in the liver of rats in Group I (Figure 3A). In the rats that received 1000mg/kg of paracetamol without treatment, the central vein was suffused with blood, being observed as severe centrilobular congestion and hemorrhage which was seen only in this group. There was also collapse of the sinusoidal walls in this group as there was no clear sinusoids in this group. Lymphocytic infiltration was evident in the hepatic stroma surrounding the central vein (Figure 3B). The micrograph representing the group treated with 200mg/kg of *Zingiber officinale* and 1000mg/kg of paracetamol is represented by Figure 3C. The architecture of the liver was similar to the control group. The sinusoids were clear and hepatocytes were arranged in a bicycle spoke-like orientation. The high dose group which received 400mg/kg of *Zingiber officinale* along with 1000mg/kg of paracetamol. also had lymphocytic infiltration around the central vein. There was however no congestion of the central vein, as was observed in the liver of rats in Group II (Figure 3D). In the rats that were treated with silymarin, the architecture of the liver was not altered as observed in Figure 3E. No lymphocytic infiltration was seen around the central vein and the sinusoidal spaces were clear and hepatocyte arrangement was similar to the control group.

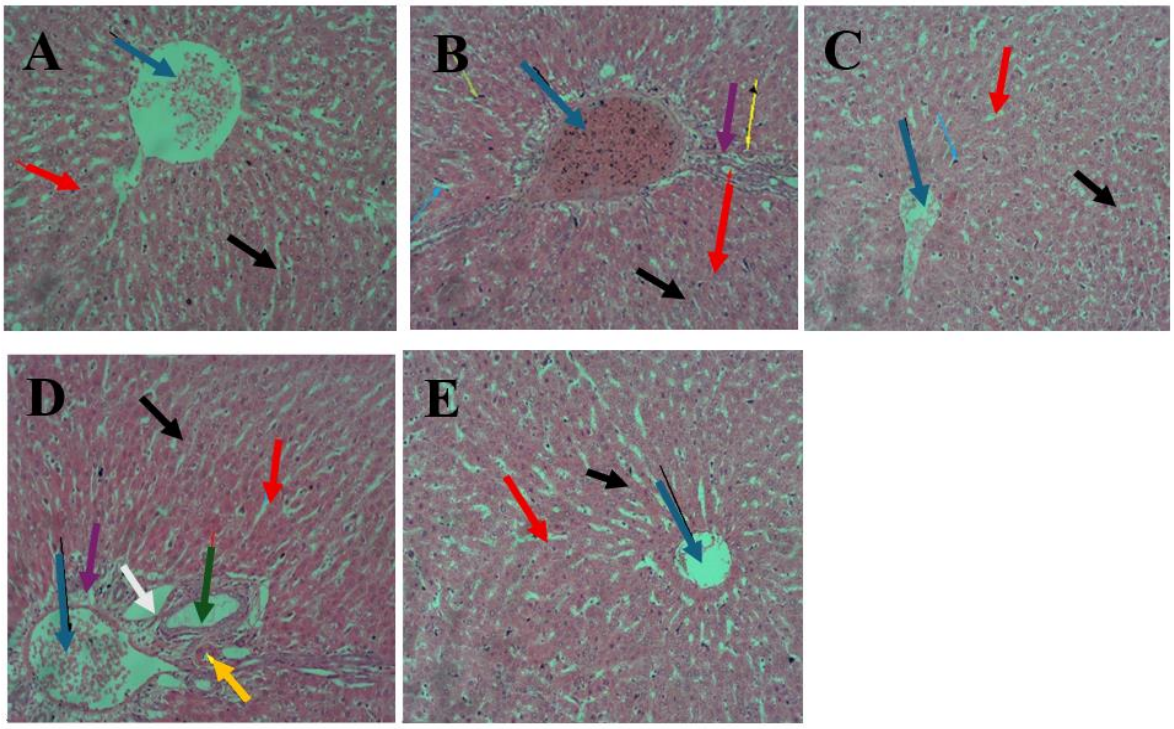

Figure 3: showing the micrograph of the liver tissue in all groups. A-Group I, B- Group II, C-Group III, D- Group IV, E- Group V. Black arrows – hepatocyte cords, blue arrow – central vein, red arrow – sinusoidal space, green arrow – hepatic artery, white arrow – portal vein, yellow arrow – bile ductule, purple arrow – lymphocytic infiltration. H and E X100.

DISCUSSION

The liver breaks down paracetamol into safe byproducts; however, when there is an overdose, it leads to an accumulation of the toxic by-product known as N-acetyl-pbenzoquinone imine (NAPQI). Glutathione which usually destroys NAPQI is overwhelmed, leading to damage of hepatocytes, leading to liver failure (Rajala et al., 2025).

Paracetamol toxicity as observed histologically in the current study led to severe centrilobular congestion and hemorrhage. This structural breakdown specifically points to pericentral (zone 3) hemorrhagic necrosis, where hepatocytes immediately surrounding the central vein are affected. This correlates with studies carried out by Fontana (2008).

Although the current study did not carry out extensive studies to determine the mechanistic effect of paracetamol hepatotoxicity, other studies describe how these hepatocytes contain the highest concentration of enzymes cytochrome P450 2E1 enzyme (CYP2E1) which is responsible for breaking down both natural body chemicals and foreign substances. The enzyme converts paracetamol to its highly toxic metabolite NAPQI (Rajala et al., 2025). As NAPQI overwhelms and depletes local glutathione stores, it induces mitochondrial collapse, ATP depletion and rapid congestive necrosis of zone 3 hepatocytes.

There was also sinusoidal wall collapse as the hepatocytes which surround the central vein die and this causes disintegration of the adjacent endothelial cells wall which forms the hepatic sinusoids. This is also as reported by Saxena (2017). Paracetamol-induced necrosis also allows sparse inflammatory infiltration in the early stages as observed in the current study and also as reported by Burt et al., (2022). There is also congestion of small blood vessels around the dying cells which become engorged and congested with blood (Penmetcha et al., 2019).

Zingiber officinale has been used in traditional Chinese medicine and Ayurveda in the treatment of several conditions (Verma et al., 2025). In many research studies, *Zingiber officinale* has been used to protect the liver from toxins through its strong antioxidant and anti-inflammatory properties (Alshatly, 2019).

Administration of *Zingiber officinale* in the current study protected the liver tissue by protecting the zone 3 hepatocytes and the hepatic architecture from paracetamol-induced toxicity. In similar studies, *Zingiber officinale* also prevented cellular damage, reduced fatty deposits, stopped tissue scarring by neutralizing harmful molecules and supporting natural repair of hepatocytes (Gholampour et al., 2017). The protective effect of *Zingiber officinale* has been attributed to the presence of gingerols which has antioxidant and anti-inflammatory properties that help to prevent cell death and reverse liver damage produced by toxins, poor diet and disease (El Deen et al., 2025). It has been known to decrease inflammation by lowering the number of inflammatory lymphocytes in related studies (Oke et al., 2019). This is in agreement with the current investigation where there was reduced infiltration of lymphocytes around the central vein and sinusoidal spaces. Also similar to the current study, Badawi et al., (2019) performed similar experimental studies that showed that *Zingiber officinale* downregulated the expression of proteins that causes cell death and upregulated the production of proteins that promoted cellular survival. *Zingiber officinale* also reduced tissue scarring by reducing collagen deposition around hepatocytes (Hamman et al., 2022, Badawi et al., 2019).

Silymarin is an extract from the milk thistle that is used to protect the liver from oxidative stress, inflammation, steatosis and fibrosis (Li et al., 2024). There was also preservation of hepatic tissue following the administration of silymarin. There was reduced lobular inflammation as the infiltration of lymphocytes, stopping ongoing tissue damage caused by immune responses, silymarin also stopped hepatocyte ballooning where the cell swells up and dies as a result of toxin overload or fat accumulation. In the current study, it also prevented liver fibrosis by blocking pathways that create excess collagen. This is in agreement with studies carried out by Federico et al., (2017), Faryadi et al., (2024).

The aqueous extract of *Zingiber officinale* produced statistically significant changes in body weight but not in liver index during paracetamol-induced hepatotoxicity. There was a dose-dependent trend in which the 400 mg/kg extract resulted in greater body weight gain and partial restoration of liver index toward normal values, suggesting a possible protective effect that was more clearly demonstrated by the histological findings.

Conclusion

The present study demonstrated that aqueous extract of *Zingiber officinale* exerts a protective effect against paracetamol-induced liver injury in albino rats. Treatment with the extract did significantly altered body weight but not liver

index and histopathological evaluation revealed marked preservation of hepatic architecture, reduced centrilobular congestion, maintenance of sinusoidal integrity, and decreased lymphocytic infiltration compared with the untreated paracetamol group. The hepatoprotective effect was more evident at the lower dose (200 mg/kg), producing liver histology that closely resembled that of the normal control and the silymarin-treated group.

The observed protective effects are likely attributable to the antioxidant and anti-inflammatory phytochemicals present in *Zingiber officinale*, which mitigate oxidative stress and inflammatory responses associated with paracetamol-induced hepatotoxicity. These findings support the potential therapeutic value of *Zingiber officinale* as a natural hepatoprotective agent. In the current study, one of the limitations was the low base-line weight in Group III. Further studies should ensure a closer weight range of rats in each group. In addition, further studies involving larger sample sizes, longer treatment durations, biochemical liver function markers, oxidative stress biomarkers, and molecular mechanisms are recommended to further validate its efficacy and elucidate its mechanisms of action. In further studies, an additional group in which only *Zingiber officinale* is administered should be included to determine the effect of the extract on the liver. Future studies should incorporate a predefined and blinded semi-quantitative histopathological scoring system, with appropriate statistical analysis, to provide objective comparisons between groups

Ethical Considerations

All procedures involving the use of the rats comply with the ethical guidelines for the care and use of animals in research by the National Research Council (NRC) and the ARRIVE Guidelines. The Department of Human Anatomy Ethical Committee, University of Maiduguri gave the approval for the study.

Acknowledgement

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Financial Statement

The current study did not receive any financial assistance/funding/grants

Conflict of Interest

The Authors do not have any conflicts of interest to declare

Consent to Publish

Not applicable

Data Availability

The data used and/or analyzed in the present study are available from the corresponding author upon request.

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