PRINT ISSN 1119-8362
Electronic ISSN 2659-1499

Full-text Available Online at
https://www.ajol.info/index.php/jasem
https://www.bioline.org.br/ja

J. Appl. Sci. Environ. Manage.
Vol. 30 (1) 18-25 January 2026

Effects of Combined Exposure to Ibuprofen and Ethanol Bark Extract of *Spondias mombin* (Hog Plum) on Liver Injury and Liver Enzyme Markers in Albino Rats: Pre-Treatment and Post-Treatment Study

ODIGIE, EB; *OGEYEMHE, BE

Department of Medical Laboratory Science, School of Basic Medical Sciences, University of Benin, P.M.B. 1154, Benin City, Nigeria

**Corresponding Author Email: blessing.atoigwe@uniben.edu*
**ORCID: https://orcid.org/0009-0002-9244-2131*
**Tel: +2348065210159*

Co-Author Email: bolaji.odigie@uniben.edu

ABSTRACT: Drug-induced liver injury remains a major concern associated with the widespread use of non-steroidal anti-inflammatory drugs such as ibuprofen. This study evaluated the effects of combined exposure to ibuprofen and ethanol bark extract of *Spondias mombin* (hog plum) on liver injury, liver enzyme markers, and hepatic histology in albino rats using pre-treatment and post-treatment models. Adult albino rats were administered ibuprofen alone or in combination with *S. mombin* bark extract following standard experimental procedures. Liver function was assessed using serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin, and conjugated bilirubin, while liver tissues were examined histologically using hematoxylin and eosin staining. Ibuprofen administration caused mild but significant elevations in ALT (41.50 ± 1.06 IU/L) and AST (31.50 ± 1.77 IU/L) compared with control values of 37.00 ± 2.83 IU/L and 31.00 ± 0.71 IU/L, respectively, with variable ALP responses. Total and conjugated bilirubin levels remained stable across all groups (0.20 ± 0.00 mg/dL and 0.10 ± 0.00 mg/dL). Histological findings revealed preserved hepatic architecture, particularly in extract-treated groups. Pre-treatment with *S. mombin* bark extract demonstrated the most pronounced protective effect. The study concludes that *S. mombin* bark extract exerts hepatoprotective and restorative effects against ibuprofen-induced liver alterations, supporting its potential therapeutic relevance in mitigating drug-induced hepatic injury.

DOI : https://dx.doi.org/10.4314/jasem.v30i1.3

License: CC-BY-4.0

Open Access Policy: All articles published by **JASEM** are open-access and free for anyone to download, copy, redistribute, repost, translate and read.

Copyright Policy: © 2026. Authors retain the copyright and grant **JASEM** the right of first publication. Any part of the article may be reused without permission, provided that the original article is cited.

Cite this Article as: ODIGIE, E. B; OGEYEMHE, B. E. (2026). Effects of Combined Exposure to Ibuprofen and Ethanol Bark Extract of *Spondias mombin* (Hog Plum) on Liver Injury and Liver Enzyme Markers in Albino Rats: Pre-Treatment and Post-Treatment Study. ***J.** Appl. Sci. Environ. Manage.* 30 (1) 18-25

Dates: Received: 01 December, 2025; Revised: 29 December 2025; Accepted: 11 January 2026; Published: 31 January 2026

Keywords: *Spondias mombin*; Ibuprofen; Hepatoprotective effect; Hepatic injury; Liver enzymes

Drug-induced liver injury (DILI) remains a significant clinical and toxicological challenge due to the liver's central role in xenobiotic metabolism and detoxification. Many commonly used therapeutic agents undergo hepatic biotransformation, during which reactive intermediates and oxidative stress may be generated, predisposing hepatocytes to structural and functional injury (Skat-Rørdam *et al.*, 2025; Wang *et al.*, 2025). Non-steroidal anti-inflammatory drugs, including ibuprofen, are widely prescribed for analgesic and anti-inflammatory purposes, yet increasing evidence indicates that repeated or prolonged exposure can disrupt hepatic redox balance, mitochondrial function, and enzyme homeostasis (Arif and Aggarwal, 2023; Elshaer and Lizaola-Mayo, 2024). Experimental studies have shown that ibuprofen metabolism may induce oxidative stress, alter aminotransferase activities, and

**Corresponding Author Email: blessing.atoigwe@uniben.edu*
**ORCID: https://orcid.org/0009-0002-9244-2131*
**Tel: +2348065210159*

provoke adaptive or injurious hepatic responses depending on exposure pattern and biological context (Villanueva-Paz *et al.*, 2021; Borgne-Sanchez and Fromenty, 2025).

Growing interest in plant-derived natural products has highlighted their potential role in mitigating drug-induced hepatic stress through antioxidant, anti-inflammatory, and cytoprotective mechanisms. *Spondias mombin* (Hog Plum) is a medicinal plant extensively used in traditional medicine across tropical regions (Ogeyemhe and Innih, 2025), with its bark reported to contain bioactive phytochemicals such as flavonoids, tannins, phenolic acids, and saponins (Gonfa *et al.*, 2024; Hu *et al.*, 2025). These compounds are known to scavenge reactive oxygen species, modulate inflammatory signaling pathways, and stabilize cellular membranes, thereby contributing to hepatocellular protection and functional preservation (Allameh *et al.*, 2023; Liao *et al.*, 2024). Experimental investigations have demonstrated that *S. mombin* and related medicinal plants can attenuate alterations in liver enzyme markers and preserve hepatic architecture in chemically induced liver injury models, supporting their hepatoprotective potential (Chen *et al.*, 2025; Ogeyemhe and Atoyebi, 2025; Okpashi *et al.*, 2022).

Although the hepatoprotective properties of *S. mombin* have been reported, limited attention has been given to how the sequence and duration of administration influence its protective or restorative effects following drug-induced hepatic stress. Distinguishing between preventive, concurrent, and post-exposure interventions is essential for understanding the translational relevance of plant-based therapies in real-world pharmacological scenarios, where exposure timing often varies (Hassan *et al.*, 2025; McGill and Jaeschke, 2018; Ogeyemhe and Atoyebi, 2025). Experimental models using Wistar albino rats provide a reliable platform for evaluating such effects due to their well-characterized hepatic physiology and responsiveness to xenobiotic-induced injury (Hora and Wuestefeld, 2023; Kobayashi *et al.*, 2023). Therefore, the objective of this study is to evaluate the effects of combined exposure of ibuprofen and ethanol bark extract of *Spondias mombin* (Hog Plum) on liver injury and liver enzyme markers in albino rats as pre-treatment, and post-treatment.

MATERIALS AND METHODS

Study area: This study was conducted in a biomedical research laboratory equipped for experimental animal handling, biochemical analysis, and histopathological processing. All experimental procedures were performed using standard laboratory facilities and equipment suitable for in vivo studies and tissue analysis.

Experimental animals: Adult male Wistar albino rats were obtained from the animal facility of the institution. The animals were housed under standard laboratory conditions with a 12 h light-dark cycle, controlled temperature (22-24 °C), and free access to standard pellet feed and water. Animals were allowed to acclimatize for one week prior to commencement of the experiment.

Plant material collection and authentication: Fresh bark of *S. mombin* (Hog Plum) was collected and taxonomically authenticated by a qualified plant taxonomist. A voucher specimen was prepared and deposited in a recognized herbarium for future reference under voucher number UBH-S345. Authentication was performed prior to extraction to ensure botanical identity and reproducibility of the study.

Preparation of plant extract: The bark was washed, air-dried under shade, and pulverized into fine powder. The powdered material was extracted using ethanol by maceration for 48-72 h with intermittent agitation. The extract was filtered, and the filtrate concentrated under reduced pressure using a rotary evaporator at controlled temperature. The concentrated extract was stored at 4 °C until use.

Drug preparation and administration: Ibuprofen tablets were obtained from a certified pharmaceutical source and freshly prepared daily by crushing and suspending in distilled water. A dose of 20 mg/kg body weight was administered orally, reflecting clinically relevant exposure levels linked to modulation of liver metabolic pathways and oxidative stress in rodent models (AlKandari *et al.,* 2024; Li and Liu, 2024). The *S. mombin* bark extract dose (1000 mg/kg) was selected based on established safety and organ-protective evidence in rodent studies (Adesina *et al.*, 2025; Ogeyemhe and Atoyebi, 2025). All treatments were administered orally using calibrated gavage needles according to the assigned sequence and duration.

Experimental design and treatment protocol: Thirty rats were randomly assigned into six groups (n = 5 per group). Group I served as the control and received feed and distilled water only. Group II received ibuprofen at 20 mg/kg body weight. Group III received *S. mombin* bark extract at 1000 mg/kg body weight. Group IV received simultaneous administration of ibuprofen (20 mg/kg) and *S.*

mombin extract (1000 mg/kg). Group V received *S. mombin* extract (1000 mg/kg) for one week followed by ibuprofen (20 mg/kg) for another week. Group VI received ibuprofen (20 mg/kg) for one week followed by *S. mombin* extract (1000 mg/kg) for another week. All treatments were administered orally.

Sample collection: Twenty-four hours after the final administration, animals were humanely anesthetized and sacrificed. Blood samples were collected by cardiac puncture into plain tubes and centrifuged to obtain serum for biochemical analysis. The liver was excised, rinsed in normal saline, and fixed in 10 % neutral buffered formalin for histological examination.

Liver Enzymes analysis: Serum activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin, and conjugated bilirubin were determined using standard colorimetric methods. Enzyme activities were measured spectrophotometrically following established protocols.

Histological processing and microscopy: Fixed liver tissues were processed using standard paraffin-embedding techniques. Sections of 3-5 µm thickness were cut and stained with hematoxylin and eosin. Stained sections were examined under a light microscope at appropriate magnifications, and representative photomicrographs were captured for documentation (Suvarna *et al*., 2019). Histological assessment and interpretation were performed independently by a qualified histopathologist affiliated with a government-approved biomedical research institute, using established criteria for hepatic architecture and cellular integrity.

Statistical analysis: Data were expressed as mean ± standard error of mean (SEM). Statistical analysis was performed using one-way analysis of variance, and differences were considered significant at $p < 0.05$.

RESULTS AND DISCUSSION

The effects of ibuprofen and *S. mombin* on body and liver weights are presented in Table 1. Rats administered ibuprofen alone exhibited a mild reduction in body weight gain alongside subtle changes in liver weight when compared with the control group, suggesting systemic stress and early hepatic adaptation following repeated ibuprofen exposure. In contrast, animals treated with *S. mombin* alone, as well as those receiving combined or sequential treatments, showed relatively stable body and liver weights. Notably, both pre-treatment and post-treatment with *S. mombin* attenuated ibuprofen-associated alterations, indicating improved physiological tolerance and preservation of organ integrity.

Similar stabilization of body and liver weights has been reported in studies evaluating plant-derived interventions against drug-induced hepatic stress (Okpashi *et al.*, 2022; Adesina *et al.*, 2025). Biochemical indices of liver function are summarized in Table 2 and further illustrated in Figure 1A-E.

Administration of ibuprofen alone resulted in measurable elevations in serum alanine aminotransferase and aspartate aminotransferase activities, with ALT rising to 41.50 ± 1.06 IU/L compared with 37.00 ± 2.83 IU/L in the control group, indicating hepatocellular membrane perturbation. Aspartate aminotransferase showed a similar upward trend in the ibuprofen group (31.50 ± 1.77 IU/L) relative to controls. Alkaline phosphatase activity also varied across groups, reflecting possible biliary or canalicular stress associated with ibuprofen exposure.

These biochemical disturbances are consistent with reports describing ibuprofen-associated hepatic stress and enzyme leakage following repeated administration (Jan-Roblero and Cruz-Maya, 2023; Skat-Rørdam *et al.*, 2025). In contrast, rats treated with *S. mombin* alone maintained enzyme activities comparable to control values, indicating the absence of intrinsic hepatotoxicity at the administered dose. More importantly, co-administration, pre-treatment, and post-treatment with *S. mombin* markedly moderated the ibuprofen-induced elevations in liver enzymes.

The most pronounced improvement was observed in the pre-treated group, where ALT values declined to 32.00 ± 2.83 IU/L, approaching baseline levels. These trends are clearly depicted in Figure 1, where enzyme responses in *S. mombin*-treated groups consistently shifted toward normalization compared with the ibuprofen-only group.

Total and conjugated bilirubin levels remained constant across all groups (0.20 ± 0.00 mg/dL and 0.10 ± 0.00 mg/dL, respectively), indicating preserved bilirubin conjugation and excretory function and suggesting that the hepatic insult induced by ibuprofen was mild and reversible.

Comparable biochemical protection has been documented in histo-biochemical studies of *S.*

mombin and related medicinal plants (Gonfa *et al.*, 2024; Ogeyemhe and Atoyebi, 2025).

Table 1: Body and liver weight changes in adult albino rats following ibuprofen and *S. mombin* treatments

Parameters	Group 1 (control)	Group 2	Group 3	Group 4	Group 5	Group 6
Initial body weight (g)	213.67 ± 4.25	196.5 ± 5.3	209.3 ± 3.06	187.7 ± 7.25	184.0 ± 4.50	191.7 ± 10.80
Final body weight (g)	236.0 ± 4.32	219.5 ± 10.96	216.3 ± 4.38	201.7 ± 13.20	187.0 ± 0.00	216.3 ± 18.40
Liver weight (g)	8.7 ± 0.57	7.35 ± 0.03	7.03 ± 0.65	8.23 ± 0.47	6.17 ± 0.22	6.93 ± 0.96

Values are expressed as Mean ±SEM

Table 2: Liver function enzyme and bilirubin profile following ibuprofen and *S. mombin* treatments

Parameters	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
AST (IU/L)	31.00 ± 0.71	31.50 ± 1.77	29.50 ± 2.47	29.50 ± 1.06	33.50 ± 1.06	30.50 ± 2.47
ALT (IU/L)	37.00 ± 2.83	41.50 ± 1.06	40.00 ± 2.83	32.00 ± 2.83	33.00 ± 4.24	36.50 ± 2.47
ALP (IU/L)	113.00 ± 4.95	104.00 ± 8.49	117.00 ± 3.54	100.00 ± 0.71	113.00 ± 3.54	117.00 ± 2.83
Total bilirubin (mg/dL)	0.20 ± 0.0	0.20 ± 0.0	0.20 ± 0.0	0.20 ± 0.0	0.20 ± 0.0	0.20 ± 0.0
Conjugated bilirubin (mg/dL)	0.10 ± 0.00	0.10 ± 0.00	0.10 ± 0.00	0.10 ± 0.00	0.10 ± 0.00	0.10 ± 0.00

Values are expressed as Mean ±SEM

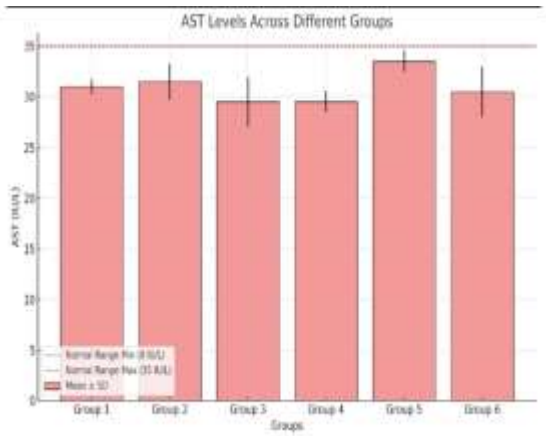


Fig. 1A: Aspartate aminotransferase levels across all experimental groups

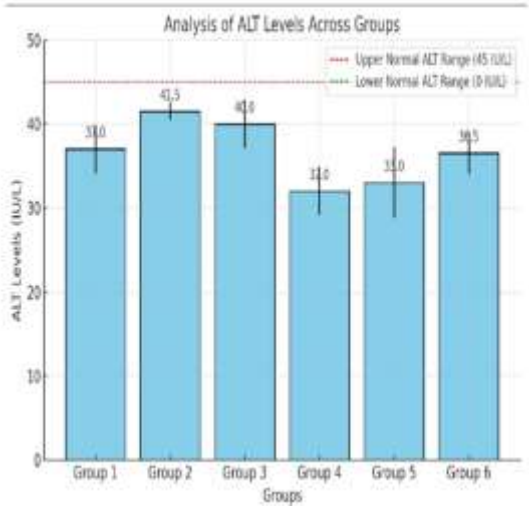


Fig. 1B: Alanine aminotransferase levels across all experimental groups

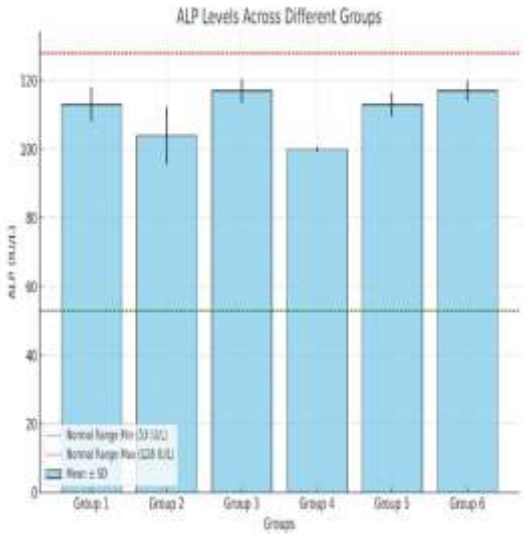


Fig. 1C: Alkaline phosphatase levels across all experimental groups

Histological findings further substantiated the biochemical results and are presented in Plate 1-6. Liver sections from the control group (Plate 1) displayed normal hepatic architecture, with well-arranged hepatocytes, intact sinusoids, and preserved central veins. In contrast, the ibuprofen-treated group (Plate 2) showed mild histopathological alterations, including hepatocellular disorganization and vascular congestion, consistent with early hepatic injury and correlating with the elevated enzyme activities observed in Table 2. Liver sections from rats treated with *S. mombin* alone (Plate 3) exhibited preserved architecture comparable to controls, confirming the

non-toxic nature of the extract at the administered dose.

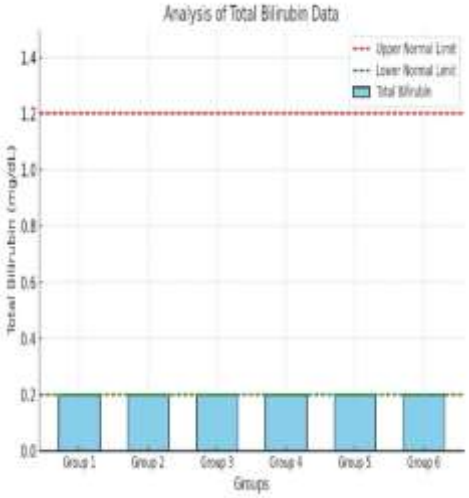


Fig. 1D: Total bilirubin levels across all experimental groups

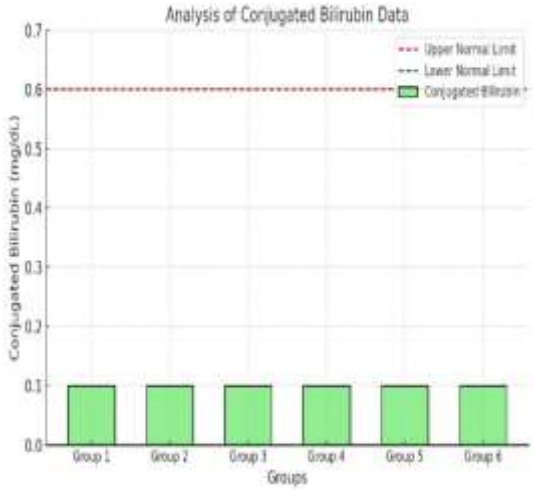


Fig. 1E: Conjugated bilirubin levels across all experimental groups

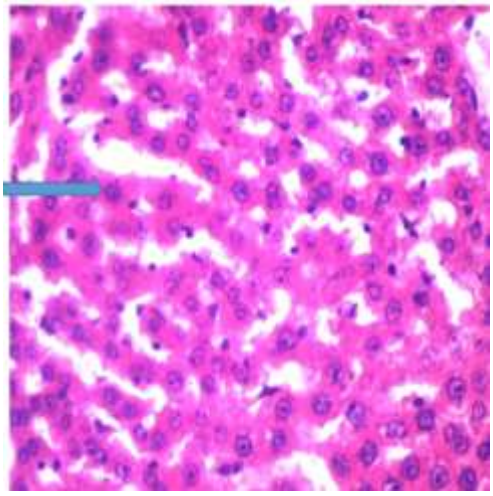


Plate. 1: Photomicrograph of liver tissue (control group) fed with only food and distilled water, showing normal hepatic architecture (H&E, X400 magnification).

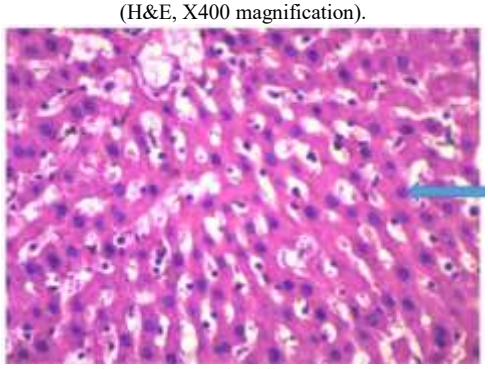


Plate. 2: Photomicrograph of liver tissue from animals administered a single daily dose of 20 ml/kg of ibuprofen, showing normal hepatic architecture (H&E, X400 magnification).

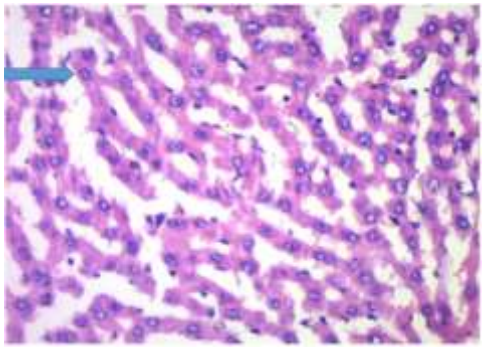


Plate. 3: Photomicrograph of liver tissue from rats administered 1000 mg/kg body weight of *Spondias mombin* bark extract (H&E, X400 magnification).

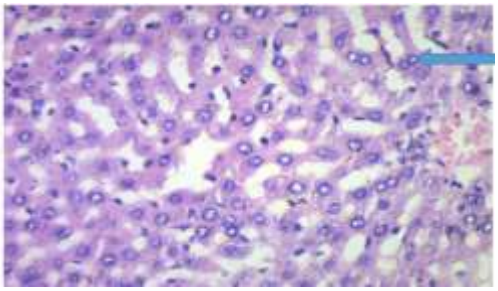


Plate. 4: Photomicrograph of the liver tissue from Group IV rats, administered a simultaneous dose of 1000 mg/kg of *Spondias mombin* bark extract and 20 mg/kg of ibuprofen (H&E, X400 magnification).

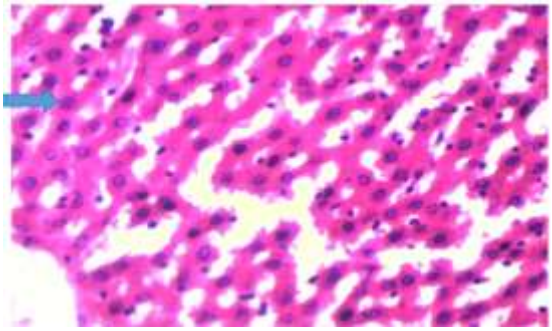


Plate. 5: Photomicrograph of the liver tissue from Group V rats, administered 1000 mg/kg *Spondias mombin* extract for one week, followed by 20 mg/kg ibuprofen for another week (H&E, X400 magnification).

Notably, groups receiving *S. mombin* alongside ibuprofen demonstrated varying degrees of histological improvement. Simultaneous administration (Plate 4) resulted in reduced structural distortion, while pre-treatment (Plate 5) showed near-complete restoration of hepatocellular arrangement with minimal vascular changes. Post-treatment with *S. mombin* (Plate 6) also produced appreciable recovery, although less pronounced than pre-treatment, indicating both protective and reparative effects. These histological observations are consistent with earlier reports describing tissue preservation and recovery following *S. mombin* intervention in drug-induced organ injury models (Ogeyemhe and Innih, 2025; Chen *et al.*, 2025).

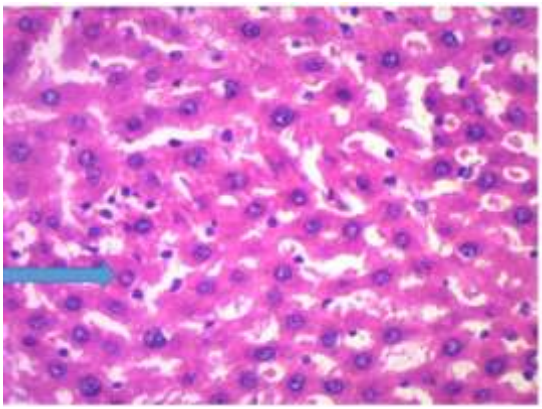


Plate. 6: Photomicrograph of liver tissue from rats administered 20 mg/kg body weight of Ibuprofen followed by 1000 mg/kg body weight of *Spondias mombin* bark extract.

Taken together, the integrated findings from Table 1, Table 2, Figure 1, and Plate 1 to 6 demonstrate that administration of ibuprofen at 20 mg/kg produced mild but measurable biochemical alterations in liver enzyme markers without corresponding structural damage on histological examination. Although serum ALT, AST, and ALP showed elevations relative to controls, liver architecture in the ibuprofen-treated group remained preserved, suggesting that the dose and duration employed were sufficient to induce functional hepatic stress rather than overt morphological injury (McGill and Jaeschke, 2018; Skat-Rørdam *et al.*, 2025). This observation is consistent with reports indicating that ibuprofen, particularly at low to moderate experimental doses, may elicit enzyme perturbations that precede or occur independently of detectable histopathological damage (Jan-Roblero and Cruz-Maya, 2023; Villanueva-Paz *et al.*, 2021).

In contrast, *S. mombin* administration, whether alone or in combination with ibuprofen, was associated with stabilization of body and liver weights, normalization of biochemical indices, and sustained preservation of hepatic architecture, reflecting improved hepatic functional integrity (Okpashi *et al.*, 2022; Ogeyemhe and Atoyebi, 2025). The convergence of biochemical modulation and histological integrity supports the hepatoprotective and restorative potential of *S. mombin*, while also indicating that its effects may be more pronounced at the level of cellular function and enzymatic regulation than gross tissue remodeling under mild injury conditions (Hora and Wuestefeld, 2023; Gonfa *et al.*, 2024). Overall, these findings suggest that *S. mombin* mitigates early hepatic stress responses induced by ibuprofen and may play a protective role before the onset of irreversible structural damage (Chen *et al.*, 2025; Skat-Rørdam *et al.*, 2025).

*Conclusion***:** This study establishes that *Spondias mombin* bark extract confers hepatoprotective and restorative benefits against ibuprofen-associated liver stress in albino rats, with protective efficacy influenced by treatment sequence and duration. The findings contribute to knowledge by demonstrating the potential of *S. mombin* as a natural intervention capable of moderating early drug-induced hepatic alterations. Its hepatoprotective relevance in mitigating biochemical disturbances associated with non-steroidal anti-inflammatory drug exposure is thereby highlighted. These outcomes support the therapeutic promise of *S. mombin* bark extract as a complementary hepatoprotective agent. Further studies are recommended to investigate broader dosing regimens, extended treatment durations, and underlying molecular mechanisms to enhance translational relevance.

DECLARATIONS

Ethical Approval: The study involved the use of experimental animals, and ethical clearance was obtained prior to commencement under approval number MAFSAEC: 025-01/09/0013. All animal-related procedures were performed in accordance with internationally accepted standards for the care and use of laboratory animals and applicable regulatory guidelines.

Disclaimer (Artificial Intelligence): Author(s) hereby declare that generative Artificial Intelligence (AI) technologies such as Large Language Models were used only for language editing. No AI tools were used for data generation, analysis, or interpretation.

Declaration of Conflict of Interest: The authors declare that there are no financial, professional, or

personal relationships that could be perceived as influencing the outcomes or interpretation of this study.

Declaration of Data Availability: The data supporting the findings of this study can be made available upon reasonable request from the corresponding author.

REFERENCES

Adesina, AF; Apata, JT; Babalola, OO; Otuechere, CA; Adekola, MB; Ogunleye, GS; Asaolu, F (2025). Hepatoprotective activity of *Alstonia boonei* stem bark in isoniazid-induced Wistar rats: antioxidant, anti-inflammatory and in silico evaluations. *Pharmacol. Res. Mod. Chin. Med.* 14:100558. DOI: https://doi.org/10.1016/j.prmcm.2024.100558

AlKandari, FM; Mohamed, HS; Ahmed, SA; Mahmoud, B; Mahmoud, AM (2024). Protective effects of propolis and chitosan nanoparticles against ibuprofen-induced hepatotoxicity in albino rats. Diseases 12(3): 49. DOI: https://doi.org/10.3390/diseases12030049

Allameh, A; Niayesh-Mehr, R; Aliarab, A; Sebastiani, G; Pantopoulos, K (2023). Oxidative stress in liver pathophysiology and disease. *Antioxidants* 12(9):1653. DOI: https://doi.org/10.3390/antiox12091653

Arif, H; Aggarwal, S (2023). Salicylic acid (aspirin). *StatPearls*. StatPearls Publishing, Treasure Island, FL. DOI: https://www.ncbi.nlm.nih.gov/books/NBK519032

Borgne-Sanchez, A; Fromenty, B (2025). Mitochondrial dysfunction in drug-induced hepatic steatosis: recent findings and current concept. *Clin. Res. Hepatol. Gastroenterol.* 49(3):102529. DOI: https://doi.org/10.1016/j.clinre.2025.102529

Chen, Y; Mei, YQ; Hou, L; Li, KJ (2025). Therapeutic potential of plant-derived natural products against drug-induced liver injury. *Front. Pharmacol.* 16:1652860. DOI: https://doi.org/10.3389/fphar.2025.1652860

Elshaer, A; Lizaola-Mayo, BC (2024). Evaluating the role of aspirin in liver disease: efficacy, safety, potential benefits and risks. *Life* 14(12):1701. DOI: https://doi.org/10.3390/life14121701

Gonfa, YH; Bachheti, A; Semwal, P; Rai, N; Singab, AN; Bachheti, RK (2024). Hepatoprotective activity of medicinal plants, their phytochemistry and safety concerns: a systematic review. Z. Naturforsch. C 80(3-4):61–73. DOI: https://doi.org/10.1515/znc-2024-0116

Hassan, M; Kansky, B; Sudhakar, H; El-Feki, I; Nguyen, T; Lopera, S (2025). Detection to prediction: biomarkers in severe drug-induced liver injury. *Am. J. Clin. Med. Res.* 5(6):971. DOI: https://doi.org/10.71010/AJCMR.2025-e224

Hora, S; Wuestefeld, T (2023). Liver injury and regeneration: current understanding, new approaches and future perspectives. *Cells* 12(17):2129. DOI: https://doi.org/10.3390/cells12172129

Hu, Q; Zhang, S; Liu, J; Liu, Y; Chen, X; Wang, J (2025). A Review: hepatoprotective compounds and its mechanisms of medicine-food homology resources. *Agric. Prod. Process. Storage* 1:5. DOI: https://doi.org/10.1007/s44462-025-00009-5

Jan-Roblero, J; Cruz-Maya, JA (2023). Ibuprofen: toxicology and biodegradation of an emerging contaminant. *Molecules* 28(5):2097. DOI: https://doi.org/10.3390/molecules28052097

Kobayashi, T; Iwaki, M; Nogami, A; Yoneda, M (2023). Epidemiology and management of drug-induced liver injury: importance of the updated RUCAM. *J. Clin. Transl. Hepatol.* 11(5):1239-1245. DOI: https://doi.org/10.14218/JCTH.2022.00067S

Li, H; Xiong, H; Wang, X; Xu, T; Zhang, C; Zhang, W; Zhang, Y (2024). Ibuprofen induces hepatic Cyp7a1 expression in mice via the intestinal FXR-FGF15 signaling pathway. *Toxicol. Lett.* 398:1-12. DOI: https://doi.org/10.1016/j.toxlet.2024.05.015

Liao, Y; Lv, F; Quan, T; Wang, C; Li, J (2024). Flavonoids in natural products for the therapy of liver diseases: progress and future opportunities. *Front. Pharmacol.* 15:1485065. DOI: https://doi.org/10.3389/fphar.2024.1485065

McGill, MR; Jaeschke, H (2018). Biomarkers of drug-induced liver injury: progress and utility in research, medicine and regulation. *Expert Rev. Mol. Diagn.* 18(9):797–807. DOI: https://doi.org/10.1080/14737159.2018.1508998

Ogeyemhe, BE; Atoyebi, MF (2025). Hepatorenal consequences of *Spondias mombin* root extract: a histo-biochemical study in animal model. *Gal. Int. J. Health Sci. Res.* 10(3):134-143. DOI: https://doi.org/10.52403/gijhsr.20250314

Ogeyemhe, BE; Innih, SO (2025). Effects of *Spondias mombin* ethanol leaf extract on ibuprofen-induced ovarian toxicity in Wistar rats: a histological study. *J. Appl. Sci. Environ. Manage.* 29(8): 2553–2557. DOI: https://doi.org/10.4314/jasem.v29i8.20

Okpashi, VE; Uroko, RI; Ogana, J; Agbafor, A; Nwuke, CP (2022). Effect of *Alstonia boonei* stem bark extracts on liver marker enzymes in CCl_4-induced rats. *Baghdad Sci. J.* 19(5):7. DOI: https://doi.org/10.21123/bsj.2022.6107

Skat-Rørdam, J; Lykkesfeldt, J; Gluud, LL; Tveden-Nyborg, P (2025). Mechanisms of drug-induced liver injury. *Cell. Mol. Life Sci.* 82:213. https://doi.org/10.1007/s00018-025-05744-3

Suvarna, SK; Layton, C; Bancroft, JD (2019). Bancroft's theory and practice of histological techniques. 8th ed. Elsevier (Churchill Livingstone), London. Pp. 125–128. DOI: https://doi.org/10.1016/C2015-0-00143-5

Villanueva-Paz, M; Morán, L; López-Alcántara, N; Freixo, C; Andrade, RJ; Lucena, MI; Cubero, FJ (2021). Oxidative stress in drug-induced liver injury: from mechanisms to biomarkers. *Antioxidants* 10(3):390. https://doi.org/10.3390/antiox10030390

Wang, L; Shao, Z; Wang, X; Lu, W; Sun, H (2025). Xenobiotic-induced liver injury: molecular mechanisms and disease progression. *Ecotoxicol. Environ. Saf.* 303:118854. https://doi.org/10.1016/j.ecoenv.2025.118854