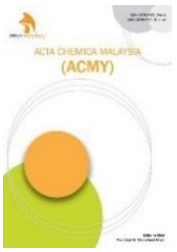
ZIBELINE INTERNATIONAL™ PUBLISHING

ISSN: 2576-6724 (Print)
ISSN: 2576-6732 (Online)
CODEN: ACMCCG

Acta Chemica Malaysia (ACMY)

DOI: http://doi.org/10.26480/acmy.01.2025.55.62



RESEARCH ARTICLE

HISTOPATHOLOGICAL ASSESSMENT OF THE HEPATOPROTECTIVE EFFECTS OF SPHENOCENTRUM JOLLYANUM STEM BARK AQUEOUS EXTRACT IN CADMIUM CHLORIDE-INDUCED LIVER INJURY IN WISTAR RATS

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ARTICLE DETAILS

Article History:

Received 07 March 2025
Revised 15 April 2025
Accepted 11 May 2025
Available online 29 May 2025

ABSTRACT

Cadmium, a pervasive environmental pollutant, is known for its hepatotoxic potential due to its ability to induce oxidative stress and disrupt cellular integrity. This study evaluated the histopathological and therapeutic effects of aqueous extract of *Sphenocentrum jollyanum* (stem bark) on cadmium chloride-induced hepatotoxicity in adult Wistar rats. A total of thirty-six (36) rats were randomly assigned into six groups (A–F) comprising six rats each. Group A served as control; Group B received cadmium chloride (10 mg/kg); Groups C and D were administered low (150 mg/kg) and high (300 mg/kg) doses of *S. jollyanum* extract, respectively; Groups E and F received cadmium chloride alongside low and high doses of *S. jollyanum* extract, respectively. Treatments were administered orally for 28 consecutive days. At the end of the treatment period, liver tissues were harvested for histopathological analysis using hematoxylin and eosin (H&E) staining. Results revealed that cadmium chloride exposure led to significant histopathological alterations in liver architecture, including hepatocellular necrosis, cytoplasmic vacuolation, and inflammatory infiltration. However, co-administration with *S. jollyanum* extract, particularly at high dose (300 mg/kg), mitigated these pathological lesions and restored hepatic architecture. This protective effect was dose-dependent and may be attributed to the antioxidant and anti-inflammatory properties of the plant extract. Conclusively, this study demonstrates that *Sphenocentrum jollyanum* stem bark extract confers hepatoprotective effects against cadmium-induced liver injury in Wistar rats, highlighting its potential as a natural therapeutic agent for managing heavy metal-induced hepatic disorders. Further studies, including molecular assays and isolation of active phytoconstituents, are recommended to support clinical relevance.

KEYWORDS

Sphenocentrum jollyanum, Cadmium chloride, Hepatotoxicity, Histopathology, Wistar rat

1. INTRODUCTION

The liver plays a central role in metabolism, detoxification, and homeostasis. As the primary organ responsible for biotransformation, it is highly susceptible to damage from xenobiotics, heavy metals, drugs, and environmental toxins (Mead, 2009). Among various environmental pollutants, cadmium is particularly notorious due to its widespread occurrence and toxicological impact (Genchi et al., 2020). Cadmium exposure is primarily occupational and environmental, arising from industrial activities such as mining, battery manufacturing, paint production, and the improper disposal of e-waste (Genchi et al., 2020). Additionally, cadmium may enter the body through the ingestion of contaminated food and water, inhalation of cigarette smoke, and long-term consumption of herbal products grown in polluted environments (Rasin et al., 2025).

Cadmium chloride ($CdCl_2$), a soluble salt form of cadmium, has been extensively used in experimental toxicology to induce organ-specific toxicity, particularly hepatotoxicity (Innih, et al., 2021). Once absorbed, cadmium accumulates in the liver and kidneys, disrupting the antioxidant defense system by generating reactive oxygen species (ROS). This leads to oxidative stress, lipid peroxidation, mitochondrial dysfunction, DNA damage, and apoptosis of hepatocytes (Qu and Zheng, 2024). Prolonged cadmium exposure has also been implicated in hepatic inflammation hepatotoxicity, fibrosis, and carcinogenesis (Xu et al., 2021; Innih, et al., 2021). These adverse effects necessitate the development of preventive and therapeutic strategies to mitigate cadmium-induced liver injury.

Conventional treatment options for heavy metal toxicity include chelation therapy, which involves the use of agents such as dimercaprol, EDTA, and DMSA (Flora and Pachauri, 2010). However, these agents are associated with significant limitations, including adverse effects, high cost, and non-specificity (Flora and Pachauri, 2010). Consequently, attention has turned toward natural remedies derived from medicinal plants, which offer promising hepatoprotective effects due to their phytochemical constituents such as flavonoids, alkaloids, tannins, saponins, and phenolic compounds. These bioactive molecules possess antioxidant, anti-inflammatory, and cytoprotective properties that can counteract the toxicological effects of cadmium and support hepatic regeneration (Unsal et al., 2020).

One such medicinal plant of growing interest is *Sphenocentrum jollyanum*, a shrub belonging to the Menispermaceae family, commonly found in West Africa. Locally known as "Aromame" in some Nigerian communities, *S. jollyanum* has been traditionally used for managing a variety of ailments

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	Website: www.actachemicamalaysia.com	**DOI:** 10.26480/acmy.01.2025.55.62

Cite the Article: Silavanus Olu Innih, Deborah Calmday-Ombo (2025). Histopathological Assessment of The Hepatoprotective Effects of Sphenocentrum Jollyanum Stem Bark Aqueous Extract in Cadmium Chloride-Induced Liver Injury in Wistar Rats. *Acta Chemica Malaysia, 9(1): 55-62.*

including malaria, fever, jaundice, gastrointestinal disorders, and inflammatory conditions (Olorunnisola, et al., 2017; Tropical Plants Database, Ken Fern, 2025). Ethnopharmacological studies have demonstrated that different parts of the plant, particularly the roots and stem bark exhibit significant pharmacological activities. Reports have highlighted its antioxidant, anti-inflammatory, antipyretic, and antimicrobial potentials, suggesting that its therapeutic benefits may extend to managing toxin-induced liver injuries (Okechukwu, et al., 2018).

Despite the plant's extensive use in traditional medicine and emerging pharmacological evidence, the hepatoprotective potential of *Sphenocentrum jollyanum*, particularly its stem bark, remains underexplored in experimental settings. Moreover, few studies have investigated its protective efficacy against heavy metal-induced hepatotoxicity, such as that caused by cadmium chloride (Olorunnisola, 2011; Olorunnisola, et al., 2021; Adebayoet al., 2021). There is a need to scientifically validate its folkloric claims and elucidate the possible mechanisms through which its bioactive constituents exert protective effects on liver tissue.

The present study, therefore, investigates the protective role of aqueous extract of *Sphenocentrum jollyanum* stem bark on cadmium chloride-induced hepatotoxicity in adult Wistar rats. The experimental model of cadmium-induced liver injury serves as a platform to evaluate both preventive and restorative potentials of the plant extract. Parameters such as body weight changes, liver-to-body weight ratio, and histopathological assessment of hepatic tissue were evaluated to provide a comprehensive understanding of the plant's protective efficacy.

The rationale for the selection of *S. jollyanum* lies in its established antioxidant and anti-inflammatory activities, which are central to combating cadmium-induced oxidative stress and hepatocellular damage (Olorunnisola, et al., 2017). The study design incorporates both low and high doses of the plant extract to determine dose-dependent responses, thereby offering insights into its therapeutic window and potential toxicity, if any. By employing an histological approach, this study aims to bridge the gap between traditional knowledge and modern scientific validation.

Ultimately, this research contributes to the growing body of literature on plant-based hepatoprotective agents, aligning with global efforts to explore natural alternatives for managing environmental and industrial toxin exposures. It also emphasizes the importance of conserving indigenous medicinal plants and validating their therapeutic applications through rigorous scientific investigation. The outcomes of this study may serve as a basis for further research into the isolation and characterization of the bioactive compounds in *Sphenocentrum jollyanum*, their mechanism of action, and potential development into standardized herbal formulations or adjunctive therapies for hepatotoxic conditions.

2. Materials and Methods

2.1 Experimental Animals

A total of thirty-six (36) healthy adult Wistar rats (both sexes), weighing between 160-220g, were obtained from the Animal House of the Department of Anatomy, University of Benin, Nigeria. The animals were housed in clean plastic cages under standard laboratory conditions (temperature 22±2°C, 12-hour light/dark cycle) and provided with standard rat pellets and clean water ad libitum. Animals were acclimatized for two weeks before the commencement of the experiment. Ethical approval for animal use was obtained from the institutional Animal Research Ethics Committee.

2.2 Plant Collection and Preparation

Fresh stem bark of *Sphenocentrum jollyanum* was collected from a local farm in Ovia North East Local Government Area of Edo State, Nigeria. The plant was identified and authenticated at the Department of Plant Biology and Biotechnology, University of Benin, with a voucher specimen number deposited for reference. The stem bark was thoroughly washed, shade-dried, and ground into fine powder using an electric grinder.

The powdered material (500g) was soaked in 2.5L of distilled water and allowed to stand for 48 hours with intermittent stirring. The extract was filtered using Whatman No.1 filter paper and concentrated using a rotary evaporator at 40°C. The final aqueous extract was stored in a refrigerator at 4°C until use. Doses of 250 mg/kg and 500 mg/kg were prepared by dilution in distilled water.

2.3 Chemical and Reagents

Cadmium chloride ($CdCl_2$) of analytical grade was procured from Sigma-Aldrich (Germany). All biochemical assay kits for liver function markers were obtained from Randox Laboratories (UK). Other reagents used were of analytical grade.

2.4 Experimental Design

The rats were randomly divided into six (6) groups, with six (6) rats per group:

- Group A (Normal Control): Received 2 mL of distilled water.
- Group B (Negative Control): Received 10mg/kg cadmium chloride solution.
- Group C (Extract Control): Received 150 mg/kg *S. jollyanum* extract.
- Group D (Extract Control): Received 300 mg/kg *S. jollyanum* extract.
- Group E: Received 10mg/kg of cadmium chloride + 150 mg/kg *S. jollyanum* extract.
- Group F: Received 10mg/kg of cadmium chloride + 300 mg/kg *S. jollyanum* extract.

All administrations were done orally using an orogastric cannula once daily for 28 consecutive days.

2.5 Sample Collection

At the end of the treatment period, rats were fasted overnight and euthanized under mild anesthesia using diethyl ether. The liver was excised, blotted dry, weighed, and processed for histological examination.

2.6 Histological Examination

Liver tissues were fixed in 10% neutral buffered formalin for 48 hours. The fixed tissues were processed using standard paraffin embedding techniques. Sections (5 µm thick) were stained with Hematoxylin and Eosin (H&E) (Drury and Wallington, 1980) and examined under a light microscope for histopathological changes, including cellular degeneration, necrosis, congestion, and inflammatory infiltration.

2.7 Statistical Analysis

Data were expressed as mean ± standard deviation (SD). Statistical analysis was performed using IBM SPSS version 25. One-way analysis of variance (ANOVA) was used to compare means among groups, followed by Tukey's post hoc test. A p-value < 0.05 was considered statistically significant.

3. Results and Discussion

3.1 Analysis of Results

3.1.1 Body Weight Changes (Chart 1 & Chart 2)

The initial and final weights of the rats after 28 days showed that cadmium chloride (Group B) significantly suppressed weight gain compared to the normal control (Group A). This weight reduction suggests systemic toxicity induced by cadmium, potentially due to anorexia, metabolic disruptions, or organ dysfunction.

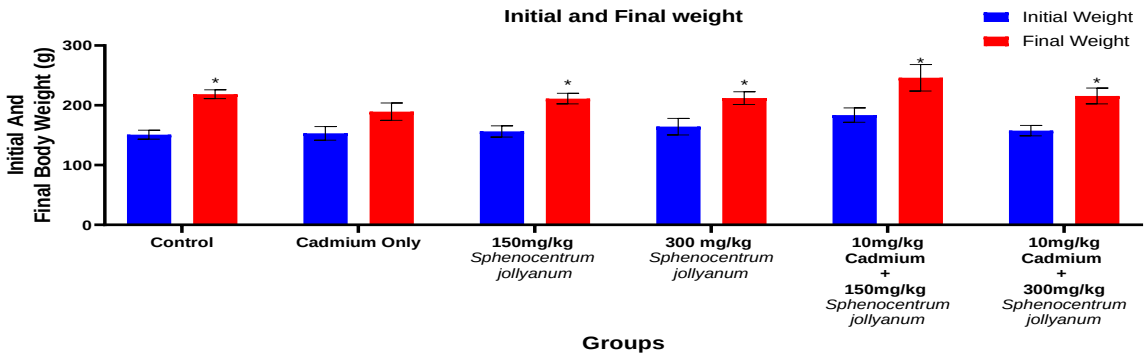

Chart 1: Initial and Final weight after 28 days of administration. Values are given as mean ± SEM. * p<0.05 compared with initial weight.

In contrast, rats co-treated with *Sphenocentrum jollyanum* extract at 150 mg/kg (Group E) and 300 mg/kg (Group F) exhibited improved weight outcomes. Although not completely restored to control levels, their weight gain was significantly better than the cadmium-only group, suggesting a dose-dependent mitigation of cadmium's toxic effects. The extract-only groups (C and D) gained weight comparably to controls, indicating no adverse effects of the extract itself.

A comparison of the net weight changes further emphasizes the protective role of *S. jollyanum*. Rats in the extract-only groups (C and D) showed positive weight changes similar to the normal control. Meanwhile, the cadmium-only group had the lowest weight gain, reinforcing the toxic burden. Co-treated groups E and F had intermediate weight gain, with Group F (300 mg/kg extract) approaching normal values, indicating enhanced resilience to cadmium-induced systemic stress.

3.1.2 Weight Change (Chart 2)

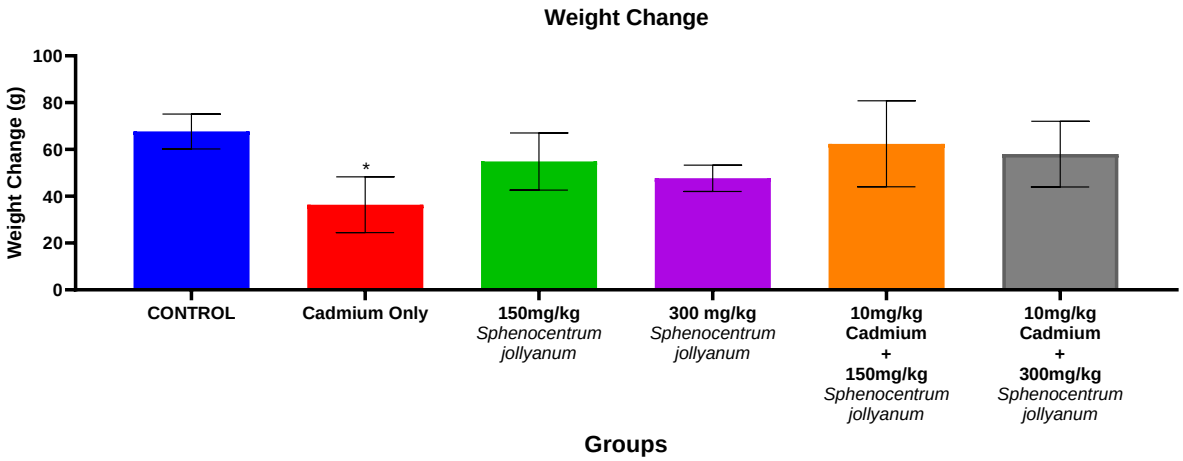

Chart 2: weight change after 28 days of administration. Values are given as mean ± SEM. * p<0.05 compared with control.

3.1.3 Liver Weight (Chart 3)

Liver weight, a direct marker of hepatic swelling or hypertrophy due to injury or inflammation, was significantly increased in the cadmium-only group. This supports evidence of liver damage. Co-treatment with the extract (especially at 300 mg/kg in Group F) significantly reduced liver weight compared to the cadmium group, suggesting protective or regenerative liver effects.

Interestingly, the extract-only groups maintained normal liver weights, reinforcing the safety profile of *S. jollyanum* at both tested doses. The reduction in liver weight in co-treated groups is consistent with reduced hepatic inflammation or congestion.

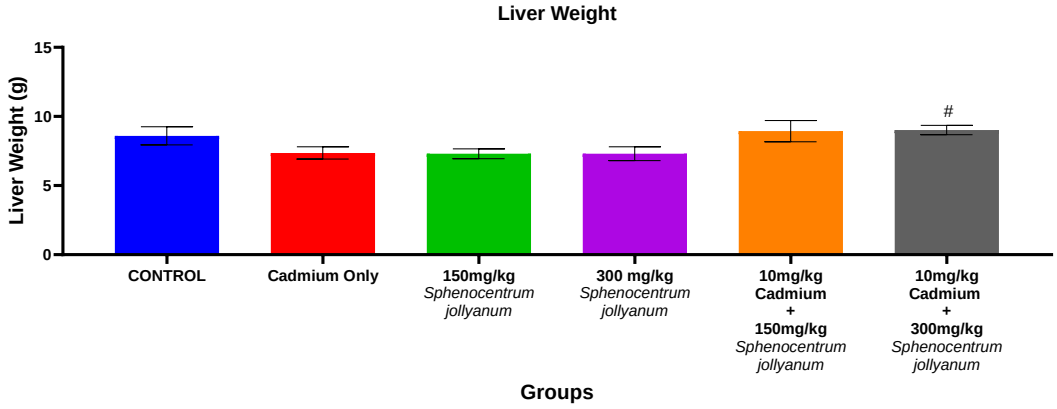

Chart 3: Liver weight after 28 days of administration. Values are given as mean ± SEM. # p<0.05 compared with cadmium only.

3.1.4 Hepatosomatic Index (Chart 4)

The hepatosomatic index (HSI), which reflects liver size relative to body weight, followed the same trend. Group B had the highest HSI, again reflecting cadmium-induced hepatomegaly. Co-treatment with *S. jollyanum* in Groups E and F significantly reduced HSI toward normal, more markedly in Group F, indicating a protective effect in proportion to dose. This further underscores the hepato-modulatory potential of the extract.

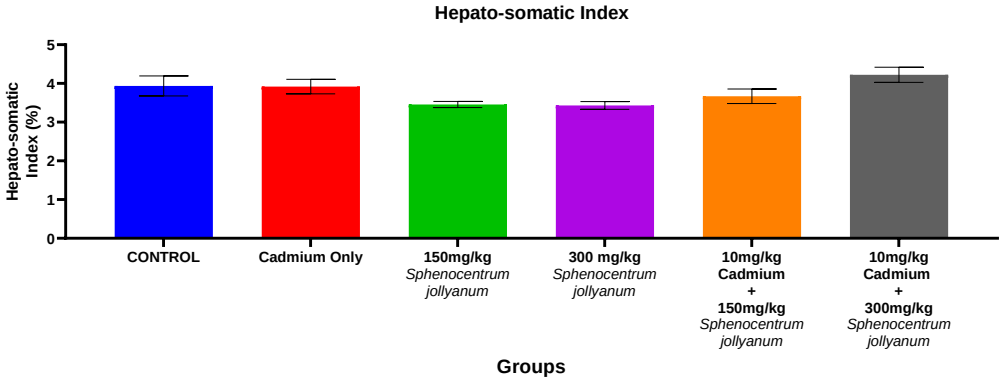

Chart 4: Hepato-somatic index after 28 days of administration. Values are given as mean ± SEM.

3.1.5 Histological Analysis (Plates 1–12)

Microscopic examination of liver tissues revealed striking differences among the groups:

- Normal Control (Plates 1 & 2): Exhibited normal liver architecture with intact hepatocytes, clear sinusoidal spaces, and distinct hepatic triads (portal vein, bile ducts, and hepatic artery).
- Cadmium Only (Plates 3 & 4): Showed severe liver damage, including zonal necrosis, extensive vasodilatation, congestion, and dense periportal inflammatory infiltrates, consistent with chemical-induced hepatotoxicity and inflammation.
- Extract Only (Plates 5, 6, 7 & 8): At 150 mg/kg, mild portal vasodilatation and congestion were observed, possibly due to increased metabolic activity or adaptive responses. At 300 mg/kg, liver architecture remained largely normal, although periportal lymphocyte mobilization suggested mild immunomodulatory activity without pathological damage.
- Cadmium + 150 mg/kg Extract (Plates 9 & 10): Demonstrated restoration of normal hepatocytes with mobilization of Kupffer cells, indicative of immunological response and tissue repair. This suggests moderate protection from cadmium toxicity.
- Cadmium + 300 mg/kg Extract (Plates 11 & 12): Still showed some vascular congestion and periportal infiltration, but significantly less necrosis than the cadmium-only group. This indicates better preservation of liver structure at higher extract doses, though not complete reversal of injury.

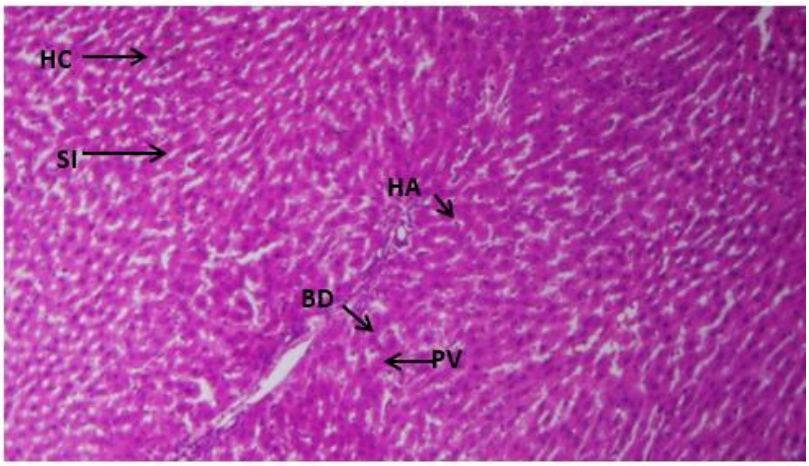

Plate 1: Sections of liver from control show: normal hepatocytes (HC), sinusoids containing Kupffer cells (SI), portal vein (PV), bile ducts (BD) and hepatic artery (HA): H&E 100x

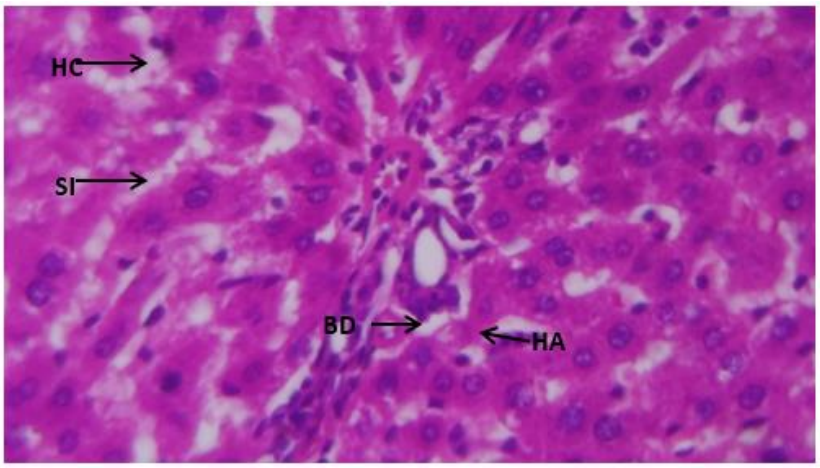

Plate 2: Sections of liver from control show: normal hepatocytes (HC), sinusoids containing Kupffer cells (SI), portal vein (PV), bile ducts (BD) and hepatic artery (HA): H&E 400x

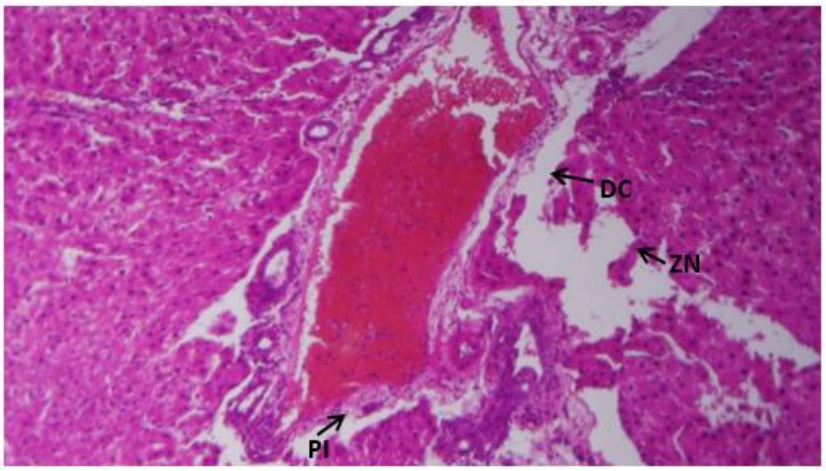

Plate 3: Sections from rats given Cadmium only show: zonal necrosis (ZN), severe vasodilatation and congestion (DC), heavy periportal infiltrates of inflammation (PI): H&E 100x

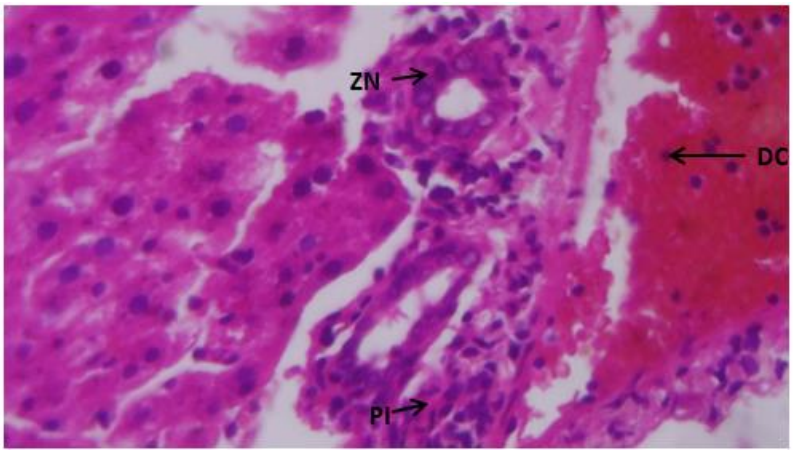

Plate 4: Sections from rats given Cadmium only show: zonal necrosis (ZN), severe vasodilatation and congestion (DC), heavy periportal infiltrates of inflammation (PI): H&E 400x

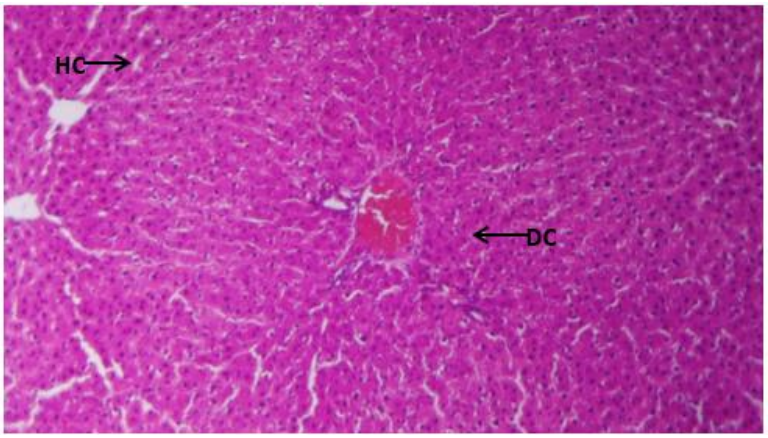

Plate 5: Sections of liver from rats given 150mg extract only show: normal hepatocytes (HC), portal vasodilatation and active congestion (DC): H&E 100x

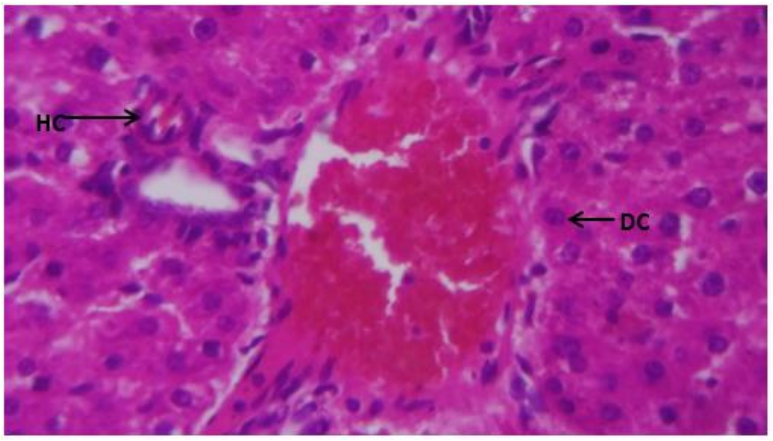

Plate 6: Sections of liver from rats given 150mg extract only show: normal hepatocytes (HC), portal vasodilatation and active congestion (DC): H&E 400x

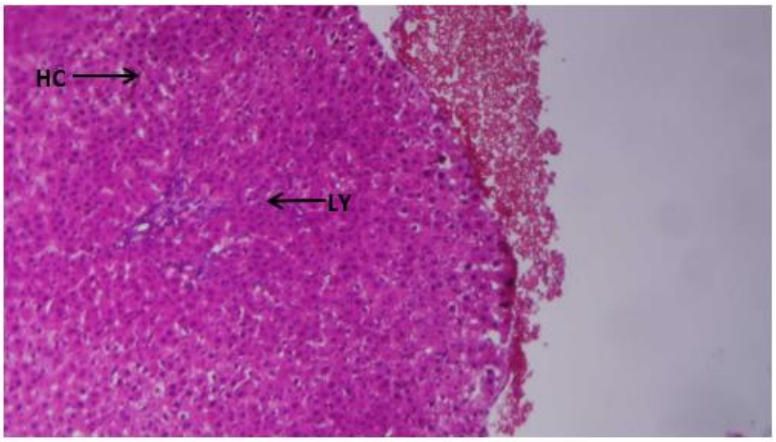

Plate 7: Sections from rats given 300mg extract only show: normal hepatocytes (HC): periportal mobilization of lymphocytes (LY): H&E 100x

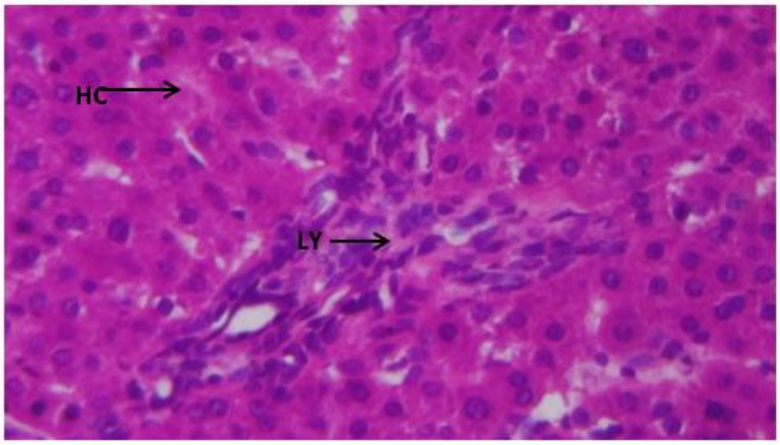

Plate 8: Sections from rats given 300mg extract only show: normal hepatocytes (HC): periportal mobilization of lymphocytes (LY): H&E 400x

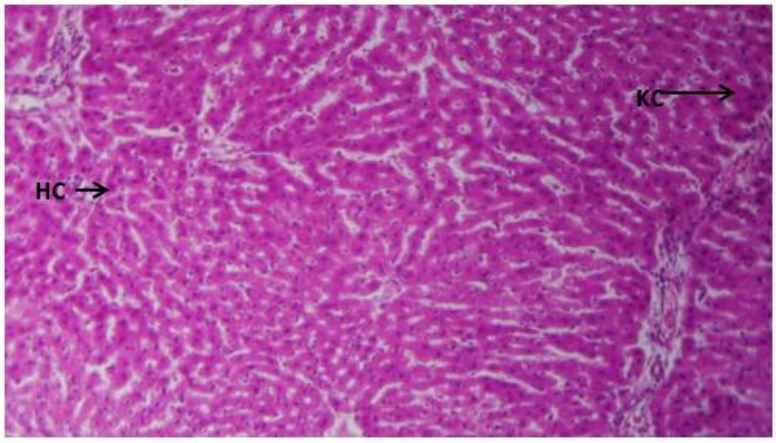

Plate 9: Sections from rats given Cadmium + 150mg extract show: normal hepatocytes (HC), sinusoidal mobilization of Kupffer cells (KC): H&E 100x

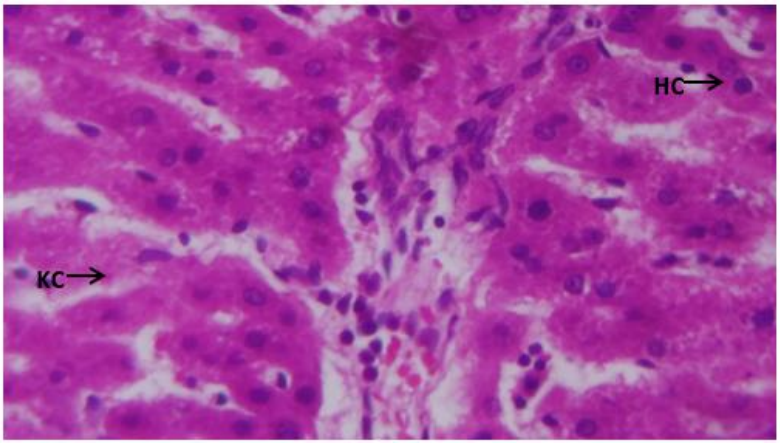

Plate 10: Sections from rats given Cadmium + 150mg extract show: normal hepatocytes (HC), sinusoidal mobilization of Kupffer cells (KC): H&E 400x

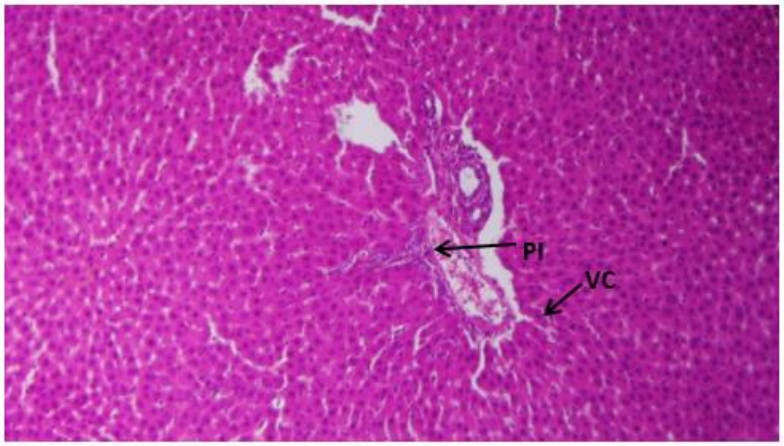

Plate 11: Sections from rats given Cadmium + 300mg extract show: vascular congestion (VC), periportal infiltrates of inflammatory cell (PI): H&E 100x

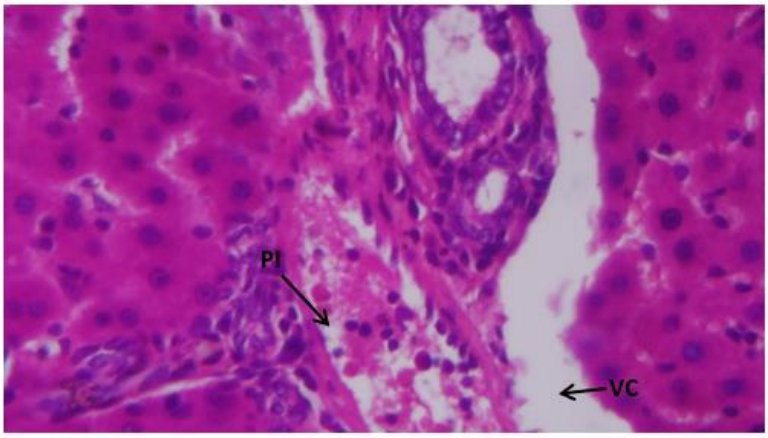

Plate 12: Sections from rats given Cadmium + 300mg extract show: vascular congestion (VC), periportal infiltrates of inflammatory cells (PI: H&E 400x.

4. Discussion

Heavy metal toxicity, particularly from cadmium, remains a critical concern due to its widespread environmental presence and detrimental effects on multiple organs, especially the liver (Innih, et al., 2021). The liver, being a central organ for detoxification and metabolism, is especially susceptible to damage from toxicants such as cadmium chloride (Mead, 2009). This study evaluated the hepatoprotective potential of *Sphenocentrum jollyanum* (S. jollyanum) extract against cadmium-induced liver toxicity in Wistar rats by assessing physical and histological parameters.

The findings from this study revealed that cadmium chloride administration (10 mg/kg) significantly impacted the overall health of the rats, as reflected in decreased weight gain, increased liver weight, elevated hepatosomatic index (HSI), and severe histological alterations. These changes affirm the hepatotoxic potential of cadmium, which is known to generate oxidative stress, disrupt mitochondrial function, and trigger inflammatory and apoptotic pathways within hepatic cells (Branca et al., 2020). The observed zonal necrosis, vascular congestion, and dense periportal inflammatory infiltration in the liver sections of cadmium-treated rats further corroborate these mechanisms of toxicity. Similar findings were reported by liver who observed liver weight gain and histopathological derangements in cadmium-exposed animals due to lipid peroxidation and cellular membrane damage (Innih, et al., 2021; Noor et al., 2022).

Conversely, rats treated with *S. jollyanum* extract alone (150 mg/kg and 300 mg/kg) did not exhibit any adverse changes in weight, liver morphology, or histoarchitecture. The hepatocytes remained structurally intact, with minor physiological alterations such as mild portal vasodilatation and periportal lymphocyte mobilization, which may indicate increased hepatic activity or mild immunomodulatory effects. These findings suggest that *S. jollyanum* extract is safe and non-toxic at the administered doses, supporting earlier reports who confirmed the non-toxic nature and organ-protective properties of *S. jollyanum* in animal models (Olorunnisola, et al., 2021).

Importantly, co-administration of *S. jollyanum* extract with cadmium chloride significantly mitigated the toxic effects of cadmium. This was evidenced by improved body weight gain in the co-treated groups (Groups E and F), an indicator of systemic recovery and reduced metabolic stress. The group treated with the higher dose of the extract (300 mg/kg) showed a better recovery profile than the 150 mg/kg group, highlighting a dose-dependent protective effect. These observations are in agreement with the findings of, who reported improved weight profiles and liver function in cadmium-exposed rats treated with antioxidant-rich plant extracts like *Curcuma longa* and *Moringa oleifera* (Toppo et al., 2015; Boulanouar, et al., 2023).

Liver weight and hepatosomatic index, which are markers of hepatic inflammation and hypertrophy, were significantly elevated in cadmium-only treated rats. These parameters were considerably normalized in the co-treated groups, especially in Group F (cadmium + 300 mg/kg extract), indicating that the extract may have reduced hepatic inflammation and/or swelling. A comparable trend was reported, where administration of *Panax ginseng* reversed cadmium-induced liver weight changes and restored normal histology through its antioxidant and hepatoregulatory effects (Kim, 2016).

The protective effects of *S. jollyanum* could be attributed to its reported phytochemical constituents, including flavonoids, alkaloids, terpenoids, and saponins, which possess strong antioxidant and anti-inflammatory properties. These compounds likely counteracted the oxidative damage and inflammatory cascade initiated by cadmium. Studies by researchers support this notion, highlighting the antioxidant-rich profile of Nigerian medicinal plants as crucial in combating xenobiotic-induced organ injury (Aiwonegbe et al., 2022; Vicidomini et al., 2024).

Histological examination provided further insight into the protective role of *S. jollyanum*. Liver sections from cadmium-only treated rats revealed extensive tissue injury, including zonal necrosis, dilated sinusoids, vascular congestion, and periportal inflammation, all hallmark features of cadmium-induced hepatocellular damage. These are consistent with histopathological findings described by liver in cadmium chloride models (Innih, et al., 2021; Noor et al., 2022). In contrast, liver sections from rats co-treated with *S. jollyanum* extract showed near-normal architecture with reduced inflammatory infiltrates and restoration of hepatocellular integrity. Kupffer cell mobilization observed in the 150 mg/kg co-treatment group suggests activation of hepatic innate immune responses, which may aid in tissue repair and clearance of toxic debris. Similar Kupffer cell responses were reported in studies involving heavy metal exposure and plant extract intervention (Diab et al., 2020).

These results align with previous studies on medicinal plants with antioxidant capacities that mitigate cadmium toxicity. The antioxidant mechanism of *S. jollyanum* may involve scavenging of reactive oxygen species (ROS), chelation of cadmium ions, inhibition of lipid peroxidation, and upregulation of endogenous antioxidant enzymes such as superoxide dismutase (SOD) and catalase (Zandi and Schnug, 2022). Moreover, the anti-inflammatory activity of the extract could contribute to the suppression of pro-inflammatory cytokines and subsequent reduction in hepatic inflammation and necrosis. This corroborates the mechanistic insights provided that regarding herbal formulations used in managing heavy metal poisoning (Gupta et al., 2024).

The findings of this study contribute to the growing body of evidence supporting the therapeutic potential of *S. jollyanum*, particularly in the context of toxicant-induced organ damage. While the results are promising, it is important to note that this study focused on short-term (28-day) exposure and treatment. Long-term studies evaluating chronic toxicity, detailed biochemical analysis of liver function enzymes (ALT, AST, ALP), oxidative stress biomarkers, and molecular pathways would provide a more comprehensive understanding of the extract's hepatoprotective mechanisms.

5. Conclusion

In conclusion, this study demonstrates that *Sphenocentrum jollyanum* possesses significant hepatoprotective activity against cadmium-induced liver damage in Wistar rats. Its ability to improve body weight, normalize liver morphology, and restore hepatic histoarchitecture suggests that it can be a potential candidate for managing heavy metal-induced hepatic toxicity. Further studies are recommended to explore its underlying molecular mechanisms and potential applications in clinical toxicology.

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