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ACUTE AND SUB-CHRONIC NEPHROTOXICITY STUDY ON ORALLY ADMINISTERED LEAF EXTRACT OF *SPONDIAS MOMBIN* IN MALE WISTAR ALBINO RAT

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ABSTRACT

Introduction: *Spondias mombin* has been reported to possess medicinal properties. **Method:** The preliminary phytochemical analysis was determined by the method described by Harbone 1973 and sofowora, 1982 and the Lethal dose was carried out and median lethal dose was calculated using modified method of Lorke (1983). Twenty five (25) apparently healthy female albino rats aged seven weeks weighing between 76-91g were randomly divided into 5 groups of 5 animals each. Group I served as control, while groups 2, 3, 4 and 5 received the aqueous leaf extract at 200,400,600 and 800 mg/kg body weight respectively. **Results:** Phytochemical constituent of *Spondias mombin* was Evaluated and the effects of aqueous leaf extract on some biochemical parameters in albino rats studied. Acute toxicity studies showed that the extract was safe at 500mg/kg body weight dose to albino rats. The results showed that liver enzymes ALT, AST and ALP increased significantly ($p<0.05$) compared to control. Total Bilirubin decreased while conjugated bilibrubin increased significantly ($p<0.05$). There were significant decrease in Lipid profile test, Cholesterol, triglyceride and Low density lipoprotein as concentration of extract administered increased from 400 mg/kg body weight while high density lipoprotein increased. Erythrocyte, hemoglobin, Leukocyte and hematocrit increased significantly ($p<0.05$). Potassium and calcium ion decreased, while Chloride increased non-significantly as Sodium concentration was not affected. These effects were dose dependent. Urea, total protein and Albumin significantly reduced ($p<0.05$) while

creatinine increased significantly. Phytochemicals present include flavonoids, alkaloids, tannin, glycosides, steroids and terpenes. Histological studies showed alterations in the architecture of the liver, kidney as the dose of extract administered increased from 400 to 800mg/kg body weight. **Conclusion**: This study has shown that the extract is safe only when administered at 200mg/kg body weight and below.

INTRODUCTION

Plants have played a major role in health care system irrespective of advance development in modern medicine. These medicinal plants are distributed worldwide, especially in tropical regions. Pharmaceutical companies have demonstrated interest in the investigation of these plants as sources for new lead structures and new development of phytotherapeutic agents with proven efficacy, safety and quality.

These plants have been in use for the treatment of man and animal diseases since prehistoric time (Ayoka*et al*., 2008).

Spondias mombin Linn belongs to the family *Anacardiacae*. It grows in the rain forest and in the coastal area. It can grow to a height of 15 – 22m.

The trunk has deep incisions in the bark, which often produces a brown resinous substance. The leaves and the flowers are at the end of the branches. Before the tree starts to flower, it strips itself from most of the leaves. The fruit, an 1½- inch long oval yellow plum, has a leathery skin and a thin layer of fruit pulp with a very exotic taste. It hangs in numerous clusters of more than a dozen on the tree. Very rich in vitamins B_1 and C, the fruit mostly exists as an oval seed. The mode of propagation of the plant is by seeds and cuttings. Other common names, according to Morton (1987) are; Bala (Costa Rica), Jobito (Panama), Joboblanco (Colombia), Jobocorronchoso (Venezuela), Hoeboe (Surinam), Acaiba, Caja, Pau da tapera (Brazil), Ubo (Peru), Hobo (Mexico), Iyeye (Yoruba), Uvuru (Igbo).

The plant is occasionally large, tree, with long compound leaves, each leaf has an odd number of leaflets, from 9 – 19. Usually, the leaves are alternate, but bunched towards the end of the branches, emanating like spokes of a wheel in all directions from the branch. The leaflets are opposite except for the terminal ones. Particularly on young plants, the leaf stalk tends to be reddish towards the outer leaflets. Crushed leaves have faint turpentine-like smell.

The chemistries of this pant has been reported (Shultes and Raffauf, 1990). Kramer *et al*. (2006), recommended its use for pregnant woman but only after five months of pregnancy. The results indicate that the cytotoxic effects of the plant may have some benefits in protecting the foetus from foreign pathogens. High level of cytotoxicity is a good indicator of analgesic properties. The use of this plant for pain ease during childbirth support this evidence (Kramer *et al*., 2006). This work is aimed at looking at the toxicological effect of this plant.

MATERIAL AND METHODS

Plant Materials and preparation of Extracts collection of Plant LEAVES

Leaves of *Spondias mombin* (Uvuru) were obtained from Ihie in Isiala Ngwa North LG.A, Abia State. The plant was identified and authenticated at the department of Plant Sciences and Biotechnology, Abia State University, Uturu, Nigeria.

Preparation of plant leaf extract of *Spondia mombin*

The plant leaves were washed with distilled water to remove dirt and contaminants. The leaves were dried under the sun to a fine powder. Two hundred (200 g) of the powdered leaf sample was soaked in 1000 ml of distilled water and allowed to stand for 48 hours with occasional stirring to allow for proper extraction (Trease and Evans, 2002). 1ml of the filtrate was pipetted into a pre-weighed 100cm^3 beaker and evaporated to dryness on a boiling water bath. The beaker was cooled and weighed again and the concentration was determined to be 70ml.

Measurement of Body WEIGHT OF THE ANIMALS

Body weight of animals was measured on days 0, 7,14, 21, and 28. Body weight of animals noted was expressed as mean body weight (g).

Experimental Designs

Twenty five (25) male albino rats of the same stock were obtained from the animal house of Abia State University, Uturu. The animals were taken to the laboratory where they were housed in plastic cages and placed on commercial feeds bought from the local market as produced by Nigeria Flour Mills, and were allowed food and water *ad libitum*. The albino rats were randomly divided into five groups of five animals each. **Group 2**: Received *Spondias mombin* leaf extract (200 mg/kg b.w), **Group 3**: Received *Spondia mombin*leaf

extract (400 mg/kg b.w), **Group 4:** Received*Spondia mombin* leaf extract (600mg/kg b.w) and **Group 5:** Received *Spondias mombin* leaf extract at (800 mg/kg b.w).

Determination of Acute Toxicity

Lethal dose was carried out and median lethal dose was calculated using modified method of Lorke (1983). In the first phase, three groups of four mice each were administered with the extract at respective oral doses of 10mg, 100mg, and 1000mg per kg body weight. The mice were observed for signs of toxicity and possible deaths for 24 hr. In the second phase, another three groups of 4 mice each were administered respective doses of 1500, 2900 and 5000mg per kg body weight of the erxtract. They were equally monitored as in phase one for toxicity signs and deaths. From data obtained, LD_{50} was determined.

Liver function indices

The serum activities of alanine aminotransferase (ALT; EC 2.6.1.1), aspartate aminotransferase (AST; EC 2.6.1.2) and alkaline phosphatase (ALP; EC 3.1.3.1), as well as the serum concentrations of total bilirubin, conjugated bilirubin, total protein and albumin were determined (Balistreri and Shaw,1987) using standard kits (Human Laboratories, Germany). The unconjugated bilirubin concentration was calculated as the difference between total and conjugated bilirubin concentrations.

Evaluation of the Haematological Parameters

Blood samples were collected from the animals by cardiac puncture into ethylenediaminetetraaceticacid (EDTA) bottles. The following haematological parameters; packed cell volume (PCV), white blood cells (WBC), neutrophil (N), eosinophil (E), lymphocyte (L) and monocyte (M) and platelets were evaluated using methods of Dacie and Lewis (1984).

Histopathology

The liver and kidney, of all the animals were removed from the animals and fixed in 10% buffered formalin in labeled bottles. Tissues were processed routinely and embedded in paraffin wax. Sections of 5 µ thickness were cut, stained with haematoxylin and eosin and examined under the light microscope.

Statistical Analysis

The results were subjected to statistical analysis using Analysis of Variance (ANOVA). Group means will be compared for significance at $p<0.05$.UsingDuncans multiple range tests data will be represented as mean ± standard deviation.

RESULTS

Table 1: Body Weight of animals before and administration of extract (g)

Groups n=5	Body weight before Experiment.	Body weight after extract administration (after 28 days)
Group 1	91.517 ± 8.565^{a}	98.550 ± 6.647^{b}
Group 2	85.883 ± 12.439^{a}	74.933 ± 12.315^{a}
Group 3	76.950 ± 3.532^{a}	110.100 ± 8.92^{c}
Group 4	85.567 ± 6.290^{a}	88.95 ± 12.065^{b}
Group 5	87.933 ± 10.999^{a}	96.133 ± 14.721^{b}

Oral administration of aqueous leaf extract of *Spondias mombiin* from 400 to 5000 mg/kg did not produce any toxicity on albino rat. Mortality was not recorded throughout the duration of this study. No death was recorded at all doses at the end of the 24 hours of study. This indicates that the LD_{50} is far above 500 mg/kg body weight.

Table 2: Acute Toxicity Test (LD_{50}) of Aqueous Leaf Extract of *Spondias mombin.*

GROUP OF RATS	DOSE(mg/kg)	NUMBER OF DEATHS RECORDED/ MOTALITY
1	400	NIL
2	800	NIL
3	1600	NIL
4	2500	NIL
5	5000	NIL

Value are Mean ± SD, of Triplicate determination. Values in the column (groups) with different superscripts are significantly different at ($p<0.05$) Mean in the column having different alphabet are statistical significant ($p< 0.05$).

Group 1 (control) showed increase in body weight from 91.517 ± 8.565 to 98.550 ± 6.647 after 28 days of treatment with extract while group 2 showed significant decrease in weight from 85.883 to 74.933, while groups 3,4 and 5 showed no significant ($p<0.05$) increase in body weight. The aqueous leaf extract of *Spondias mombin m*ay have caused the increase as seen in table 2, as the dose administered increased, body weight increase is affected, but not significantly.

Table 3: Preliminary Phytochemical Screening of Aqueous leaf Extract of *Spondias mombin*.

S/N	Phytochemical	Relative Presence in leave extract
1.	Tannin	+++
2.	Flavonoids	+++
3.	Glycosides	++
4.	Alkaloid	++
5.	Steroid	++
6.	Terpenoids	+++

KEY:

+++ Present in very high concentration

++ Present in moderate concentration

Preliminary phytochemical evaluation of aqueous leaf extract of *Spodias mombin* shows the presences of Tannin, Flavonoids, Glycosides, Alkaloid, Steroid and Terpenoids.Tannin, Flavonoids and Terpenoids were present in higher concentration compared to Glycosides, alkaloids and Steroids.

TABLE 4: EFFECTS OF AQUEOUS LEAF EXTRACTS *Spodias mombin* LIVER ENZYMES

Groups	ALT(IU/L)	AST(IU/L)	ALP(IU/L)	TOTAL BILIRUBIN (mg/dl)	CONJUGATE DBILIRUBIN (mg/dl)
Group 1	18.87 ± 0.31^{a}	20.12 ± 0.42^{a}	24.25 ± 9.09^{a}	0.540 ± 0.008^{c}	0.143 ± 0.013^{a}
Group 2	18.23 ± 0.14^{b}	20.79 ± 0.65^{b}	31.13 ± 7.34^{b}	0.520 ± 0.008^{c}	0.170 ± 0.04^{a}
Group 3	19.19 ± 0.23^{c}	23.36 ± 0.46^{c}	35.53 ± 1.61^{c}	0.500 ± 0.014^{b}	0.160 ± 0.000^{a}
Group 4	21.00 ± 0.13^{d}	36.90 ± 0.46^{d}	37.17 ± 20.70^{d}	0.485 ± 0.021^{b}	0.170 ± 0.000^{a}
Group 5	29.00 ± 0.13^{e}	42.49 ± 0.30^{e}	39.34 ± 3.38^{e}	0.468 ± 0.015^{a}	0.173 ± 0.005^{a}

Values are Mean $\pm$ SD of Triplicate determination. Values in the Colum (group) with different superscripts are significantly different ($p<0.05$)

Legend: AST = Asparate Aminotransferase

ALT = Alanine Aminotransferase

ALP = Alkaline Phosphatase

U/L = Unit per litre

ALT,AST and ALP values showed significantly ($p<0.05$) increase as dose administered exceeded 200mg/kg body weight. It was observed that as the dose administed to animals increased from 300 mg/kg body weight there was a significantly increase in ALT, AST and ALP were observed. This implies that above 200mg/kg body weight dose, the extract

becomes toxic to the animals. Total Bilirubin was not affected by the extract, but Conjugated Bilirubin increased significantly. Bilirubin is associated with serum albumin and transported to the liver where it is conjugated by Glucuronic acid to form Bilirubin Dylucuonide (Conjugated Bilirubin). The conjugated Bilirubin is soluble and then excreted into the bile.

Table 6: Effect of *Spondia mombin* leaf extract on the hematological parameters.

Treatment	Erythrocyte (10^3/µl)	Leukocyte (10^3/µl)	Hemoglobin (g/dl)	Haematocrit (%)
Group 1	7.01 ± 0.32^{d}	19.58 ± 3.40^{d}	10.61 ± 0.60^{a}	45.78 ± 2.64^{b}
Group 2	8.05 ± 0.16^{c}	20.24 ± 2.61^{b}	14.82 ± 0.24^{b}	47.92 ± 0.80^{c}
Group 3	8.10 ± 0.10^{b}	21.24 ± 2.50^{b}	16.12 ± 0.20^{c}	48.80 ± 0.85^{d}
Group 4	9.00 ± 0.15^{a}	25.02 ± 2.41^{a}	17.00 ± 0.21^{c}	5.00 ± 0.87^{a}
Group 5	9.06 ± 0.20^{a}	26.32 ± 1.50^{a}	20.00 ± 0.30^{d}	5.10 ± 0.90^{a}

Value are Mean ± SD, Mean along the column (groups) with different alphebatical superscript indicates a significant different ($p<0.05$).

There were significant improvement in hematological parameters of animal fed with of aqueous extract of *Spondias mombin* from group 1-4 when compared with the control. The hematological parameters Erythrocyte, leukocyte, hemoglobin and hematocrite measured all showed significant increase as dose of extract administered increased significantly ($p<0.05$).

The phytochemical analysis of *Spondais mombin* leaves revealed the presence of Saponins, Alkaloids, Tannins and Flavoniods. The leaves revealed high presence of Flavonoids, saponins, alkaloid, Tannins and cyanogenic glycosides. The presence of flavoniods may attribute to the anti-inflammation properties reported by Corthout *et al*., 1999, and flavoniods are known to protect against allergies. Flavonoids have been identified in *Spondia mombin* plant with anti-herpes, antioxidant and anti-aging properties (Corthout *et al*., 1999). It has also been reported by Njoku and Akumefula, 2007 that flavonoid exhibits free radical scavenging property, super antioxidants and with strong anticancer activity, also provide anti-inflammatory activity potentials. May have contributed to its usage in treatment of intestinal diseases in ethnomedicine (Okwu and Okwu,2004). Alkaloids are of therapeutic significance. Pure isolated alkaloids and the synthetic derivative used as the basic medicinal agents due to their Analgesic antispasmodic and antibacterial potentials (Stray, 1998).

Alkaloids are beneficial chemicals to plants. Alkaloids such as ergot alkaloids have been reported to elicit uterine muscles activity. This could be the reason for the use of the plant

locally to aid self delivery in goat (Esterbauer *et al*.,1991). The study show high presence of tannins; Tannins are known to improve wound healing and inflamed mucus membrane (Njoku and Akumefula, 2007). Finding from this work shows increase of high presence of tannins, this is in consonance with the report of Ayoka *et al.,* 2008 who reported high tannins in this plant. The wound healing properties ascribed to *S. mombin* may be as a result of the high tannin content. The result of the preliminary phytochemical analysis of present study may give credence to its ethonomedicinal usage.

The acute toxicity test carried out did not show any toxicity by aqueous extract of *Spondias mombin* leaf on albino rats. Mortality was not recorded throughout the duration of this study even when the extract was administered up to 5,000 mg/kg. This implies that the oral LD_{50} of *Spondias mombin* aqueous leaf extract is greater than 5000 mg/kg body weight for the rat. This shows that the extract is safe as a pharmacological agent (Akhila *et al*., 2007). Moreover there was a significant ($p<0.05$) increase in the body weight of treated rats when compared to that to the initial body weight before experiment. The significant progressive increase in body weight at doses 200 mg/kg, 400 mg/kg, 600 mg/kg and 800 mg/kg of rats during 28 days oral administration of the extract probably reflect the nutritional status of the animals, which is a clear indication that the extract did not affect the nutritional state of the treated animals.

Analysis of the activities of basic liver function enzymes in serum are used to indirectly access the integrity of tissue after exposure to pharmacological agents (Uboh *et al*., 2010). ALT, ALT and ALP are important liver marker enzymes that are associated to the hepatocellular damage, having ALT more specific. ALP involves in the transport of metabolite across cell membranes involved in protein synthesis and glycogen metabolism (Tokumitsu and Fishman, 1983) and is useful in diagnosing hepatobiliary or cholestatic obstruction (Johnson and Fody, 1992). Serum levels of ALT, AST and ALP were altered by aqueous extracts of *Spodias mombin w*hen compared with the control group. The increase was pronounced in group 5, which received 800 mg/kg when compared with the group that received 200 mg/kg. This suggests that there is a compromise on the integrity of the liver indicating dose dependent hepatotoxicity. Also there was overall reduction in the concentration of total bilirubin, which indicated the xenebiotic conjugation and excretive potentials of the organ were not affected by the administration of the extract at Group 3-5. However serum conjugated bilirubin level increased in all groups when compared with the control significant at ($p<0.05$), indicating impaired hepatic excretory function; although a significant decrease in total bilirubin was observed.

Furthermore, the extract elicited dose dependent decreases in serum total protein and albumin concentration. The liver is known as the site for synthesis of albumin which makes up approximately 60% of serum protein concentration. The observed decreases in total protein and albumin concentration of the hepatocytes shows that the liver was impaired. The decreased synthesis of albumin may also have contributed in the reduction in overall unconjugated bilirubin since it is the sole transporter of this water insoluble byproduct of haemoglobin metabolism to the liver. The significant ($p<0.05$) reduction in albumin, total protein and total bilirubin shows liver damage arising from the administration of the aqueous leaf extract. This may be an indication of diminished synthetic function of the liver which may lead to enhanced retention of fluid in the tissue spaces (Yakubu *et al*., 2006).

Thus it may be claimed that the extract may prevent hepatic cell destruction, which is usually marked by an increase in blood aminotransferases activities, increased bilirubin concentration and reduction in serum protein and albumin concentration (Igwe *et al.*, 2010).

Defective haematopoiesis is indicated by reduction in erythrocytes number and haemoglobin content, however, in this study, there was no indication of anaemia from the levels of haemoglobin found. Haemoglobin is known to be a protein used by red blood cells to distribute oxygen to other tissues and cells in the body (Choudhari and Deshmukh, 2007). The significant increase in haematocrit in the study may be indicative of the normal functioning of the bone marrow in the process of erthropoeisis. The histopathology of kidney shows normal renal histo-architecture, Glomeruli, Renal tubules, Blood vessels and Bowman's capsule from 200 mg/kg to 600 mg/kg. Sections of the kidney from group 5 which was administered the highest dose of the extract showed changes consistent with renotoxicity. Normal structures of the glomeruli and Bowman's capsules were observed. However, the renal tubules in both the cortex and outer medulla showed varying degenerative and necrotic changes in the tubular epithelial lining cells. The lesions were randomly observed affecting all the proximal convoluted tubules, pars recta and distal convoluted tubules of the cortex and outer medulla while the collecting ducts appeared normal. The changes varied from cellular swelling and vacuolar degeneration to cellular necrosis with nuclear pyknosis and/or karyorrhexis. The basement membranes of the renal tubules were unaffected.

The histopathology sections of the liver collected from groups 1 to 4 did not show any alteration from the normal hepatic histo-architecture of laboratory rodents. The sections showed normal hepatic lobules consisting of normal hepatocytes arranged in interconnecting

chords, in a radiating manner around the central veins. The hepatic chords are separated by the hepatic sinusoids and radiate towards the periphery of the hepatic lobules where they join the portal triads which are made up of normal hepatic artery, hepatic vein and bile ducts.

The group that was administered the higher dose shows a mild to moderate, widespread vacuolar degeneration of the hepatocytes (arrow). The hepatocytes appear slightly swollen and contain numerous minute vesicles (clear spaces) in their cytoplasms.

Sections of the liver collected from the animals in group 5 which was treated with the highest dose of the test extract showed changes consistent with hepatotoxicity. Mild to moderate cellular swelling were observed, involving all the described anatomic zones of the hepatic lobule (centrilobular, mid-zonal and periportal zones). The hepatic chords consisted of hepatocytes with swollen, micro-vessiculated cytoplasm. The swollen hepatocytes tend to occlude the hepatic sinusoids.

HISTOPATHOLOGY RESULTS

KIDNEY

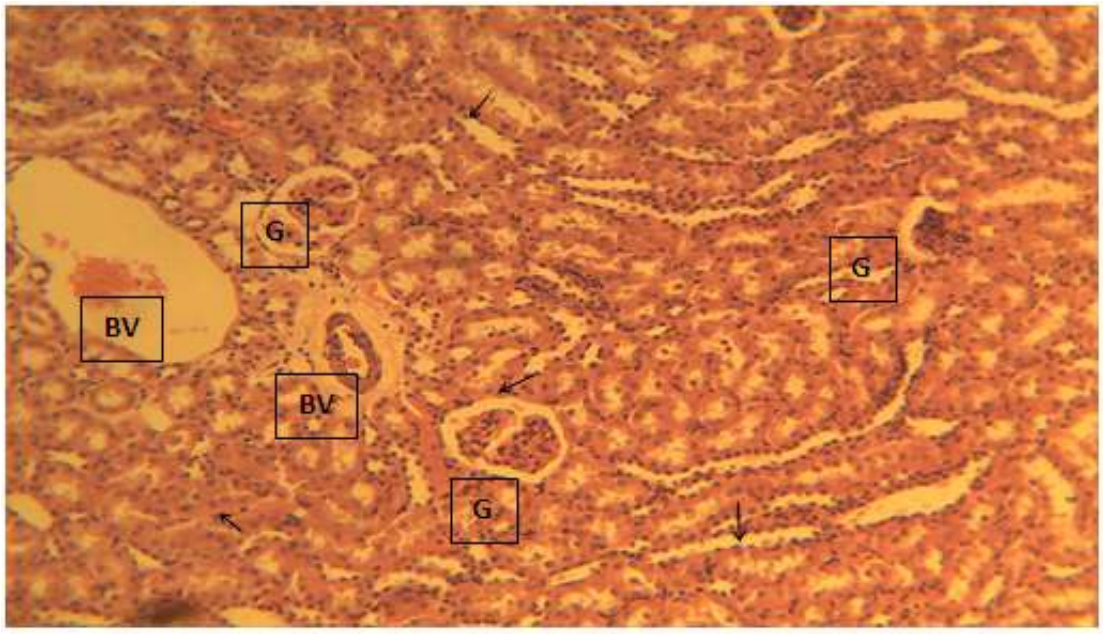

Plate 1: Photomicrograph of the kidney group 1(Control) showing the normal renal histo-architecture. Glomeruli (G); Renal tubules (arrow), Blood vessels (BV). H&Ex100.

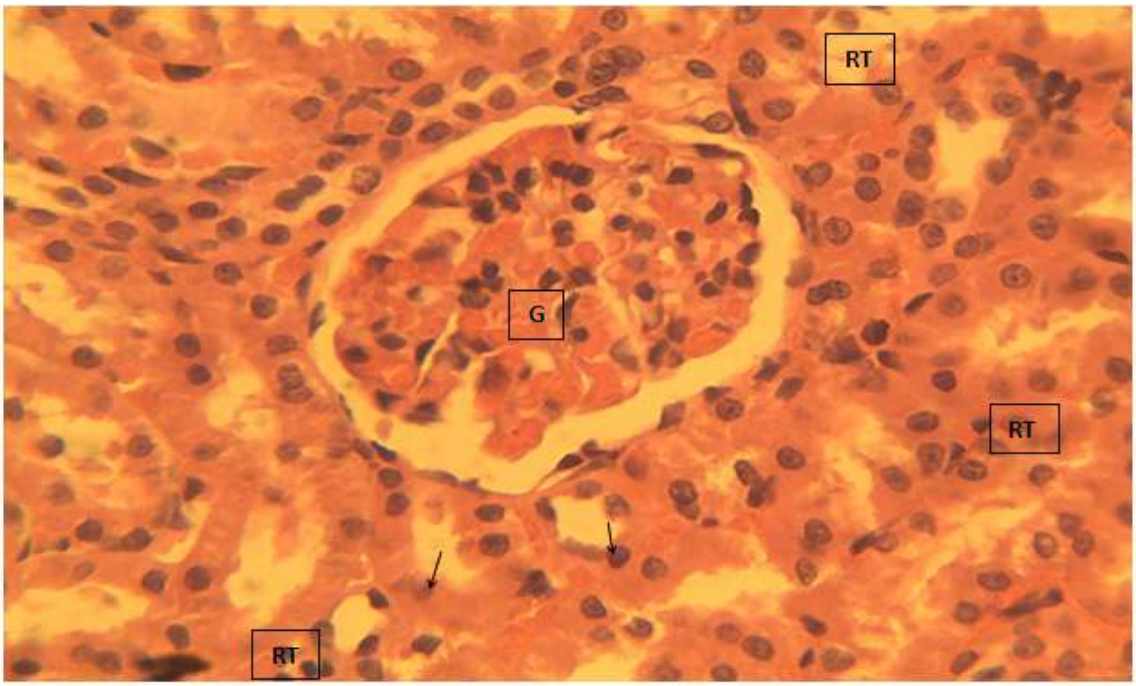

Plate 2: Photomicrograph of the kidney collected from the animals in group 2 showing the normal renal histo-architecture. Glomeruli (G); Renal tubules (RT), Bowman's capsule (arrow). H&Ex400.

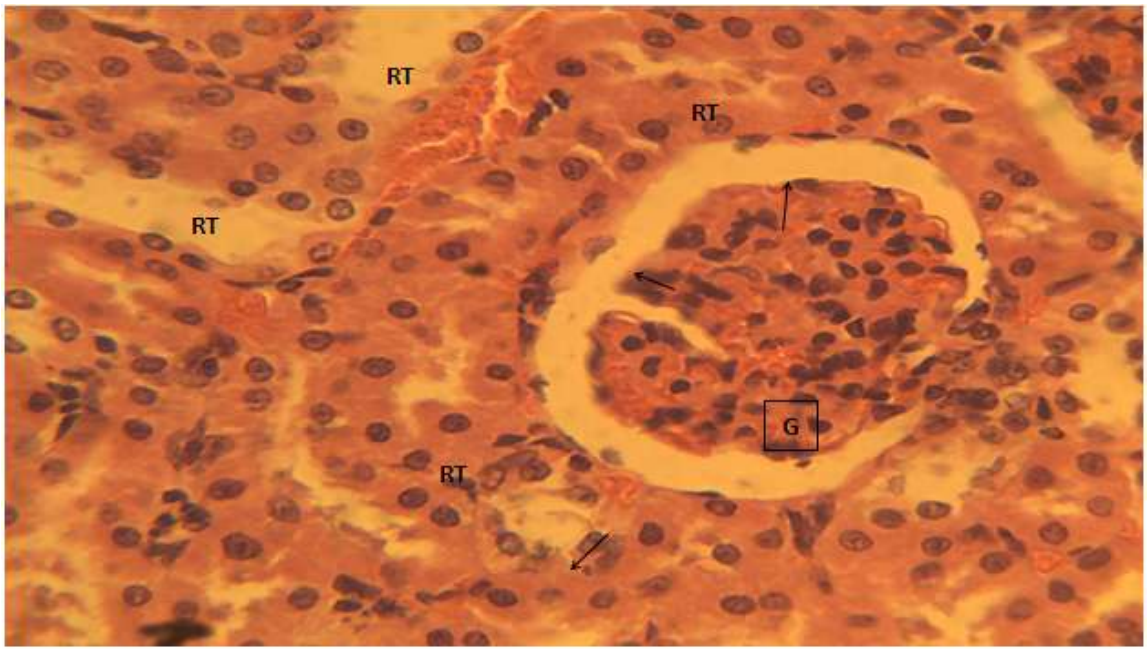

Plate 3: Photomicrograph of the kidney tissue collected from the animals in group 3 showing the normal renal histo-architecture. Glomeruli (G); Renal tubules (RT), Bowman's capsule (arrow). H&Ex400.

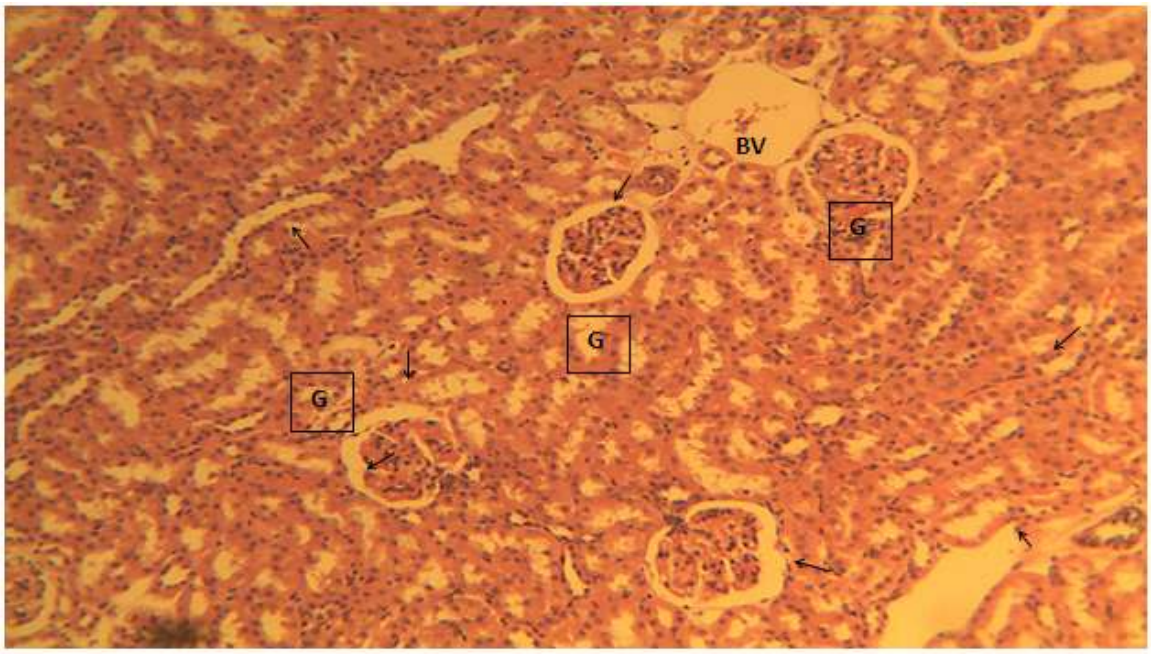

Plate 4: Photomicrograph of the kidney tissue collected from the animals in group 3 showing the normal renal histo-architecture. Glomeruli (G); Renal tubules (arrow), Blood vessel (BV). H&Ex100.

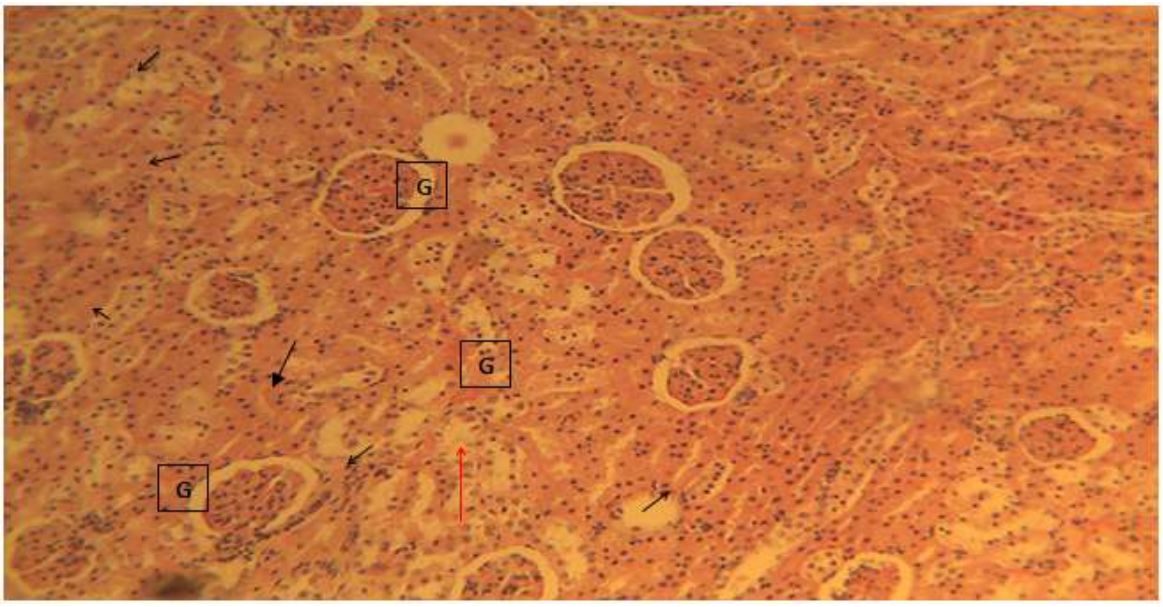

Plate 5: Section of the kidney tissue collected from group 5 showing numerous renal tubules of the cortex undergoing degenerative and necrotic changes (arrow). Glomeruli (G).Pyknotic nucleus (red arrow).H&Ex100;400.

Sections of the kidney from **group 5** which was administered the highest dose of the extract showed changes consistent with renotoxicity. Normal structures of the glomeruli and Bowman's capsules were observed. However, the renal tubules in both the cortex and outer

medulla showed varying degenerative and necrotic changes in the tubular epithelial lining cells. The lesions was randomly observed affecting all the proximal convoluted tubules, pars recta and distal convoluted tubules of the cortex and outer medulla while the collecting ducts appeared normal. The changes varied from cellular swelling and vacuolar degeneration to cellular necrosis with nuclear pyknosis and/or karyorrhexis. The basement membranes of the renal tubules were unaffected.

LIVER

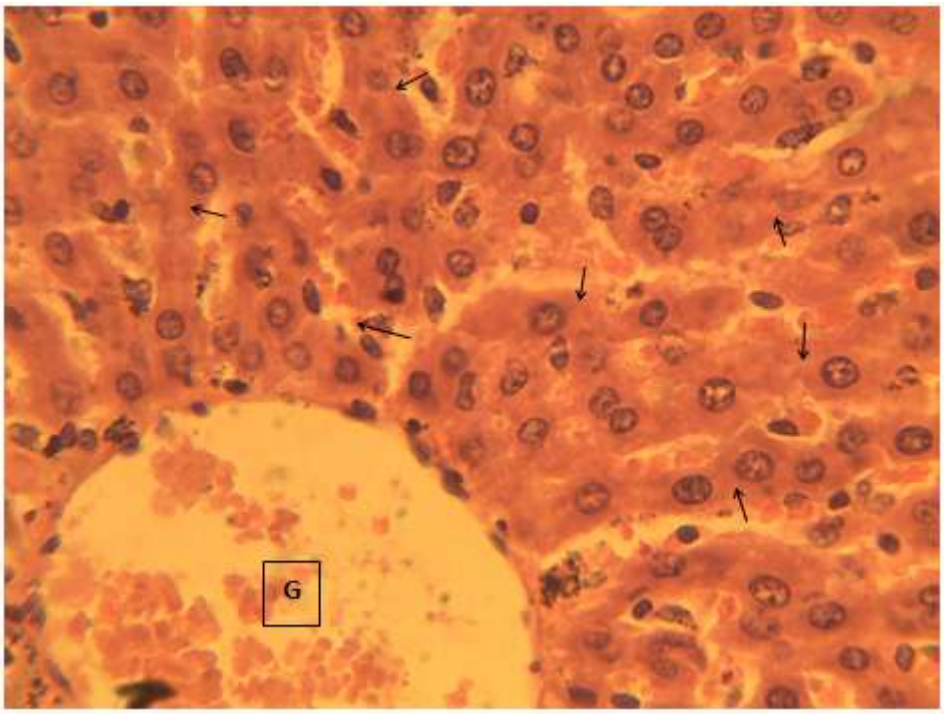

Plate 6: Photomicrograph of the liver tissue from animals in group 1 showing the arrangement of normal hepatocytes in interconnecting chords (arrow) around a central vein (V). H&EX400.

The sections of the liver collected from **groups 1 to 4** did not show any alteration from the normal hepatic histo-architecture of laboratory rodents. The sections showed normal hepatic lobules consisting of normal hepatocytes arranged in interconnecting chords, in a radiating manner around the central veins. The hepatic chords were separated by the hepatic sinusoids and radiate towards the periphery of the hepatic lobules where they join the portal triads which were made up of normal hepatic artery, hepatic vein and bile ducts.

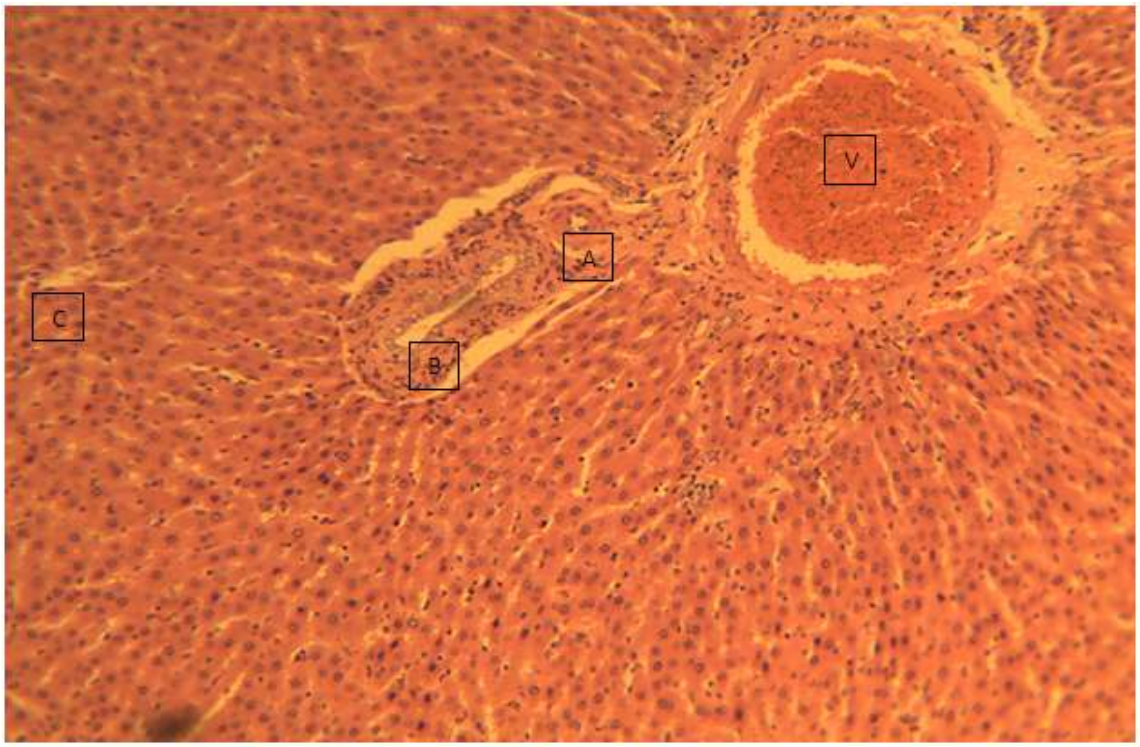

Plate 7: Photomicrograph of the liver tissue collected from the animals in group 2 showing the normal hepatic histo-architecture. The hepatocytes can be observed, arranged in chords and converging towards the portal area which contains the hepatic artery (A), hepatic vein (V) and bile duct (B). Central vein (C).H&Ex100.

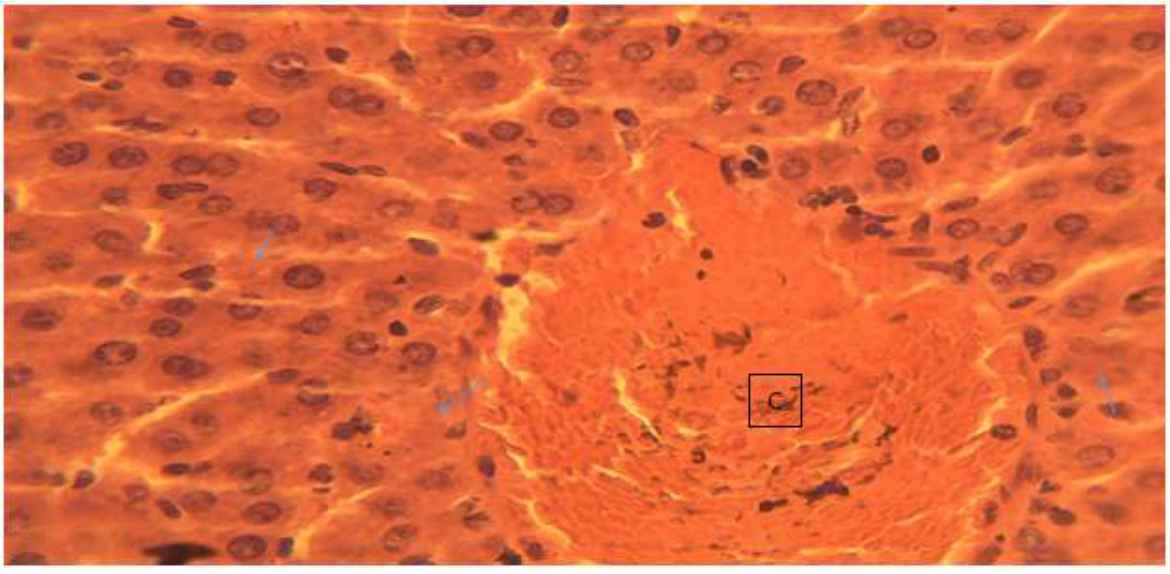

Plate 8: Photomicrograph of the liver tissue from animals in group 3 showing the normal hepatic histo-architecture. Normal hepatocytes arranged in chords (arrow) can be seen around the central vein (C). H&Ex400.

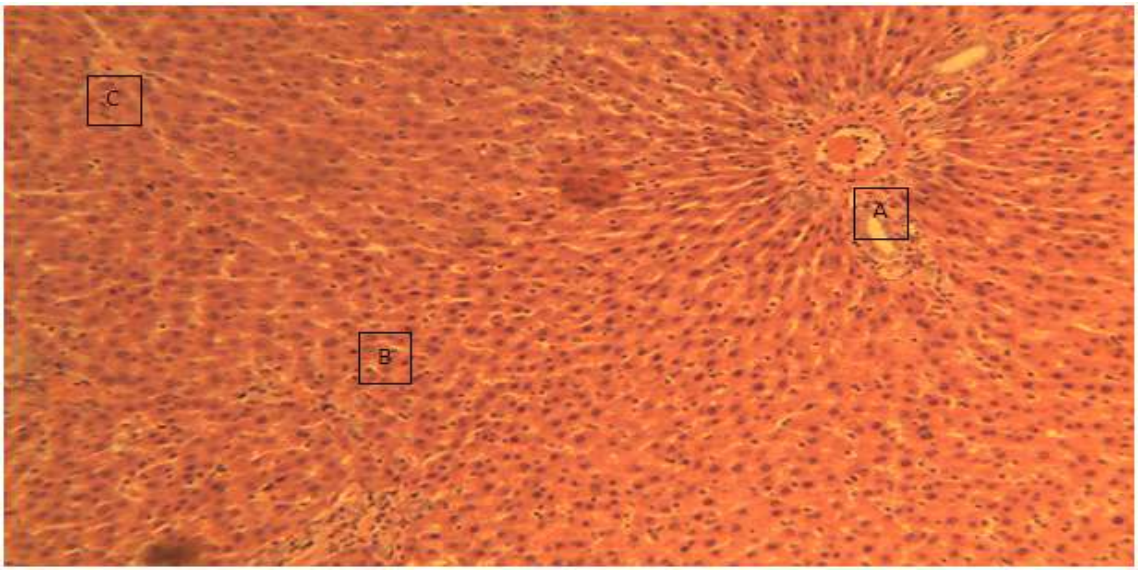

Plate 9: Photomicrograph of the liver tissue collected from the animals in group 4 showing the normal hepatic histo-architecture. Normal hepatocytes arranged in radiating chords around the central veins can be observed. Normal components of the portal area can also be observed. Hepatic artery (A), Bile duct (B),H&Ex100.

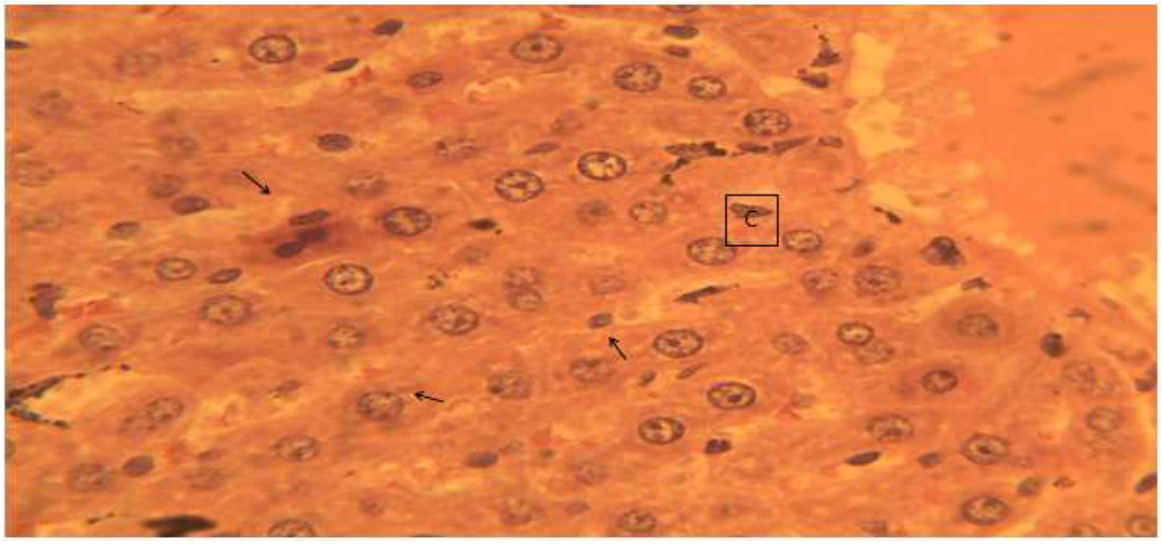

Plate 10: Photomicrograph of the liver tissue collected from the animals in group 5 showing a mild to moderate, widespread vacuolar degeneration of the hepatocytes (arrow). The hepatocytes appear slightly swollen and contain numerous minute vesicles (clear spaces) in their cytoplasms. Central vein (C).H&Ex400.

Sections of the liver collected from the animals in **group 5** which was treated with the highest dose of the test extract showed changes consistent with hepatotoxicity. Mild to moderate cellular swelling were observed, involving all the described anatomic zones of the hepatic lobule (centrilobular, mid-zonal and periportal zones). The hepatic chords consisted of

hepatocytes with swollen, micro-gesticulated cytoplasm. The swollen hepatocytes tend to occlude the hepatic sinusoids.

CONCLUSION

This research has provided information on the major bioactive constituents of the *Spondias mombins* aqueous leaf extract. It consist mainly flavonoids, saponins, alkaloid, tannins and cyanogenic glycosides, which have considerable therapeutic values. The presence of these compounds suggests that *Spondias mombins* aqueous leaf extract have the potentials of providing precursor for the synthesis of useful pharmaceutical products. The GCMS analysis of *Spondias mombin* leaf extract showed eight peaks which indicated the presence of eight bioactive compounds. The compounds posses anti-malaria, anti-inflammatary and antimicrobial properties. The study also showed the increase in levels of AST,ALT ,ALP and the changes of histopathological findings. This study suggest that this leaf extract is dose dependent.

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