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SAFETY EVALUATION OF THE AQUEOUS EXTRACT OF *Lecaniodiscus cupanioides* ROOTS IN MALE WISTAR RATS

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ABSTRACT

The benefits of herbal medicine are enormous but so are its adverse effects too. The present study was aimed at the evaluation of the toxicological impact of Lecaniodiscus cupanioides root on hematological, biochemical and histoarchitectural indices of treated rats. Twenty male Wistar rats were completely randomized into four groups (A, B, C and D) of five animals each such that the animals in group A (Control) received 0.5 ml of distilled water orally while those in groups B, C and D received equal volume (0.5 ml) of the aqueous extract of L. cupanioides root corresponding to 25, 50 and 100 mg/kg body weight respectively for 7 days. The rats were sacrificed to obtain the serum and tissue homogenate used for analysis. Administration of the aqueous extract of L. cupanioides roots significantly ($p < 0.05$) increased the concentrations of plasma erythrocytes, leucocytes, monocytes, neutrophils, malondialdehyde, reduced glutathione, urea and creatinine while there was a significant ($p < 0.05$) and dose related decrease in platelet, lymphocyte, total and urine bilirubin concentrations. There was no significant ($p > 0.05$) difference in the concentrations of plasma hematocrit, hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, direct bilirubin, total protein, albumin and globulin. The activities of ALP, ALT, AST, GPx, Gre were significantly ($p < 0.05$) decreased while the activities of CAT, SOD and G6PDHsignificantly ($p < 0.05$) increased. The aqueous extract of Lecaniodiscus cupanioides root caused structural and functional toxicity hence, it is not safe for consumption.

***Keywords**: Lecaniodiscus cupanioides, Sapindaceae, hematology, antioxidant, histopathology*

INTRODUCTION

Medicinal plants, which are the source of a large proportion of medicines, have been used for the treatment of several human ailments for thousands of years (Katkar *et al.*, 2010). Medicinal plants are also called medicinal herbs in which one or more of their organs contain substances that can be used for therapeutic functions or which are precursors for the synthesis of drugs (Shaik *et al.*, 2017). Over eons, human beings have relied on plants to meet their fundamental needs e. g. food, shelter, fuel and health. World Health Organization reports that 70% - 80% of the world population rely on traditional medicines for their primary health care (Ramandeep *et al.*, 2018). Most of these plants have their present uses rooted in traditional medicines, which play a major part in maintaining the health and welfare of both rural and urban dwellers in developing countries. Plants still remain the basis for development of modern drugs and medicinal plants have been used for years in daily life to treat diseases all over the world (Ates and Erdogrul, 2003). A vast majority of herbal plants possess pharmacological principles which have rendered them useful as curatives for numerous diseases (Das-Banani and Choudhury, 2014).

Lecaniodiscus cupanioides Planch belongs to the family Sapindaceae. It is a small tree, 6-12 m tall with low branching and widely spreading crown. It is identified by various local names in Nigeria such as *akika* (Yoruba), *kafi-nama-zaki* (Hausa), *okpu* (Igbo) and *utantan* (Edo) (Keay *et al.*, 1989). The plant is ethno-medically reported to be useful in the treatment of wounds and sores, abdominal swelling caused by liver abscess, fever, measles hepatomegaly as well as burns (Yemitan and Adeyemi, 2005). The leaves are used by the people of Ebonyi State in Nigeria as a spice for making soup for new nursing mothers as a form of postnatal care (Oselebe *et al.*, 2013). Decoction from the leaves, roots and seeds are traditionally used in the treatment of fever, burns, liver abscesses, jaundice, coughs, malaria, and as an aphrodisiac by the people of South-Western Nigeria (Olowokudejo *et al.*, 2008). The folkloric application of its

root decoction as a chemo-therapeutic agent against rheumatism in South-Western States of Nigeria was also mentioned by Ogunmefun and Gbile (2012). The aqueous pod extract from *L. cupanioides* reportedly demonstrated remarkable anti-candidal activity (Okore *et al*., 2007) and the antimalarial activity of its aqueous root extract has also been reported by Nafiu *et al*. (2013). The central nervous system depressant action of the plant has also been demonstrated (Yemitan and Adeyemi, 2005). Aqueous root extract of *L. cupanioides* is widely used in the management of sexual dysfunction in Nigeria (Nurudeen *et al*., 2015). Findings from Oladimeji-Salami *et al.* (2014) revealed that the ethanolic leaf extract of *L. cupanioides* at 800 and 1600 mg/kg body weight inhibited *in-vivo* antioxidant enzymes (CAT, SOD and GSH) with accompanying hepatotoxicity after prolonged use. Similarly, Joshua and Timothy (2011) reported significant alterations in the activities of ALT, AST and ALP following treatment with the root extract of *L. cupanioides* at 800 mg/kg body weight but recommended a further assessment and evaluation. Hence, this study was designed for a robust investigation of the toxic effects of the root extract of *L. cupanioides* plant on the liver, kidney, antioxidant, hematology and histoarchitectural changes in male Wistar rats.

MATERIALS AND METHODS

Collection and Authentication of the Plant Material

Dried roots of *L. cupanioides* were bought from herb sellers at Oja-Tuntun market, Ilorin, Nigeria. It was authenticated at the Herbarium Unit of the Department of Plant Biology, University of Ilorin, Ilorin, Nigeria, where a voucher specimen (UILH/001/954) was deposited.

Experimental Animals

Twenty healthy, male Wistar rats (*Rattus norvegicus*) weighing 143.25 ± 15.40 g were obtained from the Animal Holding Unit of the Department of Biochemistry, University of Ilorin, Ilorin, Nigeria. All the animals were strictly handled in conformation to the principle of laboratory animal care (NIH publication number 82-23,revised 1985). They were kept in a well-ventilated house (25-29°C temperature,12 hours light/dark photo period and 45-55% humidity), allowed unrestricted access to feed (Premier Feeds, Ibadan, Nigeria) and tap water *ad libitum.*

Reagents and Assay Kits

The assay kits used for the determinations of albumin, total and conjugated bilirubin, alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), glucose-6-phosphate dehydrogenase (G6PDH), catalase (CAT), reduced glutathione (GSH), glutathione reductase (GRe), glutathione peroxidase (GPx), urea, creatinine, Na^+ and K^+, superoxide dismutase (SOD) and malondialdehyde (MDA) were products of Randox Laboratory Ltd, Co-Antrim, UK. All other reagents used were of analytical grade and prepared using distilled water and stored in air-tight reagent bottles except otherwise stated.

Preparation of Plant Extract

The roots of *L. cupanioides* were washed, sliced, oven-dried at 40ºC (Quincy Laboratory Oven, Model 30 GC, Chicago, USA). The dried roots were then pulverized using an electric blender (Master Chef Blender, Model MC-BL 1980, China). A known amount (100g) of the resulting powder was extracted in 1litre of distilled water for 48 hours at 27ºC with intermittent shaking. The resulting filtrate was concentrated on a steam bath (Electric Thermostatic Waterbath DK 420, England) to give a yield of 8.46 g. This was then reconstituted in distilled water to give the required doses of 25, 50 and 100 mg/kg body weight used for the experiment.

Animal Grouping and Administration of Plant Extracts

A total of twenty male Wistar rats were completely randomized into four groups (A, B, C and D) of five animals each. The rats in group A received 0.5 ml of distilled water orally while those in groups B, C and D received equal volume of the aqueous extract of *L. cupanioides* root corresponding to 25, 50 and 100 mg/kg body weight respectively, for 7 days.

Preparation of Serum and Tissue Supernatants

The procedure described by Yakubu and Salimon (2016) was adopted for the preparation of serum and tissue supernatants. Twenty-four hours after the 7 days administration of the distilled water and plant extract, the rats were weighed and anaesthetized in diethyl ether fumes. Following loss of consciousness, the jugular veins were cut, and 3 ml of blood were collected into plain and heparin sample bottles. Clear serum was then collected using Pasteur pipette after centrifuging the clotted blood samples at 1252 × *g* for 10 minutes using Biobase Laboratory Centrifuge (Model LC-4KA, Jinan, China). The sera were kept frozen for 12 hours before being used for further analysis. The animals were then quickly dissected, and the liver and kidneys were carefully removed and blotted. The organs were weighed and placed in iced cold 0.25 M sucrose solution to maintain the integrity of the tissues. The organs were separately homogenized after which they were centrifuged at 1789 × *g* for 10 minutes. The supernatants were frozen for 12 hours before being used for the assessment of some biochemical parameters.

Hematological, Biochemical and Histological Examination

Hematological analysis was performed using an automatic hematological analyzer (Sysmex Hematology System, Model KX-21W, Kobe, Japan). The procedures described by Gornal *et al*. (1949), Doumas *et al*. (1971), Jendrassik and Grof (1938), Tietz (1995), Veniamin and Verkirtzi (1970) and Bartels and Bohmer (1972) were adopted for the determination of total protein, albumin, bilirubin (total and conjugated), globulin, urea and creatinine respectively. The concentrations of electrolytes – sodium and potassium ion (Na^+ and K^+) were determined as described by Tietz (1995) while the levels of GSH, MDA and TAC were determined following the procedures described by Sedlak and Lindsay (1968) and Buege and Aust (1978) respectively. The activities of ALT, AST, ALP, CAT, G6PDH, GRe, GPx, LDH

and SOD were determined using standard procedures described by Reitman and Frankel (1957), Wright *et al.* (1972), Aebi (1984), Krieg *et al*. (1967), Reclos *et al*. (2000), Misra and Fridovich (1972) while histological examination was carried out following procedures described by Krause (2001).

Data Analysis

Data were expressed as the mean ± SEM of five replicates. Means were analyzed using One-way Analysis of Variance and complemented with Duncan Multiple Range Test. The Statistical Package for Social Sciences, Version 23.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analyses while differences were considered statistically significant at $p < 0.05$.

RESULTS

Administration of the aqueous extract of *L. cupanioides* roots significantly ($p < 0.05$) increased the concentrations of plasma erythrocytes, leucocytes, monocytes and neutrophils (Figures 1 – 4) at all doses investigated whereas, there was a significant ($p < 0.05$) and dose related decrease in the platelet and lymphocyte concentrations (Figure 5 and 6). There was no significant ($p > 0.05$) difference in the concentrations of hematocrit (HCT), hemoglobin (Hgb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) (Figure 7 and 8). There were no treatment-related changes in the concentrations of liver total protein, albumin, globulin, A:G ratio and direct bilirubin while there was a dose-dependent increase in the total and urine bilirubin levels (Table 1). The activities of liver and serum ALP, liver AST and ALT decreased dose-dependently with a corresponding increase in the serum AST (Table 1). Furthermore, the activities of CAT, SOD, LDH and G6PDH were significantly ($p < 0.05$) increased whereas there was a dose-dependent decrease in the activities of GPx, GRe as well as the concentration of GSH (Table 2). The serum level of MDA significantly ($p < 0.05$) increased in rats treated with 50 and 100 mg/kg body weight of *L. cupanioides* root extract while there was a significant ($p < 0.05$) decrease in TAC (Table 2). Also, the aqueous extract of *L. cupanioides* root at 50 and 100 mg/kg body weight significantly ($p < 0.05$) increased the concentration of serum urea, uric acid and creatinine whereas there were no treatment related changes in concentration of sodium and potassium ions (Table 3). The liver of the control rats revealed normal sinusoids with no infiltration whereas the animals treated with the aqueous extract of *L. cupanioides* root at 25, 50 and 100 mg/kg body weight revealed a moderate congestion of the portal veins, moderate fatty infiltration of cytoplasm and hepatocellular infiltration with severe steatosis respectively (Plates 1 – 4). Similarly, the histo architecture of the kidney in control rats showed normal glomeruli with healthy mesangial cells, capsular and interstitial spaces (Plate 5). In contrast, the renal cortex of the extract treated rats at 25, 50 and 100 mg/kg body weight revealed some lack of luminar space, mild tubular necrosis and widened interstitial spaces with tubular infiltration respectively (Plates 6 – 8).

Table 1: Effect of the aqueous root extract of *Lecaniodiscus cupanioides* on liver function indices of male Wistar rats

Parameters	Control	Doses of plant extract (mg/kg) body weight		
		25	50	100
Total protein (g/dL)	8.31±0.48^a	7.80±0.36^a	7.89±0.28^a	7.95±0.31^a
Albumin (g/dL)	4.48±0.31^a	4.37±0.10^a	3.91±0.19^a	4.11±0.24^a
Globulin (g/dL)	3.83±0.28^a	4.06±0.29^a	3.98±0.17^a	3.84±0.14^a
A:G ratio	1.17±0.09^a	1.08±0.06^a	0.98±0.08^a	1.07±0.07^a
Total bilirubin (mg/dL)	1.15±0.06^a	1.52±0.11^b	1.87±0.21^c	1.80±0.11^c
Directbilirubin (mg/dL)	0.83±0.25^a	0.99±0.11^a	0.86±0.09^a	0.84±0.19^a
Urine bilirubin (mg/dL)	0.32±0.11^a	0.53±0.09^b	1.01±0.15^c	0.96±0.14^c
Liver ALP(U/I)	31.34 ± 1.21^a	24.27 ± 0.67^b	26.45 ± 0.48^b	19.30 ± 0.38^c
Serum ALP (U/I)	10.27 ± 0.19^a	6.17 ± 0.13^b	6.18 ± 0.22^b	5.88 ± 0.08^c
Liver AST(U/I)	20.87 ± 0.13^a	19.87 ± 0.11^b	17.77 ± 0.19^c	15.37 ± 0.11^d
Serum AST (U/I)	16.15 ± 0.16^a	21.70 ± 0.93^b	24.45 ± 0.34^c	28.98 ± 0.31^d
Liver ALT (U/I)	38.46 ± 2.03^a	25.17 ± 0.75^b	19.56 ± 0.35^c	19.98 ± 0.27^c
Serum ALT (U/I)	13.59 ± 0.58^a	14.73 ± 0.25^a	14.49 ± 0.34^a	13.90 ± 0.20^a

Data are mean ± SEM of five determinations. Test values with superscripts other than the control for each parameter are significantly different (P<0.05);

Table 2: Effect of the aqueous extract of *Lecaniodiscus cupanioides* root on enzymatic and non-enzymatic antioxidant parameters of male Wistar rats

Parameters	Control	Doses of plant extract (mg/kg) body weight		
		25	50	100
Catalase × 10^2 (U/l)	20.00 ± 0.01^a	22.50 ± 0.05^b	22.55 ± 0.15^b	27.50 ± 0.50^c
Superoxide dismutase (U/l)	24.88 ± 0.58^a	49.75 ± 6.05^b	99.50 ± 7.55^c	149.75 ± 10.12^d
Glutathione peroxidase (U/l)	185.77 ± 0.39^a	132.63 ± 4.11^b	80.02 ± 3.89^c	35.54 ± 1.88^d
Reduced glutathione (U/mg)	8.75 ± 0.73^a	8.78 ± 1.05^a	8.05 ± 0.34^{ab}	7.05 ± 0.72^b
Glutathione reductase (U/mg)	569.71 ± 7.51^a	334.61 ± 8.23^b	105.68 ± 5.07^c	76.87 ± 2.29^d
Total antioxidant capacity(mg/dl)	82.80 ± 1.17^a	80.93 ± 0.91^a	74.85 ± 2.50^b	74.62 ± 1.85^b
Malondialdehyde×10^{-5} (U/l)	2.30 ± 0.02^a	2.31 ± 0.02^a	2.73 ± 0.02^b	2.77 ± 0.03^b
Lactate dehydrogenase (U/l)	201.57 ± 12.45^a	209.12 ± 13.33^a	193.57 ± 12.75^a	235.42 ± 10.33^b
Glucose-6-phosphate dehydrogenase (U/l)	11.22 ± 0.33^a	22.43 ± 1.35^b	23.10 ± 0.88^b	33.65 ± 3.02^c

Data are mean ± SEM of five determinations. Test values with superscripts different from the control for each parameter are significantly different ($p<0.05$)

Table 3: Effects of the aqueous root extract of *Lecaniodiscus cupanioides* on selected kidney function parameters of male Wistar rats

Parameters	Control	Doses of plant extract (mg/kg) body weight		
		25	50	100
Urea (mmol/L)	7.83 ± 0.14^a	8.72 ± 0.27^b	8.28 ± 0.29^b	8.75 ± 0.37^b
Uric acid (µmol/L)	4.42 ± 0.18^a	4.55 ± 0.25^a	5.34 ± 0.11^b	5.45 ± 0.18^b
Creatinine (µmol/L)	14.47 ± 1.38^a	13.45 ± 3.29^a	22.74 ± 1.46^b	29.11 ± 3.10^c
Na^+ (mmol/L)	129.3 ± 1.48^a	130.5 ± 1.96^a	131.9 ± 1.86^a	129.8 ± 2.38^a
K^+ (mmol/L)	5.17 ± 0.08^a	5.37 ± 0.08^a	5.35 ± 0.24^a	5.42 ± 0.30^a

Data are mean ± SEM of five determinations. Test values with superscripts different from the control for each parameter are significantly different ($P<0.05$)

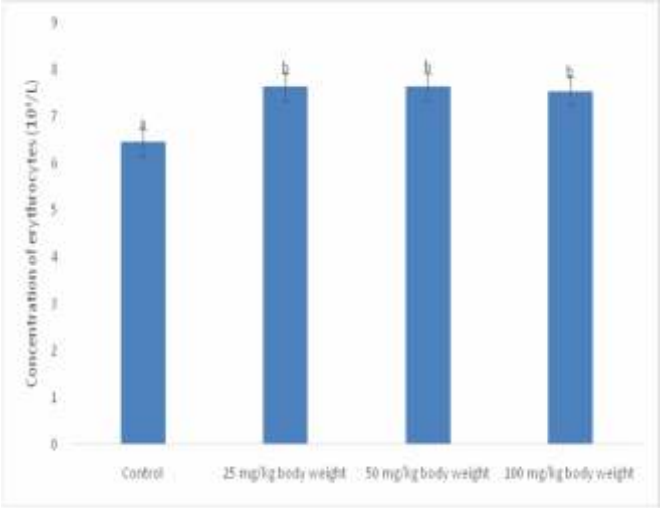

Figure 1: Effect of *L. cupanioides* root on plasma concentration of erythrocytes

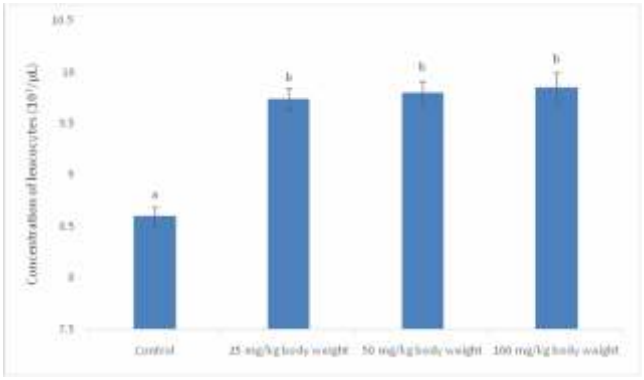

Figure 2: Effect of *L. cupanioides* root on plasma concentration of leucocytes

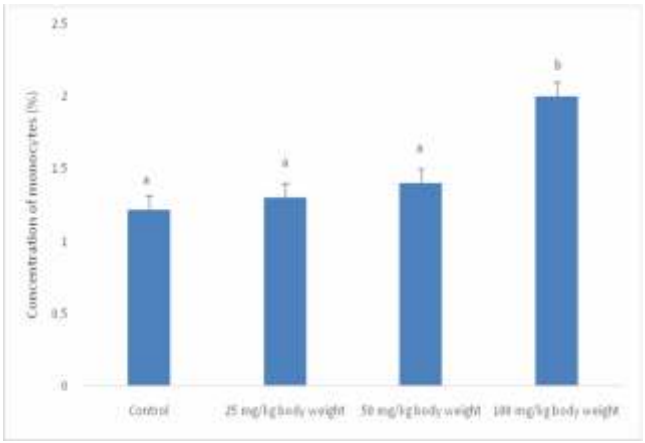

Figure 3: Effect of *L. cupanioides* root on plasma concentration of monocytes

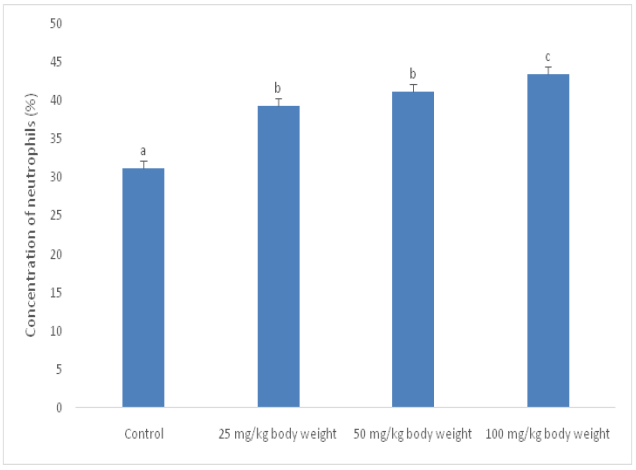

Figure 4: Effect of *L. cupanioides* root on plasma concentration of neutrophils

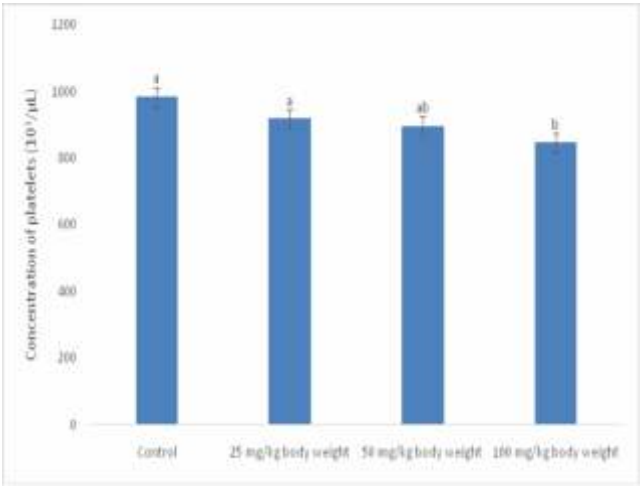

Figure 5: Effect of *L. cupanioides* root on plasma concentration of platelets

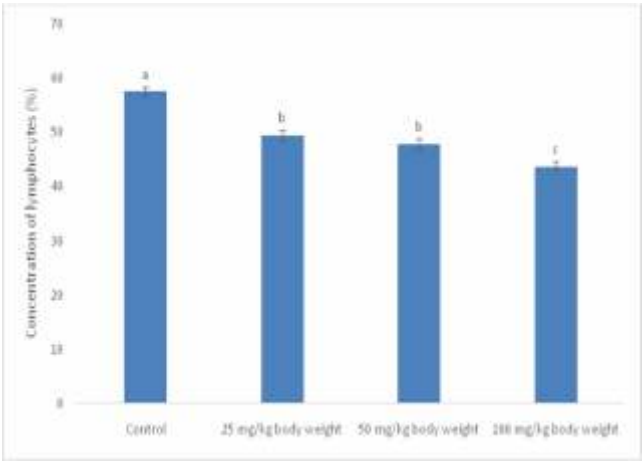

Figure 6: Effect of *L. cupanioides* root on plasma concentration of lymphocytes

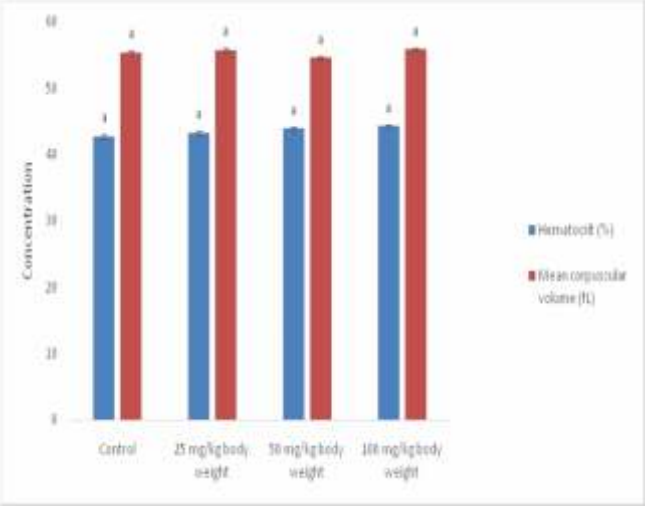

Figure 7: Effect of *L. cupanioides* root on plasma concentration of hematocrit and mean corpuscular volume

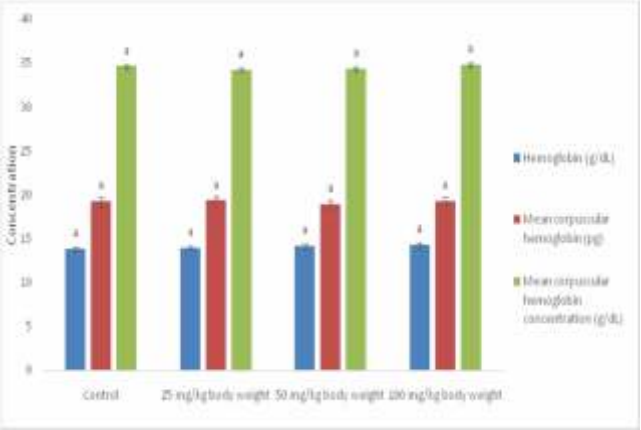

Figure 8: Effect of *L. cupanioides* root on plasma concentration of hemoglobin, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration

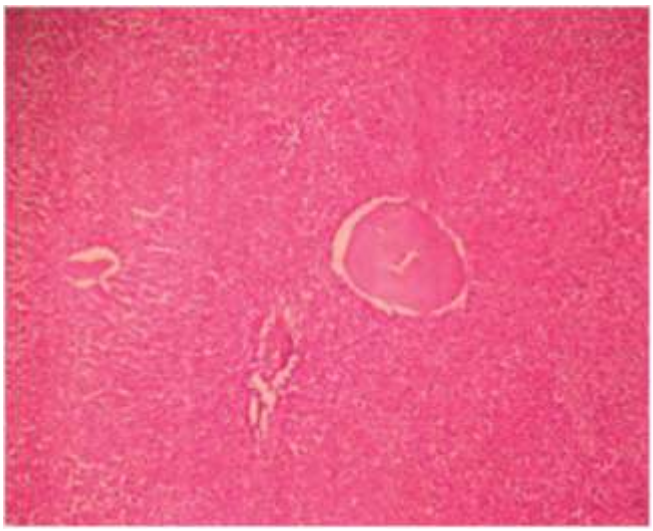

Plate 1: Cross section of the liver of control rat treated with distilled water (Mag. × 100; H & E)

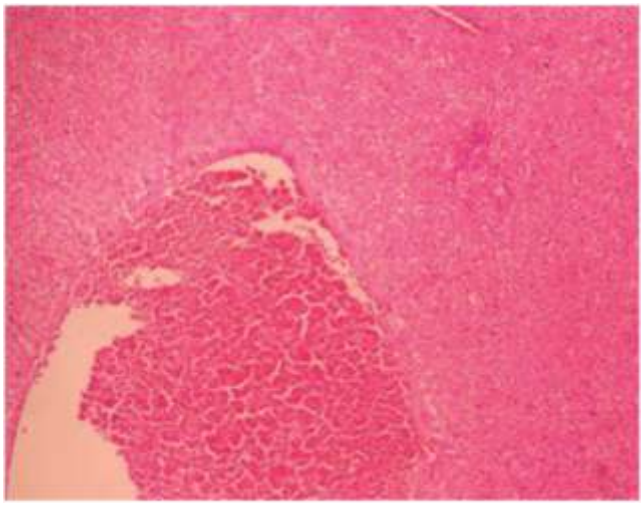

Plate 2: Cross section of the liver of rat treated with 25 mg/kg body weight of *L. cupanioides* extract (Mag. × 100; H & E)

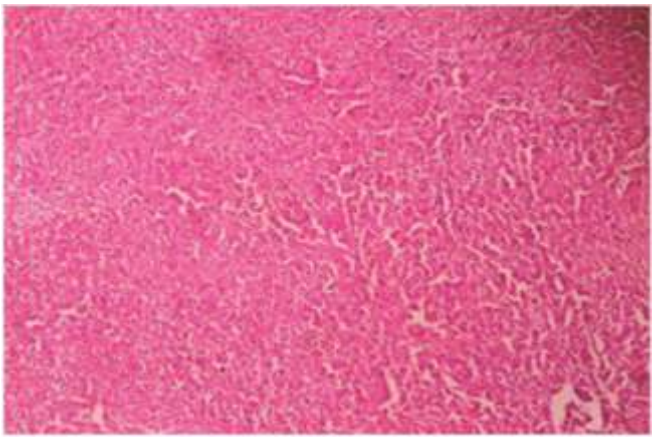

Plate 3: Cross section of the liver of rat treated with 50 mg/kg body weight of *L. cupanioides* extract (Mag. × 100; H & E)

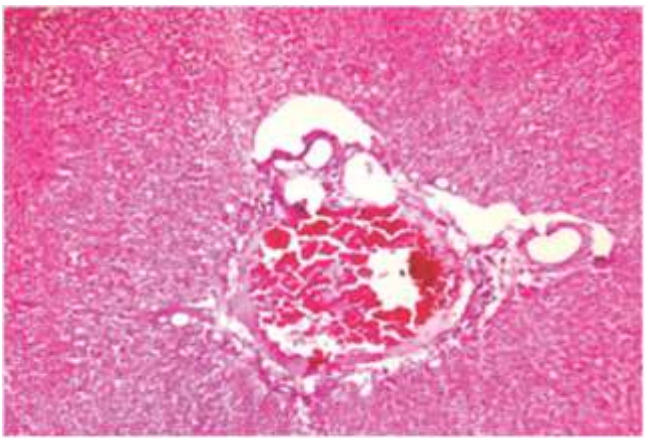

Plate 4: Cross section of the liver of rat treated with 100 mg/kg body weight of *L. cupanioides* extract (Mag. × 100; H & E)

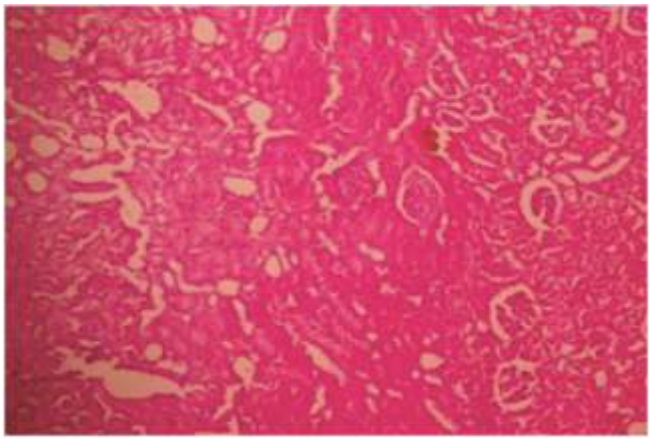

Plate 5: Cross section of the kidney of control rat treated with distilled water (Mag. × 100; H & E)

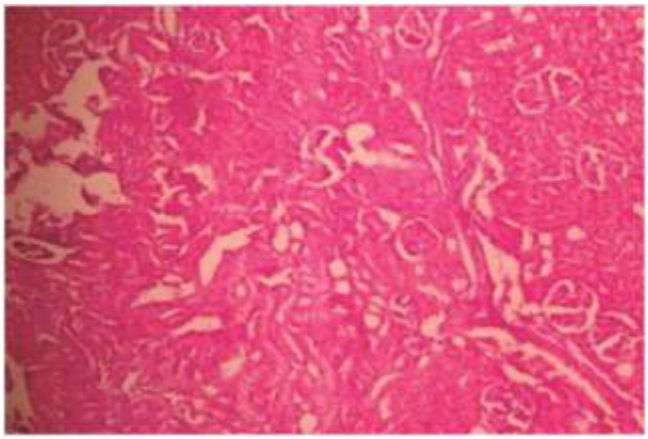

Plate 6: Cross section of the kidney of rat treated with 25 mg/kg body weight of *L. cupanioides* extract (Mag. × 100; H & E)

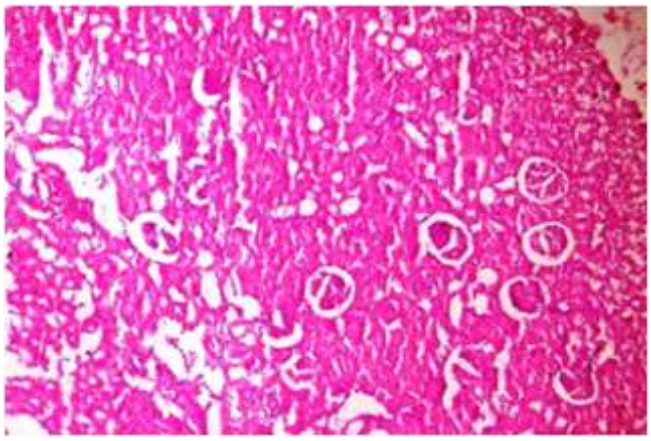

Plate 8: Cross section of the kidney of rat treated with 100 mg/kg body weight of *L. cupanioides* extract (Mag. × 100; H & E)

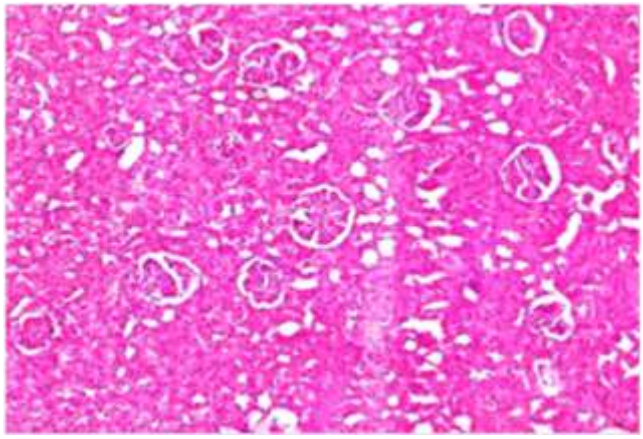

Plate 7: Cross section of the kidney of rat treated with 50 mg/kg body weight of *L. cupanioides* extract (Mag. × 100; H & E)

DISCUSSION

Worldwide, various medicinal plants and botanical drugs have been widely adapted as primary therapeutic agents for treating various human illnesses (Tulay, 2012; Raman deep *et al.,* 2018). Safety studies are accomplished by the implementation of general pre-clinical toxicity experiments to uncover potential poisonous effects of any drug majorly in liver and kidney of animals (Farzamfar *et al.*, 2008).

Hematology parameters are evaluated to obtain toxicity related information which is not usually detected by direct examination of organs and body weight analysis. Red blood indices such as the MCV, MCH, Hgb, HCT and MCHC are the most useful indicators in the diagnosis of anemia in most animals (Weingand *et al.*, 1996). The effect of the aqueous root extract of *L. cupanioides* on Hgb, HCT, MCV, MCH and MCHC were insignificant in extract treated groups compared to the control. These observations imply that the aqueous extract of *L. cupanioides* roots did not cause significant toxic effect on plasma erythrocytes at all doses investigated, thus, the absence of any macrocytic and microcytic anemia (Rogers, 2011). Elevation in the estimated erythrocyte and leucocyte count after administration of the aqueous extract of *L. cupanioides* roots compared with the control suggests increased *de-novo* synthesis of erythrocytes and stimulation of immune response respectively (Tousson *et al.*, 2011). The dose-related decrease in platelets count in the animals treated with the aqueous extract of *L. cupanioides* roots as compared to the control group might suggest inhibition of biosynthesis or enhancement in platelet destruction (Debelo *et al.*, 2016) while the alterations in monocytes, neutrophils and leucocytes count could be attributed to the adaptation of the animal to chemical assault.

In this study, total protein, albumin, globulin and bilirubin (total and direct) were monitored to assess the secretory and excretory functions of the liver. The absence of any treatment related changes in the levels of total protein, albumin and globulinare suggestive of normal hepatocellular function. However, the increase in total bilirubin implies hemolysis and blockage of the biliary tract (Sabiu *et al*., 2015) which can be attributed to the accompanying increase in urine bilirubin. The activities of ALP, ALT and AST are useful biomarkers for hepatotoxicity (Xie *et al*., 2014; Yakubu and Salimon, 2016). The dose-dependent decrease in the

activities of liver and serum ALP is indicative of disrupted bilayer of the plasma membrane. The dose dependent decrease in the activity of liver ALT and AST with corresponding increase in serum AST confirms deranged plasma membrane integrity causing the efflux of cytosolic content (Ajiboye *et al*., 2017). The enzymes CAT, SOD, GPx, GRe and G6PDH are responsible for the detoxification of noxious reactive oxygen and nitrogen species with their depletion reported in previous hepatotoxicity studies (Sabiu *et al*., 2015; Ajiboye *et al*., 2017; Nurudeen *et al*., 2020). However, the elevations in the activity of CAT, SOD and G6PDH implies the stimulation of antioxidative response following the administration of the aqueous extract of *L. cupanioides* root in male Wistar rats. The depletion in the level of GSH can be attributed to the reduction in GPx and GRe that plays coordinated role in the biosynthesis of GSH and restoration of oxidative balance (McGill *et al*., 2013). The increase in activity of LDH at 100 mg/kg body weight is suggestive of tissue degeneration which was further corroborated by the structural degeneration of the hepatocytes. The elevation in the level of MDA a biomarker of lipid peroxidation with reduction in TAC suggests oxidative stress resulting from the administration of the plant extract (Nurudeen *et al*., 2020). The increase in serum urea, uric acid, and creatinine implies the excretory function of the kidney had been dampened by the plant extract while the absence of any treatment related changes in the concentrations of Na^+ and K^+ is an indication of normal tubular function. The aqueous extract of *L. cupanioides* root caused significant structural damages of the liver and kidney which further substantiates the tissue degeneration and oxidative stress levels earlier reported in this study.

CONCLUSION

The aqueous extract of *Lecaniodiscus cupanioides* root may not be safe for use as evidenced by the distortion of antioxidant balance, hematology, structural and functional derangements of the liver and kidney. Thus, the prolonged usage of the plant is vehemently discouraged.

REFERENCES

Aebi, H. (1984). Catalase in vitro. Methods in Enzymology 105:121–126.

Ajiboye, T. O., Ahmad, F. M., Daisi, A. O., Yahaya, A. A., Ibitoye, O. B., Muritala, H. F. and Sunmonu, T. O. (2017). Hepatoprotective potential of *Phyllanthus muellarianus* leaf extract: studies on hepatic, oxidative stress and inflammatory biomarkers. Pharmaceutical Biology 55(1): 1662-1670.

Ates, D.A. and Erdogroiul, O.T. (2003). Antimicrobial activities of various medicinal and commercial plant extract. Turkish Journal of Biology 278: 157-162.

Bartels, H. and Bohmer, M. (1972). Kinetic determination of creatinine concentration. Clinica Chimica Acta 37: 193 – 197.

Buege, J. A. and Aust, S. D. (1978).Microsomal lipid peroxidation. Methods in Enzymology 52: 302-310.

Das Banani, A.D.T.D. and Choudhury, D.M. (2014). A few traditional medicinal plants used as antifertility agents by ethnic people of Tripura India. International Journal of Pharmacy and Pharmaceutical Sciences, 6(3):47-53.

Debelo, N., Afework, M., Debella, A., Makonnen, E., Ergete, W. and Geleta, B. (2016).Assessment of hematological, biochemical and histopathological effects of acute and sub-chronic administration of the aqueous leaves extract of *Thymus schimperi* in rats. Journal of Clinical Toxicology 6(286): 2161-2495.

Doumas, B.T., Watson, W.A. and Biggs, H.G. (1971). Albumin standards and measurement of serum albumin with bromocresol green. Clinical Chimica Acta. 31:87-92.

Farzamfar, B., Abdollahi, M., Kabinezhadian, S., Heshmat, R., Shah, H. M. H., Novitsky, Y. A. and Farhadi, M. (2008).Sub-chronic toxicity study of a novel herbal-based formulation (Semelil) on dogs. DARU Journal of Pharmaceutical Sciences 16: 15-19.

Gornall, A. C., Bardawill, C. J. and David, M. M. (1949). Determination of serum protein by means of biuret reaction. Journal of Biological Chemistry. 177:751-756.

Jendrassik, L. and Grof, P. (1938).Simplified photometric methods for determination of direct and total bilirubin. Biochem Zeit. 297(81): 2 – 23.

Joshua, Z. P. and Timothy, A. G. (2011). Toxicity studies of the aqueous root extract of *Lecaniodiscus cupanioides* on albino rats. Science World Journal 6(4): 27-29.

Katkar, K.V., Suthar, A.C. and Chauhan, V.S. (2010).The chemistry, pharmacologic, and therapeutic applications of *Polyalthia longifolia*. Pharmacology Review 4: 62-68.

Keay, R.W.J., Onochie, C.F.A. and Standfield, D.P. (1989).Trees of Nigeria. Revised version, Clarendon Press, Oxford, London, Pp. 361 – 362.

Krause, W.J. (2001). The art of examining and interpreting histologic preparations: A student handbook. Parthenon Publishing Group, Lancaster, UK, Pp. 9 – 10.

Krieg A.F., Rosenblum L.J. and Henry J.B. (1967).Lactate dehydrogenase isoenzymes a comparison of pyruvate-to-lactate and lactate-to-pyruvate assays. Clin. Chem. 13(3):196–203.

McGill, M.R., Lebofsky, M., Norris, H.R.K., Slawson, M.H., Bajt, M.L., Xie, Y., Williams, C.D., Wilkins, D.G., Rollins, D.E. and Jaeschke, H. (2013). Plasma and liveracetaminophen-protein adduct levels in mice after acetaminophen treatment: dose-response, mechanisms, and clinical implications. Toxicology and Applied Pharmacology. 269:240–249.

Misra, H.P. and Fridovich, I. (1972).The role of superoxide anion in the autoxidation of epinephrine and a simple assay for superoxide dismutase. Journal of Biological Chemistry. 247:3170–3175.

Nafiu, M.O., Abdulsalam, T.A. and Akanji, M.A. (2013).Phytochemical analysis and antimalarial activity of the aqueous extract of *Lecaniodiscus cupanioides* root. Journal of Tropical Medicine. 15: 1 - 4.

Nurudeen, Q.O., Ajiboye, T.O., Yakubu, M.T., Oweh, O.T. and Nosarieme, O. (2015). Aqueous root extract of *Lecaniodiscus cupanioides* restores nitric oxide/cyclic guanosine monophosphate pathway in sexually impaired male rats. Journal of Ethnopharmacology 175: 181-184.

Nurudeen, Q.O., Salimon, S.S., Falana, M.B., Oweh, O.T. and Abubakar, I.B. (2020). Antioxidant activity and

toxicological implications of the aqueous extract of *Phyllantus amarus* (Euphorbiaceae) leaves in female Wistar rats. Pacific Journal of Medical Sciences 21(1): 29 – 40.

Ogunmefun, O. T. and Gbile, Z. O. (2012).An ethnobotanical study of anti-rheumatic plants in South Western States of Nigeria. Asian Journal of Science and Technology 4(11): 63-66.

Okore, V.C., Ugwu, C.M., Oleghe, P.O. and Akpa, P.A. (2007).Selective anti-candidal action of crude aqueous pod extract of *Lecaniodiscus cupanioides*: a preliminary study on *Candida albicans* obtained from an AIDS patient. Scientific Research and Essays 2(2): 043–046.

Oladimeji-Salami, J.A., Akindele, A.J. and Adeyemi, O.O. (2014). Effects of ethanolic dried leaf extract of *Lecaniodiscus cupanioides* on antioxidant enzymes and biochemical parameters in rats. Journal of ethnopharmacology. 155(3): 1603-1608.

Olowokudejo, J.D., Kadiri, A.B. and Travih, V.A. (2008).An ethnobotanical survey of herbal markets and medicinal plants in Lagos State of Nigeria. Ethnobotanical Leaflets. 12: 851–865.

Oselebe, H.O., Nnamani, C.V. and Okporie, E.O. (2013). Ethnobotanical survey of underutilized crops and spices of some local communities in Nigeria: potentials for improved nutrition, food security and poverty reduction. IOSR Journal of Pharmacy. 3(1): 21-28.

Ramandeep, S., Satinder, K., Manisha, S. and Rishab, J. (2018). Some medicinal plants withanti-fertility potential: A current status. Journal of Basic and Clinical Reproductive Sciences 7(1):7-19

Reclos, G.J., Hatzidakis, C.J. and Schulpis, K.H. (2000). Glucose-6-phosphate dehydrogenase deficiency neonatal screening: preliminary evidence that a high percentage of partially deficient female neonates are missed during routine screening. Journal of Medical Screening. 7(1): 46-51.

Reitman, S. and Frankel, S. (1957).A colorimetric method for determination of serum glutamate-oxaloacetate and pyruvate transaminase. American Journal of Clinical pathology. 28:56-59.

Rogers, K. (2011). Blood: Physiology and Circulation (The Human Body), 1st Edition. Encyclopedia Britannica 42: 121-225.

Sabiu, S., Sunmonu, T.O., Ajani, E.O. and Ajiboye, T.O. (2015). Combined administration of silymarin and vitamin C stalls acetaminophen-mediated hepatic oxidative insults in Wistar rats. Revista Brasilera Farmacognosia 25:29–34.

Sedlak, J. and Lindsay, R.H. (1968).Estimation of total, protein-bound, and non-protein sulfhydryl groups in tissue with Ellman's reagent. Analytical Biochemistry 25: 192-205.

Shaikh, A., Yalavarthi, P. and Bannoth, C. (2017). Role of anti-fertility medicinal plants on male and female reproduction. Journal of Complementary and Alternative Medical Research, 3:1-122.

Tietz, N.W. (1995). Clinical Guide to Laboratory Tests.3rd edition. W. B. Saunders Company, Philadelphia, USA. p. 972,

Tousson, E., El-Moghazy, M. and El-Atrsh, E. (2011).The possible effect of diets containing *Nigella sativa* and *Hymus vulgaris* on blood parameters and some organs structure in rabbit. Toxicology and Industrial Health 27: 107-116.

Tülay, A.C. (2012). Potential Genotoxic and Cytotoxic Effects of Plant Extracts. A Compendium of Essays on Alternative Therapy. Edited by Arup Bhattacharya, ISBN 978-953-307–863-2, 292.

Veniamin, M.P. and Varkirtzi, C. (1970).Chemical basis of the carbamidodiacetyl micro-method forestimation of urea, citrulline and carbamyl derivatives. Clinical Chemistry. 16: 3 – 6.

Weingand, K., Brown, G., Hall, R., Davies, D., Gossett, K., Neptun, D., Waner, T., Matsuzawa, T., Salemink, P., Froelke, W. and Provost, J. P. (1996). Harmonization of animal clinical pathology testing in toxicity and safety studies. Fundamental and Applied Toxicology. 29(2): 198-201.

Wright, P.J., Leathwood, P.D. and Plummer, D.T. (1972). Enzymes in rat urine alkaline phosphatase. Enzymologia 42:317-327.

Xie, Y., McGill, M.R., Dorko, K., Kumer, S.C., Schmitt, T.M., Forster, J. and Jaeschke, H. (2014). Mechanisms of acetaminophen-induced cell death in primary human hepatocytes. Toxicology and Applied Pharmacology 279:266–274.

Yakubu, M.T. and Salimon, S.S. (2016). Biochemical and histological changes in female Wistar rats following oral administration of the aqueous extract of *Mangifera indica* L. leaves. Nigerian Journal of Natural Product Medicine 20: 4 – 11.

Yemitan, O.K. and Adeyemi, O.O. (2005).CNS depressant activity of *Lecaniodiscus cupanioides*. Fitoterapia 76(5): 412–418.