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TOXICITY STUDIES OF THE AQUEOUS ROOT EXTRACT OF *Lecaniodiscus cupanioides* ON ALBINO RATS.

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INTRODUCTION

Lecaniodiscus cupaniodes shrub widely distributed throughout deciduous and non deciduous rain forest, part of the plants which have been used medicinally, are the leaf, bark, young shoots and roots. The leaf infusion with *Dialium guinensis* used for body washing during illness, the crushed leaves as dressing for boils, bumps, cut and wounds. Decoction of the roots and stem twigs is given for abnormal swelling caused by liver abscess, bark infusion as purgative, while the twigs are chewed for oral hygiene.

Gill (1992) undocumented claims suggest that the root extract of *L. Cupaniodes* is used in folk medicine, particularly among the Yoruba people of Nigerian to manage epilepsy. During the screening of various plants for anticonvulsant activities, the anticonvulsant activities of *L. cupaniodes* and the aqueous root extract of *Dalbergia saxatilis* was demonstrated (Yemitan & Adeyemi, 2001).

Plant Materials: Fresh root part of *L. cupaniodes* growing in the wild was collected and identified by Forestry Research Station, Jos, where voucher specimen (FHI 106116) is preserved.

Extract preparation: The root part of *L. cupaniodes* was washed with distilled water and dried at room temperature for 24 hours. The material was pounded to obtain a homogenous powder. 100 g of the powder was boiled in 2 litres of distilled water for 30 minutes then left for 24 hours for further extraction. The residue was filtered and oven-dried in beakers at 40 ^{0}C. The dried extract was reconstituted in distilled water before administration.

Animals: Albino rats of either sex weighing between 150 g and 70 g were obtained from the laboratory animal house of the National Veterinary Research Institute Vom, Plateau State, Nigeria. The rats were housed in polypropylene cages at root temperature throughout the study, and fed on standard rodents feed .Water was given to the rats throughout the period of the study.

Acute Toxicity test: Rats were fasted for 12hrs, and administered with *L.cupniodes* to 200mg/kg, orally. In the same manner, *L. cupaniodes* (100 to 800mg/kg) was administered to another set of groups of mice, intraperitoneally. The control mice were given distilled water (10 ml/kg). Mice were closely observed for toxic symptoms and behavioral changes for first two hours of administration and mortality recorded within 24hrs. LD_{50} was calculated using the method of Miller &Tainter (1994).

Chronic Toxicity test: A total of 32 rats were randomly allotted to four groups, consisting of the control and three extract- treated groups, 80 mg/kg, 400 mg/kg, and 2g/kg (which represented one-fifth of the pharmacologically active dose, the pharmacologically active dose, and five times the pharmacologically active dose, respectively of the extract (Qureshi *et al.,* 92; Yemitan *et al.,* 2001). The doses were administered daily through gastric gavages, through out 45-days period. The rats in the different groups were observed closely for any behavioral changes, feeding and drinking habits, as well as body weight changes and general morphological changes. They were later sacrificed for internal macroscopic, hematological and biochemical investigations.

Effect of vital organs: At the end of the study, qualitative data on the weights of vital organs (heart, lungs, liver, kidneys, and spleen) were assessed by carefully dissecting each organ from the sacrificed animals into 10 % formalin contained in a Petri dish. Isolated organs were dried with a blotting paper and weighed on a sensitive balance. Each weighed organ was then standardized for 100g- body weight of each rat.

Hematological Parameters: Blood samples were collected through heart puncture of anaesthetized rat into different bottles, the blood samples were analyzed for red blood cells (RBC), haemoglobin (Hb), packed cell volume (PVC) and white blood cells (WBC) and WBC differentials (neutrophil, eosinophil, basophil, lymphocyte and monocytes) using light compound microscope connected to a CVCTV (WT/CP410/G) Panasonic camera monitoring system.

Biochemical parameters: The effect of the plant extract on certain biochemical parameters were compared with those of the control. Serum from the blood of each rat was collected from the tubes mixed with necessary reagents and read in a screen master colorimeter set at 37 ^{0}C. The activities of the serum alkaline phosphates (SAP) was determined at 405nm using a standard method of Bassey *et al.,* (1946), serum alkaline amino transferase (AST), at 340nm using the method of Reitman & Frankel (1957). Uric acid levels were determined at 500nm using the urease cleavage Berthelot's reaction, according to the principles described by Fawcett & Scott (1960).

Statistical analysis: Results are reported as mean $\pm$ SEM. Statistical analysis was carried out using student's t test. Significance was considered at values of $p<0.05$.

The results from the study showed that irrespective of the treatment dose administered orally to the rats no mortality was recorded. Their was no significant change $p<0.05$ in organ weight when *Lecaniodiscus cupaniodes* was administered except for the liver which showed an insignificant decrease $p<0.05$ in weight and the lungs which increases $p>0.05$ when 200mg/kg was administered (Table 1). Table 2 indicated that their was increased weight gain in all the study groups of rats after six weeks of administering different doses of the extract of *L. cupaniodes.* All the heamatological parameters showed insignificant change, except for heamoglobin which showed a significant decrease $p<0.05$ when 400 mg/kg and 200 mg/kg was administered to the rats (Table 3). The WBC differentials showed a significant decrease in neutrophil at 200 mg/kg and 400 mg/kg. Monocytes showed a significant decrease in WBC differentials when 800mg/kg, 200 mg/kg and 400 mg/kg of *lecaniodiscus cupaniodes* extract were administered to the rats (Table 4). Table 5 showed the biochemical parameters, with alkaline phosphatase showing a significant increase when 200 mg/kg of *L. cupaniodes* was administered to the rats and alanine transaminase showing a significant decrease when 800 mg/kg of the extract was administered.

TABLE 1. EFFECT OF TREATMENT OF EXPERIMENTAL RATS WITH *Lecaniodiscus cupaniodes* ON THEIR VITAL ORGANS.

Treatment and Dose	Mean organ weight per body weight ± S.E.M				
	Heart	Lungs	Liver	Kidney	Spleen
Control	0.33±0.03	0.66±0.03	3.10±0.06	0.83±0.03	0.32±0.02
800mg/kg	033±0.02	0.68±0.03	3.08±0.12	0.80±0.3	0.36±0.02
400mg/kg	0.32±0.02	0.69±0.03	3.06±032	0.82±0.03	0.33±0.02
200mg/kg	0.34±0.03	0.77±0.06	3.10±0.15	0.86±0.03	0.34±0.02

*Significant, p<0.05

TABLE 2. MEAN BODY WEIGHT OF RATS TREATED WITH EXTRACT OF *L. cupaniodes.*

Treatment and dose	Mean body weight± S.E							Mean weight. gain/wk
	Day 1	Day 7	Day14	Day21	Day28	Day35	Day42	
Control	152.6	156.6	161.5	166.6	169.8	174.3	180.8	28.2
800mg/kg	155.5	157.7	161.9	167.3	171.6	176.5	181.5	29.0
400mg/kg	158.6	159.3	162.8	168.1	172.4	178.4	186.1	27.4
200mg/kg	157.7	158.6	161.5	167.8	172.8	178.1	185.3	27.7

TABLE 3. HEMATOLOGICAL STUDIES ON RATS AFTER SUB-CHRONIC TREATMENT WITH *L. cupaniodes.*

Treatment an d dose	RBC(x10^6)±SEM	Hb (g/dl) ± SEM	PVC(%)± SEM	WBC(x10^3)±SEM
Control	8.62±0.36	17.2±0.56	34.1±1.01	3.36±0.21
800mg/kg	8.15±0.40	17.7±0.61	34.0±1.23	2.98±0.32
400mg/kg	7.7±0.29*	17.6±0.60	34.6±1.05	2.95±0.29
200mg/kg	6.4±0.26*	17.1±0.59	34.1±1.40	2.93±0.39

*Significant, P<0.05

TABLE 4. QUANTITATIVE DATA ON WBC DIFFERENTIALS IN RATS AFTER SUB-CHRONIC TREATMENT WITH *L. cupaniodes*

Treatment and dose	NEUTROPHIL%	EOSINOPHIL%	BASOPHIL%	LYMPHOCYTE%	MONOCYTES%
Control	53.7±1.78	3.0±0.23	6.5±0.60	21.9±1.24	8.1±0.30
800mg/kg	52.2±1.56	13.8±0.86	6.6±0.72	22.1±1.68	6.9±0.18*
400mg/kg	48.2±2.01*	14.0±0.94	6.7±0.58	22.0±1.43	6.2±0.32*
200mg/kg	45.5±1.95*	14.8±0.79	6.8±0.64	22.5±1.54	5.4±0.28*

*Significant, P<0.05

TABLE 5. METABOLIC PARAMETERS AFTER SUB-CHRONIC TREATMENT WITH *L. cupaniodes*

TREATMENT AND DOSE FOR 6 WEEKS	ALP (U/L,405nm, 37^{0}C)	AST(U/L,340nm,37 ^{o}C)	URIC ACID (mg/dl,500nm,37^{o}C)	ALT (U/L, 340nm, 37 ^{0}C)
Control	330±10	16.0±1.02	1.78±0.19	31.8±1.78
800mg/kg	288±09	4.8±0.88	1.780.23	27.7±1.23*
400mg/kg	360±12	16.2±0.98	1.83±0.20	28.6±1.31
200mg/kg	530±09*	16.6±0.94	1.89±0.24	31.2±1.40

The aqueous root extract of *Lecaniodiscus cupaniodes* was found not to produce any serious toxicity or mortality when administered orally, up to 200 mg/kg, within 14 days of single treatment in mice. When given daily up to 45 days, neitmortality nor any visible signs of lethality were also observed in the rat, at the doses tested. The vital organs were not affected, except for the lungs of rats given 200 mg/kg. A notable insignificant reduction in the weight of the liver was observed, as doses increased (Table 1). This observation could be the reason behind the claim of administering the decoction of different part of the plant in traditional medicine to treat abnormal swelling cause by liver abscess. Chronic treatment caused by a significant ($p < 0.05$) reduction in RBC at doses of 400 mg/kg and 200 mg/kg, interestingly, without recording any significant changes in the PCV and Hb levels (Table 3). WBC counts revealed a significant decrease in neutrophil (at 400 mg/kg and 200 mg/kg; in monocytes at all doses tested (Table 4). This might be due to impossible anti-inflammatory activity of *Lecanodiscus cupaniodes,* though causes of neutropenia might include bone injury or infiltration of bone marrow by malignant cell or nutritional deficiency, monocytopenia has not been related to unknown clinical condition (Turgeon, 1993). Biochemical parameters such AST, ALT, ALP, and uric acid were not significantly altered compared with the control (Table 5). Significant changes in such classical enzymes ALP, ALT, and AST may suggest liver impairment since these are reliable indices of liver toxicity (Hayes, 1989), or altered integrity of cellular

membrane as well as cell lyses or death (Olagunju *et al.,* 2000). The decrease in liver enzymes suggests its use for treatment for acute hepatitis (Celia & Wilkinson, 1989). The significant increase in ALP, recorded at 200 mg/kg may, therefore may be attributable to altered metabolism of the skeletal muscle (Billing, 1978; Nerbely, 1982). These findings provide some basis about the safety of this plant where initial results suggest that aqueous root extract of this plant, especially at lower doses, may be safe. However, some of the result obtained suggests the need for further assessment and evaluation of the medicinal uses and safety, especially when administered for a much longer period.

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