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Original Research Article

Histological Effects of Kepok Banana (*Musa paradisiaca* L.) Heart Extract on the Kidneys and Liver of Mice

Elidahanum Husni*, Yufri Aldi, Wiwing N. Putri, and Zikri H. Hamdi

Faculty of Pharmacy, Andalas University, Padang, West Sumatera, 25163, Indonesia

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ABSTRACT

Kepok banana (*Musa paradisiaca* L.) heart is rich in secondary metabolites and has found wide applications in traditional medicine. This study aimed to assess the safety of Kepok banana heart extract on the kidney and liver histology in male albino mice. *Musa paradisiaca* heart extract was obtained by maceration in 70% ethanol, and the extract was formulated into a suspension. Thirty-six male albino mice were divided into four groups: a control group and three treatment groups which received oral administration of the extract for 7, 14, and 21 days at doses of 200, 400, and 800 mg/kg body weight (bw). Liver and kidney samples were taken for histological examination. The observed parameter was histological tissue damage in the kidneys and liver. The outcome indicated that the administration of *Musa paradisiaca* heart extract at doses of 200 - 800 mg/kg bw did not cause significant damage across all time points. However, at 800 mg/kg bw, histological changes, such as hyperemia (day 7) and inflammatory cell infiltration (days 14 and 21), were observed. On day 14, liver analysis revealed that the 200 and 400 mg/kg bw groups' hepatocytes and central vein architectures were normal. Mild periportal inflammatory infiltration was noted in the 800 mg/kg bw group. These findings suggest that *Musa paradisiaca* heart extract is relatively safe at doses of 200 - 400 mg/kg bw but may induce mild tissue alterations at 800 mg/kg bw. Further investigation is recommended to evaluate long-term toxicity and establish safety thresholds for potential therapeutic applications.

Keywords: *Musa paradisiaca*, Kepok banana, Histological analysis, Kidneys, Liver, *In vivo*.

Introduction

Kepok banana (*Musa paradisiaca* L.) hearts thrive in tropical and subtropical regions. They are often grown in locations at an altitude of approximately 800 meters above sea level.[1] In traditional medicine, the heart of *Musa paradisiaca* has been used as an antioxidant and antidiabetic agent and to promote lactation.[2,3] The heart of *Musa paradisiaca* contains many secondary metabolites. Plants synthesize various secondary metabolites that primarily function to protect them against predators and microbes by acting as toxins and repellents of microorganisms and herbivores.[4] In the study conducted by Mahmood *et al*. (2011), *Musa paradisiaca* was reported to contain active metabolites, including alkaloids, saponins, tannins, flavonoids, and total phenols or phenolic compounds.[5] The kidneys and liver are vital organs with critical roles in maintaining overall health. The kidneys are responsible for regulating acid-base balance, maintaining fluid levels, managing electrolytes, like sodium and potassium, and removing waste products from the body. They also reabsorb essential substances, such as glucose and amino acids, help regulate blood pressure, produce key hormones, including erythropoietin, and are involved in the activation of vitamin D.[6]The liver, being the body's largest internal organ, is crucial for metabolic processes, detoxifying harmful substances, and producing important biochemicals necessary for digestion.[7]

*Corresponding author. Email: elidahanumhusni@gmail.com
Tel: +6281363989864

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Toxicity testing plays a crucial role in evaluating newly developed drugs before they are approved for human use. Animal models play a crucial role in biomedical research, including toxicity testing. They enable a better understanding of pathophysiological mechanisms and the development of novel therapies while also providing a reliable platform for toxicological evaluation prior to clinical trials in humans.[8] The aim of this study was to examine the histological effects of *Musa paradisiaca* heart extract on the liver and kidney tissues of mice.

Materials and Methods

Plant collection and identification

A total of ten kilograms of *Musa paradisiaca* heart were collected in August 2024 from Sumanik area in Tanah Datar Regency, West Sumatra, Indonesia (Coordinates: 0.3806° S, 100.5776° E). The samples were identified at the Andalas Herbarium, Department of Biology, Faculty of Mathematics and Natural Sciences, Andalas University, Padang, Indonesia. Herbarium specimen with voucher number 625/K-ID/ANDA/VIII/2024 was deposited in the herbarium unit.

Extract preparation

Powdered *Musa paradisiaca* L. heart (0.5 kg) was extracted with 70% ethanol at 1:10 ratio (w/v) by maceration at room temperature for 5 days. The extract was filtered. The residue was re-extracted with the same solvent, and the extraction process was carried out 3 times. The combined extract was concentrated in a rotary evaporator running at 45°C and a pressure of 150 bar.[9]

Preparation of sodium carboxymethyl cellulose suspension

Sodium carboxymethyl cellulose (Na CMC) powder (500 mg) was placed in a mortar. The powder was dissolved by gradual addition of 10 mL of hot water. After homogenizing the suspension by trituration, it was made up to 100 mL by addition of distilled water.[10]

Preparation of extract suspension
Na CMC (100 mg) was placed into a mortar, and 10 mL of hot water was added. After expansion, the suspension was crushed until homogeneous. The suspension was mixed with *Musa paradisiaca* heart extract (1, 0.5, and 0.25 g) for doses of 800, 400, and 200 mg/kg bw. The extract was homogenized and then adjusted to 20 mL with distilled water.[11]

Animals
Thirty-six (36) healthy male Balb/c mice age 2-3 months weighing between 20 - 30 g were purchased from the animal facility of the Faculty of Pharmacy, Andalas University, Padang, Indonesia. The mice were maintained under standard laboratory conditions (temperature 25 ± 2°C, light/dark cycles of 12/12 h) and fed with standard rodent pellets and drinking water *ad libitum*. Albino mice were acclimatized to the laboratory conditions for 7 days before being administered *Musa paradisiaca* L. extract.

Ethical approval
The study was approved by the Animal Ethics Committee, Faculty of Pharmacy, Andalas University, Padang, West Sumatera, Indonesia (Ethical approval no.: 79/UN16.10.D.KEPK-FF/2024).

Animal grouping and treatment
Thirty-six male albino mice were divided into four groups (A – D) of 9 mice each. Group A served as the control group and received 0.5% Na CMC. Groups B, C, and D served as the treatment groups and received suspension of banana heart extract at doses of 200, 400, and 800 mg/kg bw, respectively. The volume of the test extract administered to the animals was 0.32 mL/20 g body weight. The test preparations were administered orally once daily for 7, 14, and 21 days.

Histopathological examination
On days 8, 15, and 22, three mice from each group were humanely sacrificed under ether anaesthesia, followed by cervical dislocation. The animals were then dissected for the collection of kidneys and liver. The harvested organs were rinsed with 0.9% physiological saline, preserved in buffered formalin solution, and labeled according to their respective identities. The organs were subsequently submitted to a qualified professional for histopathological preparation. Histopathological examination was carried out with the assistance of a specialist in anatomical pathology. Tissue analysis was performed using a microscope at 20× magnification with a 1:20 scale. The degree of tissue damage was observed and recorded based on histopathological damage scores, thereby providing an overview of the histological changes occurring in the liver and kidney organs.

Statistical analysis
Descriptive characterizations of the histological damage of the kidneys and livers were recorded. Histological data of the kidneys were analyzed using two-way analysis of variance (ANOVA) followed by Duncan's multiple range test. Histological data of the liver was analyzed using Kruskal-Wallis test, followed by the Mann-Whitney test. Significant differences between groups were established at p-value < 0.05.

Results and Discussion

Damage scores of the kidneys
Based on the results of the two-way ANOVA, there was no significant difference between histological scores for the kidneys and duration of extract use ($p > 0.05$). However, the analysis of the histological scores in relation to dosage demonstrated a significant difference ($p < 0.05$). Based on Duncan's multiple range test, the histological score of Group D was found to be significantly different from that of the control, Groups B and C. As shown in Figure 1, the average scores of the control, Groups B and C were nearly the same, classifying these three groups as normal. No significant damage was recorded in these groups. The Group D, on the other hand, scored higher on histology than the other groups. This group was classified as normal-minimal damage. The classification of this group is based on the score obtained, referring to Table 1.

Histological findings of the kidneys on day 7
The effects of the administration of *Musa paradisiaca* heart extract on the kidneys after 7 days demonstrated that Groups B and C did not appear different from the control group. The glomerulus and tubules were neatly arranged without any damage, which falls within the normal category. On the other hand, the histological features of the kidneys in Group D showed damage in the form of hyperemia, as indicated by black arrows (Figure 2). No significant necrosis was observed in the kidneys of mice after administering banana heart extract for 7 days. Reactive hyperemia is a response to local ischemia, in which active arteriolar vasodilation leads to increased blood flow to the tissue followed by redness caused by vascular engorgement with oxygen-rich blood.[14] A common cause of kidney hyperemia is the entry of toxic substances that impact the blood vessel walls within the organ. If this condition persists, it may result in tissue hemorrhage.[15] Hyperemia can return to normal if the underlying cause is eliminated and the body is able to restore blood flow to a balanced condition.

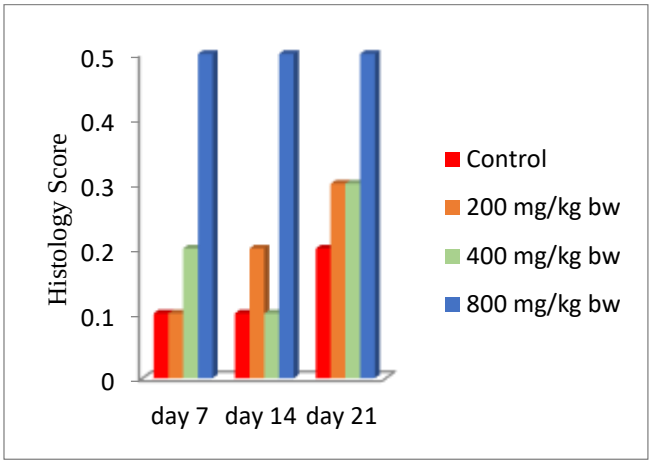

Figure 1: Kidney histological damage scores after administration of banana heart extract

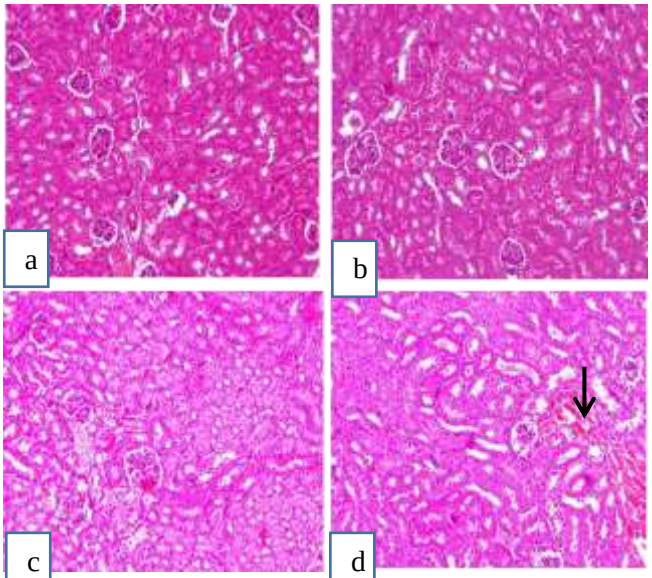

Figure 1: Histopathological findings of the kidneys in male albino mice after administration of kepok banana (*Musa paradisiaca* L.) heart extract for 7 days. Hematoxylin-Eosin staining; objective lens magnification: 20x; scale: 1:20; **a:** Control group; **b:** 200 mg/kg bw group; **c:** 400 mg/kg bw group; **d:** 800 mg/kg bw group; G: glomerulus; T: tubules; V: vein; black arrow: hyperemia

Histological findings of the kidneys on day 14

The effects of the administration of kepok banana heart extract on the kidneys after 14 days showed that Groups B and C did not appear different from the control group. The glomerulus and tubules were neatly arranged without any damage, which falls within the normal category. In contrast, the kidney histoarchitecture revealed damage in the form of inflammatory cell infiltration in Group D, as indicated by red arrows (Figure 3). No significant necrosis was observed in the kidneys of mice after administering kepok banana heart extract for 14 days. Inflammation is a complex response at the cellular and molecular levels, initiated by tissue damage, infections, or other pathological conditions. Inflammation while acting as a vital defense system, is characterized by clinical symptoms including redness, swelling, pain, and increased body temperature.[16]

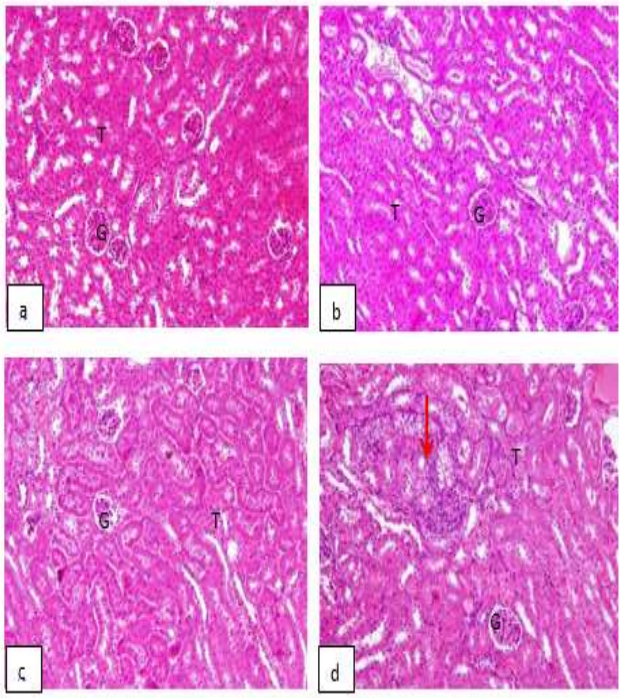

Figure 3: Histopathological findings of the kidneys in male albino mice after administration of kepok banana (*Musa paradisiaca* L.) heart extract for 14 days. Hematoxylin-Eosin staining; objective lens magnification: 20x; scale: 1:20; **a:** Control group; **b:** 200 mg/kg bw group; **c:** 400 mg/kg bw group; **d:** 800 mg/kg bw group; G: glomerulus; T: tubules; V: vein; red arrow: inflammatory cell infiltration

Histological findings of the kidneys on day 21

The effects of the administration of banana heart extract for 21 days on the kidneys of mice is shown in Figure 4. The results indicated that Groups B and C did not differ from the control group. The glomeruli and tubules appeared well-organized without any damage, classifying them as normal. However, in Group D, the image showed damage in the form of inflammatory cell infiltration, indicated by red arrows (Figure 4). No significant necrosis was observed in the kidneys of mice after 21 days of banana heart extract administration. Inflammation at the tissue level appears as redness, swelling, heat, pain, and loss of function, resulting from immune responses, changes in blood vessels, and localized reactions to injury or infection.[17] When tissue injury occurs, the body triggers a series of chemical signals that promote healing in the affected areas. These signals stimulate the movement of leukocytes from the bloodstream to the site of damage. Once activated, these leukocytes release cytokines that initiate inflammatory responses.[18]

Table 1: Histopathological grading of kidney lesions[12]

Score	Description
0	Normal histology
1	Minimal damage Degeneration of tubular epithelial cells occurs without notable signs of necrosis or apoptosis.
2	Mild damage Tubules exhibiting necrosis or apoptosis of epithelial cells, along with additional accompanying structural changes < 25%.
3	Moderate damage Tubules exhibiting necrosis or apoptosis of epithelial cells, along with additional accompanying structural changes <50%.
4	Severe damage Tubules exhibiting necrosis or apoptosis of epithelial cells, along with additional accompanying structural changes <75%.
5	Extremely severe damage Tubules exhibiting necrosis or apoptosis of epithelial cells, along with additional accompanying structural changes >75%.

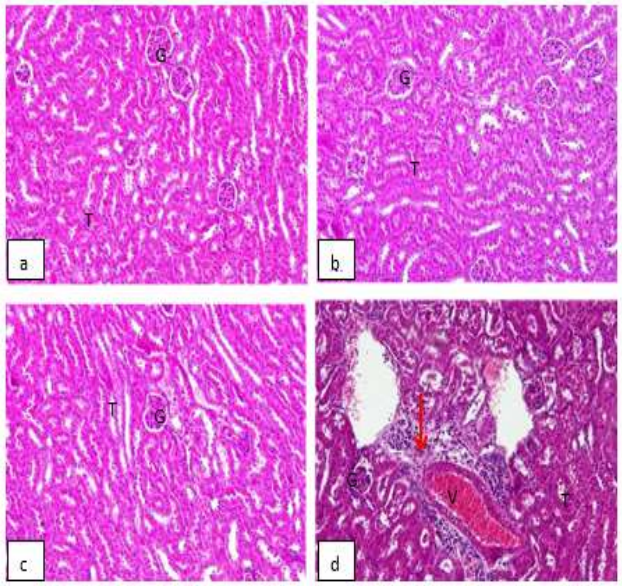

Figure 4: Histopathological findings of the kidneys in male albino mice after administration of kepok banana (*Musa paradisiaca* L.) heart extract for 21 days. Hematoxylin-Eosin staining; objective lens magnification: 20x; scale: 1:20; **a:** Control group; **b:** 200 mg/kg bw group; **c:** 400 mg/kg bw group; **d:** 800 mg/kg bw group; G: glomerulus; T: tubules; V: vein; red arrow: inflammatory cell infiltration

Damage scores of the liver

The analysis using the Kruskal-Wallis test showed a significant ($p < 0.05$) difference in histological scores of the liver among the different groups. Further analysis using the Mann-Whitney test revealed that the 800 mg/kg bw dose group (Group D) was significantly ($p < 0.05$) different from the control and Groups B and C. The histological damage scores indicated that the mean histological scores of the control, Groups B and C were nearly the same and fell within the normal range (Figure 5). Meanwhile, Group D had a score of 0.5, which is categorized as normal-minimal damage. The classification of this group is based on the score obtained, referring to Table 2.

Histological findings of the liver on day 14

After administering banana heart extract at doses of 200-800 mg/kg bw

for 14 days, the area surrounding the central vein of the liver appeared normal. No significant pathological changes were observed in the central vein region, and there was no damage to the liver cells in this area (Figure 6). The lobule is hexagonally shaped with the central vein located in the middle of the lobule. It is called the central vein because of its position at the center or in the middle.[19]

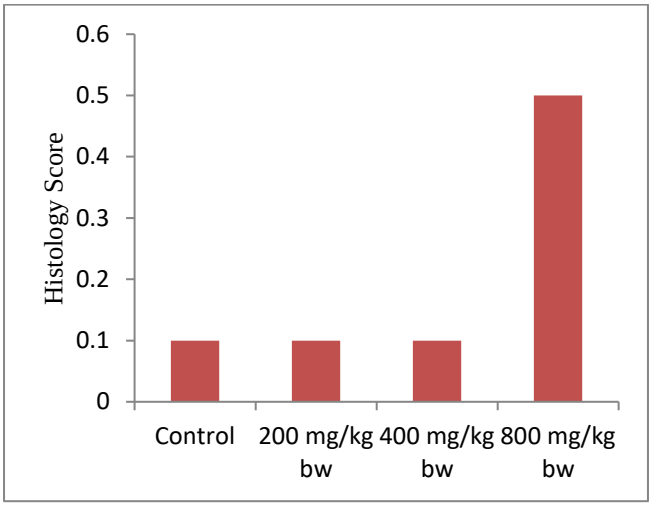

Figure 5: Liver histological damage scores after administration of kepok banana heart (*Musa paradisiaca* L.) extract for 14 days

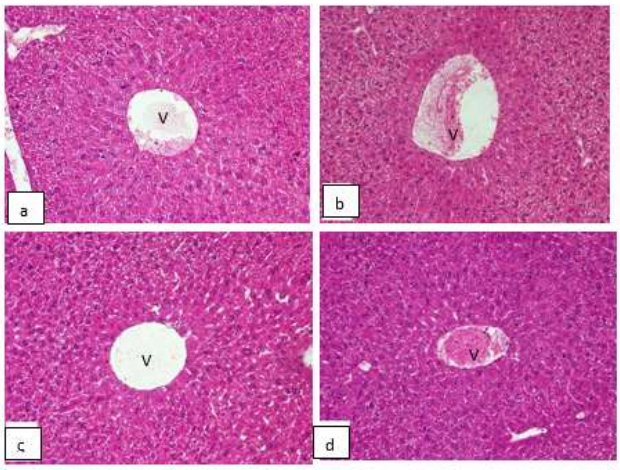

Figure 6: Histopathological findings of the liver (at central vein) in male albino mice after administration of kepok banana (*Musa paradisiaca* L.) heart extract for 14 days. Hematoxylin-Eosin staining; objective lens magnification: 20x; scale: 1:20; **a:** Control group; **b:** 200 mg/kg bw group; **c:** 400 mg/kg bw group; **d:** 800 mg/kg bw group; V: vein.

The arrangement of central vein branches differs between humans and rats. In humans, each central vein connects directly to a sublobular vein, while in rats, two to four central veins usually converge before draining into the sublobular vein.[20] The liver is composed of multiple interacting cell types, with hepatocytes accounting for around 60% of the total cell population. These hepatocytes are spatially arranged into hexagon-shaped structures known as lobules, typically containing about 15 layers of concentric cells. Oxygenated blood, hormones, and nutrients are delivered via the hepatic artery and portal vein, entering at the outer edge of each lobule and flowing inward toward a central vein.[21] The research findings showed that the hepatocyte cells forming the liver were in a normal condition.

After administering banana heart extract at doses of 200-400 mg/kg bw for 14 days, the histology of the liver in the periportal region showed no differences compared to the control group. Hepatocytes around the periportal zone appeared normal without any damage, classifying Groups B and C as normal. However, in Group D, inflammatory cells were present in a small portion of the periportal zone (indicated by red arrows) (Figure 7), categorizing Group D as normal with minimal damage. Inflammation in the liver serves as a defense mechanism against infection and injury. However, excessive inflammation can result in significant hepatocyte loss, ischemia-reperfusion damage, and metabolic disturbances.[22] The liver functions to eliminate harmful substances from the body through a process known as detoxification, which is performed on all substances entering the body, including toxic compounds.[23]

Table 2: Liver injury scores and histopathological changes in hepatocytes following acetaminophen exposure[13]

Score	Description
0 (-)	Normal histology No necrosis of hepatocytes
1 (+)	Minimal-mild Focal, confined to the centrilobular region, with necrosis affecting <25% of the lobules.
2 (+2)	Mild-moderate Focal and multifocal lesions extending from the central to midzonal areas of the lobule, involving regions affected by necrosis <50% of the lobules.
3 (+3)	Moderate–severe Multifocal (centrilobular-portal region) 50% < X < 75% affected lobules are necrotic
4 (+4)	Severe > 75% affected lobules are necrotic
5 (+5)	Severe (whole lobules) The loss of hepatocytes spreads from the central vein toward the portal region, impacting neighboring lobules

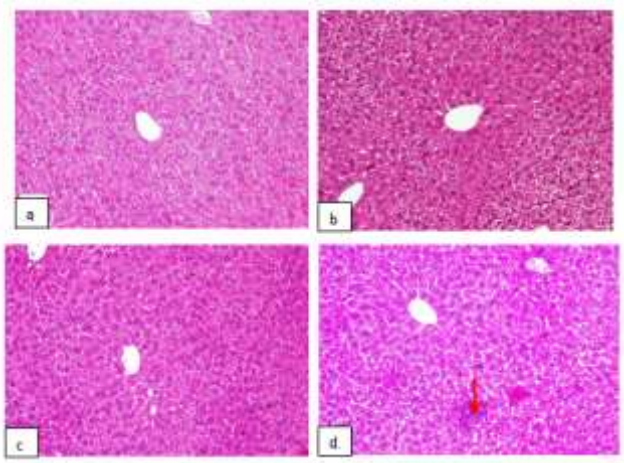

Figure 7: Histopathological findings of the liver (at periportal region) in male albino mice after administration of kepok banana (*Musa paradisiaca* L.) heart extract for 14 days. Hematoxylin-Eosin staining; objective lens magnification: 20x; scale: 1:20; **a:** Control group; **b:** 200 mg/kg bw group; **c:** 400 mg/kg bw group; **d:** 800 mg/kg bw group; red arrow: inflammatory cell infiltration

The kidneys are more susceptible to the accumulation of toxic substances due to their continuous filtration process. Therefore, testing was conducted on days 7, 14, and 21 to observe whether there were progressive toxic effects over time. The liver, although playing a primary role in toxin metabolism, tends to exhibit changes more rapidly and has a higher capacity for recovery. Observation at a single time point (day 14) may be considered sufficient to assess toxic effects

without the need for long-term evaluation. Histological testing of *Musa paradisiaca* extract is essential if it is to be developed into a standardized herbal medicine. Histopathological assessment of drug-induced toxicity plays a crucial role in pharmacovigilance, offering valuable information about how drugs may negatively impact different tissues and organs. As pharmaceutical innovation progresses and new treatments are introduced, evaluating their safety through histopathological studies has become more essential than ever.[24]

Conclusion

This study provides preliminary histological evidence supporting the safety of *Musa paradisiaca* L. heart extract at doses of 200–400 mg/kg bw in mice, while suggesting caution at higher doses due to mild tissue alterations. These findings open opportunities for its development as a standardized herbal product, provided that further investigations address its long-term safety, dose optimization, and potential therapeutic applications. Future studies should explore its effects on other vital organs, assess biochemical and molecular toxicity markers, and clarify its pharmacological mechanisms to ensure both efficacy and safety for prospective clinical use.

Conflict of Interest

The author`s declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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