Acute Toxicity Study of *Euphorbia heterophylla* in Normal Wistar Albino Rats

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Abstract

This study investigated the safe dosage range of aqueous extract of the aerial parts of *Euphorbia heterophylla* by acute toxicity study in wistar albino rats. Acute oral toxicity of aqueous extract of the aerial parts of *Euphorbia heterophylla* was evaluated adopting the guidelines and procedure of organization for Economic Cooperation and Development (OECD). Twenty five non-pregnant female wistar rats weighing 150g and 170g were obtained and were grouped into five groups five rats per group. Group 1 served as control. Group 2 was orally

administered 500 mg/kg b.wt for seven days. Group 3 was administered 1000 mg/kg b.wt. Group 4 was administered 1500 mg/kg b.wt while group 5 was administered 2000 mg/kg b.wt. The treated groups were observed for signs of toxicity and mortality for seven days after exposures to the extract. Signs of toxicity were observed and recorded following the methods and procedure of OECD. Haematological and biochemical parameter were evaluated and compared to the control group. Doses of the extract at 1500 mg/kg b.wt values for seven days exposure cause a significantly increased RBC (49.54±0.05 $X10^{12}$/L), PCV (49.54±0.05 %), Hb (25.36±0.06 g/dl), platelet count (268.45±0.10 X^9/L) and WBC (34.45±0.0 X^9/L) concentrations. Liver biomarkers, total protein (71.78±0.04 g/L), albumin (53.12±0.04 mmol/l), total bilirubin (7.44±0.01 mmol/l), concentrations were significantly decreased with respect to the control value. More so, the alkaline phosphatase (137.97±0.12 U/L), alanine amino transferase (37.94±0.45 U/L), aspartate transaminase (177.17±0.07 U/L) and gamma glutamyl transaminase (2.55±0.10 U/L) activities were significantly decreased following exposure to the extract at 1500 mg/kg b.wt and similar trend occurred with 2000 mg/kg treatment. Aqueous extract of *Euphorbia heterophylla* elicited a non-toxic effect at 500 and 1000. Toxicity effects was elicited at 1500 and 2000 mg/kg.

Keywords: Toxicity, *Euphorbia heterophylla* Liver biomarkers, Kidney biomarkers, lipid profile, Wistar albino rats

1. INTRODUCTION

Herbal therapies have been commonly used in rural areas for the treatment of numerous diseases, impairments and disorders (1). Survey stated that about 12% of the population in United States used herbal regiments as a complementary source in 1993 (2). Due to the fact that natural herbal treatment are being used in considerable amount against diseases, impairments and disorders, it is now the major focus of the researchers to conduct studies on efficacy and safety of medicinal plants (3). Plants that possess and elicit medicinal properties should have minimal toxicity due to their prolong used in human . Countless of medicinal plants have been shown to possess and elicit toxicity effects while yielding their pharmacological effects. In this present times, a considerable amount of modern drugs are produced from natural products of which many of them are dependent on using agents in traditional system of medicine (4). *Euphorbia heterophylla* is commonly known as desert milk weed which grows up to 2.5-6cm is used in traditional system of medicine for the treatment of several diseases, impairments and disorders (5). The plant is reported to possess and elicit diuretic and purgative effects in addition to its use in the treatment of liver damage, kidney dysfunction and proximal bronchial relaxation (6). The plant is used by traditional healers for the treatment of bacterial, plasmodial, gonorrhoeal and inflammatory diseases (7,8).

Several pharmacological substances and chemicals being used in today's life, have greatly increased to almost an innumerable amount. These are forms of chemical compounds found in food substances and other household products. These pharmacological chemical substances may lead to acute or chemical toxicity when used over a long period of time. Depending on the nature and concentration of the pharmacological substance and the effect may be mild (9). Acute toxicity could be explained as effects that are not desired which occur immediately or a period of seven days after the administration of a chemical agent (drug). It can occur within a short time

interval after administration of a single or multiple graded doses of a chemical agent which produced biochemical lesion that could alter the functioning of vital organs in the body (Enegide *et al*., 2013). The median lethal lethal dose of ethanol extract of E*uphorbia heterophylla* has been determined in mice by Nalule *et al.*, (2017). However, Wellington *et al*., (2019) investigated the chemical composition of phytochemicals and essential oil profile of *Euphorbia heterophylla*. Their evaluation showed that the plant is rich in bioactive ingredients or phytonutrients such as alkaloids, saponins, sterols, flavonoids, isopflavanoiods, anthraquinones, anthocyanins, lignans, terpenoids, and phenolic acids which are responsible for the medicinal or therapeutic properties elicited by the plant. This studies investigated the acute toxicity effect of four graded doses of aqueous extract of the aerial parts of *Euphorbia heterophylla* for seven days exposure to wistar albino rats based on the determine median lethal dose by (10).

II. METHODOLGY

1. PLANT COLLECTION AND PREPARATION OF PLANT EXTRACT

The fresh aerial parts of *E. heterophylla* were harvested from Obinze West Local Government Area Imo State. They were washed and air-dried under shade for five weeks . The dried aerial parts were pulverized into coarse powder. Two hundred and fifty grams (250 g) of the coars powdered sample was macerated in 500 ml of distilled water at room temperature for 72 hours. The mixture was filtered using a Whatzman filter paper grade 1 (542 mm) and the filtrate condensed while water molecules were evaporated to dryness using a rotary evaporator and water bath at 50˚C. The extract which weighed 85 g was stored in air-tight containers in a refrigerator until when required for analysis.

2. EXPERIMENTAL DESIGN

Twenty five (25) non-pregnant female wistar rats (nine weeks old) weighing between 150 and 170g were used for this study. The rats were obtained from the Biochemistry Animal House

University of Port Harcourt, Choba, Nigeria. They were grouped into five groups five rats per group. Group 1 was give *ad libitum* (Vet Store in Choba, Rivers State, Nigeria) and distilled water, serving as control. Group 2 was orally administered 500mg/kg b.wt of aqueous extract of *Euphorbia heterophylla, ad libitum* and distilled water for seven days. Group 3 was administered 1000 mg/kg b.wt of the extract, ad libitum and distilled water. Group 4 and 5 were administered 1500 and 2000 mg/kg b.wt of the extract, *ad libitum* and distilled water. The rats in the respective groups were observed for signs of toxicity for seven days and on the 8th day, the rats were sacrificed and blood samples were collected by cardiac puncture under anaesthesia with isoflurane and plasma was separated for biochemical and haematological evaluations. Vital organs were excised and preserved in 10% formalin for histological examination. Throughout the duration of the study the rats were maintained in Makrolon cages (model 1291, 425x266x185mm^3, 185mm^3, 800cm^2) under controlled environment conditions (temperature of (23 - 26 ^{o}C), humidity 45 - 55%, 12/12-h light/dark cycle. The rats were given ad libitum following the OECD Test Guide 425, non-pregnant female wistar albino rats. The animal investigation procedures were approved by the Ethical Committee of University of Port Harcourt.

3. BIOCHEMICAL AND HAEMATOLOGICAL ASSAYS.

Urea, creatinine, sodium ion (Na^+), potassium ion (K^+), chloride ion (Cl^-), total protein, albumin, total bilirubin, alkaline phosphatase (ALP), alanine amino transferase (ALT), aspartate transaminase (AST) and gamma glutamyl transferase (GGT), hemoglobin (Hb), total RBC, packed cell volume (PVC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), platelet count, white blood cells (WBC) count were measured by using Randox kits.

4. HISTOLOGICAL STUDY

The vital organs isolated from sacrificed rats were liver and kidney and were fixed in 10% formalin, then after processing embedded in paraffin wax. Paraffin sections were made at 5 mm and stained with hematoxylin and eosin. The slides were studied under a light microscope and captured the magnified images of tissues structure for further study.

5. STATISTICAL ANALYSIS

Data expressed as means ± standard deviation (M ±SD were analyzed using Statistical Package foe Social Sciences (SPSS) for window version 16 USA. Descriptive statistics was done by one way analysis of variance (ANOVA) and multiple comparison was done using Turkey Post hoc at ($p \leq 0.05$) confidence interval.

III. RESULTS

Mortality did not occur following oral administration of the extract at 500, 1000, 1500 and 2000 mg/kg b.wt even though the signs of acute toxicity were observed, measured and written as of behavioural patterns. Observations were recorded on regular bases morning and evening throughout the study period. All results are as follows:

1. BEHAVIOURAL PATTERN

Behavioural observation of the test animals after oral administration of 500mg/kg of the extract showed increased sleep from day 1-2, 1000 mg/kg showed increased sleep and salivation from day 1-4, 1500mg/kg treated showed increased sleep from day 1-4, salivation and urination and 2000 mg/kg showed increased sleep, urination and salivation from day 1-5 as presented in Table 1-5.

Table 1 Observation of the control and 500mg/kg extract treated group

Parameter	Da1		Day2		Day3		Day4		Day5		Day6		Day7	
	C	T_1	N	T_1	N	T_1	N	T_1	N	T_1	N	T_1	N	T_1
Fur and skin	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Eyes	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Salivation	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Respiration	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Urination	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Faeces														
Consistency	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni
Sleep	N	*	Ni	*	N	N	N	N	N	N	N	N	N	N
Mortality	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Key: C= control, T_1=treated, Ni=not found, N=normal, *=increased sleep

Table 2 Observation of the control and 1000 mg/kg extract treated group

Parameter	Da1		Day2		Day3		Day4		Day5		Day6		Day7	
	C	T_1	N	T_1	N	T_1	N	T_1	N	T_1	N	T_1	N	T_1
Fur and skin	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Eyes	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Salivation	N	S	N	S	N	S	N	N	N	N	N	N	N	N
Respiration	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Urination	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Faeces														
Consistency	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni
Sleep	N	*	Ni	*	N	*	N	*	N	N	N	N	N	N
Mortality	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Key: C= control, T_1=treated, Ni=not found, N=normal, *=increased sleep , S=saliva occurred

Table 3 :Observation of the control and 1500 mg/kg extract treated group

Parameter	Da1		Day2		Day3		Day4		Day5		Day6		Day7	
	C	T_1	N	T_1	N	T_1	N	T_1	N	T_1	N	T_1	N	T_1
Fur and skin	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Eyes	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Salivation	N	S*	N	S*	N	S*	N	S*	N	N	N	N	N	N
Respiration	N	N*	N	N*	N	N*	N	N	N	N	N	N	N	N
Urination	N	P	N	P	N	N	N	N	N	N	N	N	N	N
Faeces														
Consistency	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni
Sleep	N	*	N	*	N	*	N	*	N	*	N	N	N	N
Mortality	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Key: C= control, T_1=treated, Ni=not found, N=normal, *=increased sleep, S*=increase saliva occurred, N*=respiration, P=increased urination

Table 4 Observation of the control and 2000 mg/kg extract treated group

Parameter	Da1		Day2		Day3		Day4		Day5		Day6		Day7	
	C	T_1	N	T_1	N	T_1	N	T_1	N	T_1	N	T_1	N	T_1
Fur and skin	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Eyes	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Salivation	N	S*	N	S*	N	S*	N	S*	N	S*	N	N	N	N
Respiration	N	N*	N	N*	N	N*	N	N	N	N	N	N	N	N
Urination	N	P	N	P	N	P	N	P	N	P	N	N	N	N
Faeces														
Consistency	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Convulsion	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni	Ni
Sleep	N	*	N	*	N	*	N	*	N	*	N	N	N	N

Mortality	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Key: C= control, T_1=treated, Ni=not found, N=normal, *=increased sleep , S*=increase saliva occurred, N*=respiration, P=increased urination

2. EFFECT OF AQUEOUS EXTRACT OF THE AERIAL PARTS OF *EUPHORBIA HETEROPHYLLA* ON THE PLASMA HAEMATOLOGICAL PARAMETERS .

The results of the effect of aqueous extract of the aerial parts of *Euphorbia heterophylla* on the haematological parameters of wistar albino rats are presented in Table 5 and 6. Oral administration of the extract at 500, 1000, 1500 and 2000 mg /kg b.wt for seven days exposure cause a significantly increased RBC, PCV, Hb, platelet count and WBC concentrations when compared to the control value as shown in Table 5. The most significant effects were observed in group 4 and 5 orally administered 1500 and 2000 mg/kg b.wt of the extract. The plasma concentrations of MCV, MCH and MCHC were significantly increased following exposure to the extract for seven days and the most significantly increased levels were observed in group 4 and 5 orally administered 1500 and 2000 mg/kg b.wt when compared to the control values as shown in Table 6. Similar trends were also noted on the plasma concentrations of Haematocrit, haemoglobin, MCH, MCHC, RDW and WBC.

Table 5 The effect of aqueous extract of the aerial parts of *Euphorbia heterophylla* on the plasma haematological parameters of wistar albino rats

Group	RBC($X10^{12}$/L)	PCV (%)	Hb (g/dl)	Platelet($X10^{9}$/L)	WBC($X10^{9}$/L)
Control	7.19±0.05[a]	47.72±0.06[a]	23.98±.07[a]	200.66±0.03[a]	21.18±0.02[a]
500mg/kg	7.98±0.08[abc]	48.19±0.05[abc]	24.04±0.03[abc]	224.33±0.04[abc]	23.30±0.03[abc]
1000mg/kg	8.24±0.06[abc]	48.98±0.02[abc]	24.88±0.03[abc]	237.04±0.1[abc]	27.00±0.04[abc]
1500mg/kg	8.77±0.03[abc]	49.54±0.05[abc]	25.36±0.06[abc]	268.45±0.10[abc]	34.45±0.04[abc]
2000mg/kg	9.50±0.06[abc]	50.02±0.05[abc]	26..24±0.04[abc]	295.80±0.12[abc]	41.88±0.04[abc]

Data are reported as mean ± standard Deviation (M ± SD), n =5. Values bearing similar Superscript"[(abc)]" down the group are significantly ($p \leq 0.05$) different from the control.

Table 6 Effect of aqueous extract of the aerial parts of *Euphorbia heterophylla* on red blood cell indices of wistar albino rats

Group	MCV (fl)	MCH (Pg)	MCHC(g/dl)
Control	70.46±1.19[a]	23.26± 12.08[a]	41.02± 0.l1[a]
500mg/kg	71.23± 1.23[abc]	24.74± 0.19[abc]	37.91± 0.23[abc]
1000mg/kg	72.07± 0.02[abc]	29.65± 9.00[abc]	37.78± 0.04[abc]
1500mg/kg	77.22± 0.30[abc]	33.56± 0.29[abc]	34.01± 0.20[abc]

2000mg/kg	85.12± 9.00^{abc}	38.21± 12.01^{abc}	34.76± 0.33^{abc}

Data are reported as mean ± standard Deviation (M ± SD), n =5. Values bearing similar Superscript"$^{(abc)}$" down the group are significantly ($p \leq 0.05$) different from the control.

3. EFFECT OF SEVEN DAYS EXPOSURE TO AQUEOUS EXTRACT OF THE AERIAL PARTS OF *EUPHORBIA HETEROPHYLLA* ON BIOCHEMICAL PARAMETERS

The effects of exposure to aqueous extract of the aerial parts of *Euphorbia heterophylla* on biochemical parameters is shown in Table 7 and 8. Kidney Na^+, K^+, Cl^-, urea and creatinine biomarkers concentrations were significantly increased following exposure to the extract for seven days particularly at 1500 and 2000 mg/kg b.wt when compared to the control values as shown in Table 7. Liver total protein and albumin biomarkers concentrations were significantly decreased following exposure to the extract from group 2-5 when compared to the control values as shown in Table 8. While total bilirubin concentration, ALP, ALT, AST and GGT activities were significantly decreased following exposure of the extract from group 2-5 when compared to the control values as shown in Table 8.

Table 7 Effect of aqueous extract of *Euphorbia heterophylla* on kidney biomarkers of wistar albino

Group	Na^+ (mmo/l)	K^+ (mmol/l)	Cl^- (mmol/l)	Urea (mmol/l)	Creatinine (mmol/l)
Control	141.20 ± 2.09^{a}	3.00 ± 0.02^{a}	77.12 ± 2.05^{a}	4.25 ± 0.02^{a}	0.5 ± 1.08^{a}
500mg/kg	146 ± 1.03^{abc}	3.46 ± 1.13^{abc}	95.33 ± 0.11^{abc}	4.87 ± 0.05^{abc}	0.5 ± 3.01^{a}
1000mg/kg	149 ± 12.0^{abc}	4.00 ± 2.02^{abc}	100.12 ± 0.05^{abc}	5.02 ± 11.02^{abc}	0.6 ± 0.00^{abc}
1500mg/kg	155 ± 0.00^{abc}	6.68 ± 0.14^{abc}	143.04 ± 11.07^{abc}	5.25 ± 0.25^{abc}	0.7 ± 1.08^{abc}
2000mg/kg	162 ± 1.02^{abc}	8.00 ± 0.01^{abc}	162.61 ± 0.00^{abc}	5.77 ± 0.34^{abc}	0.7 ± 12.02^{abc}

Data are reported as mean ± standard Deviation (M ± SD), n =5. Values with the Superscript"$^{(abc)}$" down the group are significantly ($p\leq0.05$) different from normal and constipated control.

Table 8 Effect of aqueous extract of the aerial parts of *Euphorbia heterophylla* on liver biomarkers of wistar albino rats

Group	TP (g/l)	ALB (mmol/l)	TBIL (µmol/L)	ALP (U/L)	ALT (U/L)	AST (U/L)	GGT (U/L)

Control	63.01±0.02[a]	43.51±0.2[a]	8.0±0.02[a]	135.91±1.1[a]	41.60±1.5[a]	175.40±2.0[a]	2.98±0.0[a]
500mg/kg	63.78±0.04[bc]	43.23±0.0[a]	7.87±0.03[b]	135.16±0.0[b]	41.12±0.0[bc]	175.42±0.0[a]	2.95±0.0[a]
1000mg/kg	67.21±0.04[b]	43.45±0.04[a]	7.44±0.01[b]	134.88 ±0.1[b]	38.77±0.12[b]	175.69±1.09[b]	2.93±0.2[a]
1500mg/kg	71.78±0.04[b]	53.12±0.04[b]	7.02±0.01[b]	137.97±0.12[b]	37.94±0.4[b]	177.17±0.0[b]	2.55±0.1[b]
2000mg/kg	75.00±0.07[b]	57.37±0.05[b]	6.64±0.02[b]	141.20±3.11[b]	76.41±0.1[b]	184.34±0.0[b]	2.32±0.0[b]

TP: total protein, ALB: albumin, TBIL: total bilirubin, ALP: alkaline phosphatase, ALT: alanine amino transferase, AST: aspartate transaminase, GGT: gamma glutamyl transferase.Data are reported as mean ± standard Deviation (M ± SD), n =5. Values with the Superscript"[(bc)]" down the group are significantly ($p \leq 0.05$) different from normal and constipated control.

Table 9 Effect of aqueous extract of the aerial parts of *E. heterophylla* on lipid profile of albino wistar rats.

Group	Total CHOL (mg/dl)	HDL-CHOL (mg/dl)	LDL-CHOL (mg/dl)	VLDL-CHOL (mg/dl)	Triglyceride (mg/dl)
Control	73.32±0.08[a]	47.24± 0.57[a]	49.23± 0.07[a]	8.51± 0.09[a]	42.52± 0.03[a]
500 mg/kg	73.36± 0.05[a]	47.24± 0.57[a]	49.28± 0.07[a]	8.53± 0.05[a]	42.71± 0.03[ab]
1000 mg/kg	73.52± 0.03[a]	47.87± 0.03[a]	49.79± 0.03[a]	8.62.52±0.03[a]	42.82± 0.03[ab]
1500 mg/kg	77.09± 0.13[ab]	44.52± 0.17[ab]	51.52± 0.02[ab]	9.04± 1.11[ab]	39.12± 0.05[ab]

2000 mg/kg	77.92± 1.04 [ab]	44.78± 2.01 [ab]	52.12± 0.07 [ab]	9.52± 0.06 [ab]	39.78± 0.03 [ab]

Data are reported as mean ± standard Deviation (M ± SD), n =5. Data are reported as mean ± standard Deviation (M ± SD), n =5. Values bearing similar Superscript"[(ab)]" down the group are significantly ($p \leq 0.05$) different from the control ("[a]").

IV. DISCUSSION OF FINDINGS

Adverse changes including behavioural patterns usually occure following a short or single period of exposure to a chemical substance or drug when investigating safe doses in rats and also in humans following treatment of illnesses (11). Administration of a single or multiple graded doses of a chemical agent via the oral cavity for a period of 24h or days can produce a functional impairment of vital organs and biochemical lesions that may in turn affect the performance of an organism (11). In this study, the moderate sleep and salivation following exposure to the extract at 500 and 1000 mg/kg b.wt from day 1-2 and 1-4 were indicative of non-toxic effect of the extract at 500 and 1000 mg/kg b.wt while the increased sleep, salivation and urination following exposure to the extract at 1500 and 2000 mg/kg b.wt were indicative acute toxicity yet mortality was did not occur. The toxicity effects observed following exposure to the extract at 1500 and 2000 mg/kg b.wt is mainly due to closeness of these doses to the median lethal of the extract (2244 mg/kg) as determined by Nalule *et al.*, (2017) which agrees with the report of Sabiu *et al*., (2016) on the toxicological implication of ethanol leaf extract of *Morrella serata* in rats. However, the significantly increased RBC, PCV, Hb, platelet count and WBC concentrations observed when compared to the control values as shown in Table 5 were indicative of anti-anaemic effect facilitated by exposure to aqueous extract of *Euphoria heterophylla* for seven days. This is in line with the report of (12) the pharmacological assessment of anti-anaemic

activity of aqueous leaves extract of *Telfairia occidentalis* and Spondias mombin in rats. RBC shows the magnitude of MCV and concentration of Hb such as MCH and MCHC of the RBC which helps in establishment of the diagnosis of anaemia (11). However, the increased concentrations of MCV, MCH and MCHC following exposure to the extract particularly at 1500 and 2000 mg/kg body weight is reflective of the onset of anti-normocytic anaemia effect which is also in consistency with the claim made by Sylvester (12) as stated above. This could ascribed to the capacity of the extract to stimulate and enhance bone erythropoiesis and this could be one of the reason the plant is used as blood booster in traditional system of medicine against anaemic condition. . Immediate decrease in serum urea, creatinine and electrolytes concentration occur in renal insufficiency (13). In this study, the significant increases observed in the plasma urea, creatinine, Na^+, K^+ and Cl^- were reflective of the capacity of aqueous extract of the aerial parts of *Euphorbia heterophylla* to stimulate the release of electrolytes and enhancement of the functional capacity of the glomerula filtration rate (GFR) in the metabolism of urea and creatinine. These results are in agreement with the report of (14) on the amelioration of cisplatin-induced nephrotoxicity by extracts of *Hemidesmus indicus and Acorus calamus.*

Elevated serum levels of total protein, albumin, ALP, AST, ALT and GGT activities is associated with severe liver toxicity and injury to the muscles as well as other impairments [15]. In this research, the significantly increased plasma total protein and albumin concentrations and decreased ALP, ALT, AST and GGT activities when compared to the control value following exposure to the extract is reflective of the capacity of the extract in the enhancement of liver functional capacity. This is in line with work of (15) on the ameliorative effect of methanol extract of *Rumex vesicarius* on CCl4-induced liver damage in wistar albino rats. Also, dose at

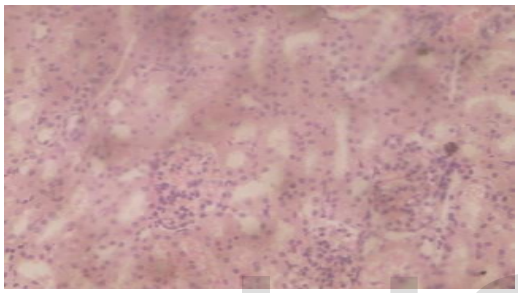
500 and 1000 mg/kg showed very little toxicity signs while treatment at 1500 and 2000 mg/kg showed increased salivation, tremor, urination from 1-5 but mortality did not occur.

Exposure of rats to 1500 and 2000 mg/kg of aqueous extract of the aerial parts of *Euphorbia heterophylla* significantly increases on the plasma levels of low density lipoprotein (LDL) and very low density lipoprotein cholesterol (VLDL). The significantly increased plasma levels of LDL and VLDLD cholesterols observed following exposure of rats to 1500 and 2000 mg/kg is indicative of toxicity effects of the extract at the stated doses when compared to the control value which means treatment of diseases or any complication using therapeutic agents designed from *Euphorbia heterophylla* will cause minimal side effects while eliciting it therapeutic effects. Also, significant decrease were observed on the plasma high density lipoprotein cholesterol (HDL) and triglyceride levels at same doses of the extract which is also indicative of toxicity of the extract at 1500 and 2000 mg/kg. This is agreement with the report of (16) on acute oral toxicity evaluation of aqueous ethanolic extract of *Saccharum munja* Roxb roots in albino mice as per OECD 425 TG.

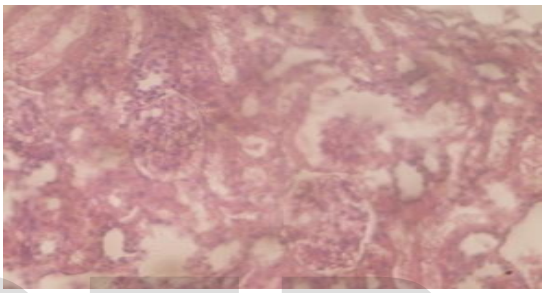
Histological examination of the kidney and liver of rats exposed to 500, 1000 and 1500 mg/kg body weight of the extract shown improvement on the kidney architecture when compared to the control. But treatment at 2000 mg/kg b.wt resulted in disruption and interrupted architecture of the liver and kidney, severe inflammation, distended Bowman's capsule and mild glomerulosclerosis which is also responsible for significantly increased electrolytes, urea and creatinine concentration, ALP, ALT and GGT activities. The disruption and interrupted architecture of the liver and kidney, severe inflammation, distended Bowman's capsule and mild glomerulosclerosis facilitated by exposure to 2000 mg/kg b.wt which is reflective of toxicity

effects. This is also in line with (16) report on acute oral toxicity evaluation of aqueous ethanolic extract of *Saccharum munja* Roxb. roots in albino mice as per OECD 425 TG.

Effect of Aqueous Extract of the Aerial Parts of *E. heterophylla* on the Histology of the Kidney and Liver of Wistar Albino Rats for Seven Exposures

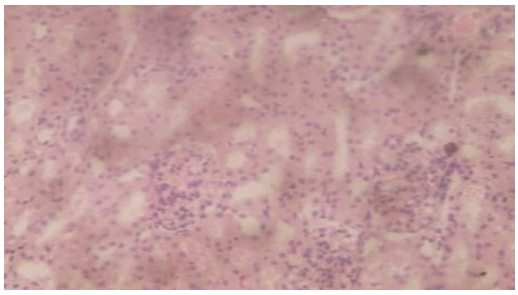


A

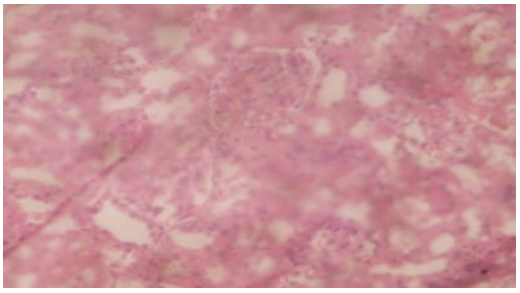


B

Figure 1: Histological presentation histology of the kidney of untreated control wistar albino rat A and at 500 mg/kg body weight rat B, magnification x 10. The control showing normal architecture with no pathology and B orally administered with 500 mg/kg body weight of aqueous extract of the aerial parts of *Euphorbia heterophylla* showing improved architecture of the kidney with no pathology.

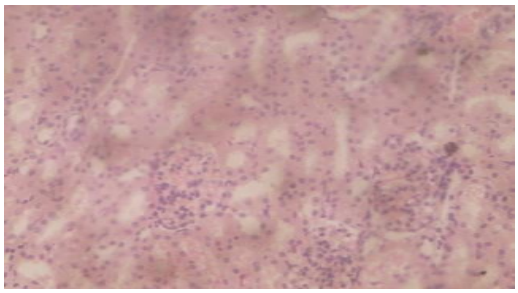


C

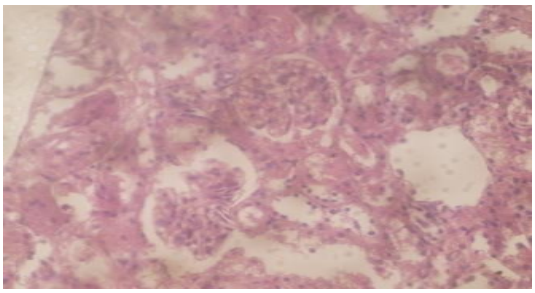


D

Figure 2: Histological presentation histology of the kidney of untreated control wistar albino rat C and at 1000mg/kg body weight rat D, magnification x 10. The control showing normal architecture with no pathology while 1000mg/kg body weight treatment showing a more improved capsular lining and renal tubule.

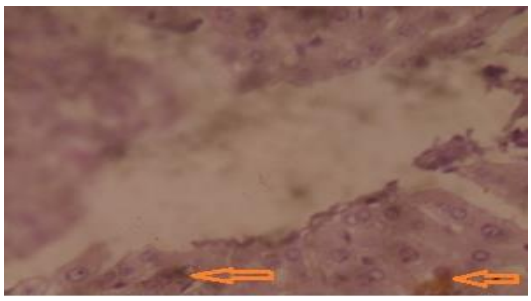


E

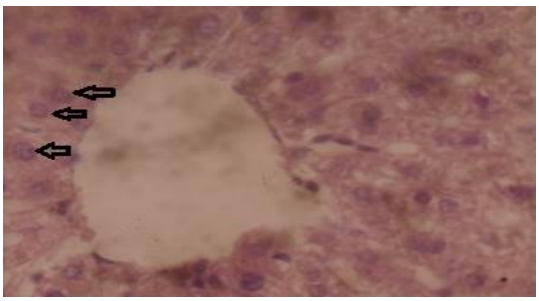


F

Figure 3: Histological presentation histology of the kidney of untreated control wistar albino rat which received feed and distilled water for seven days and 2000 mg/kg body weight rat F, magnification x10. The control showing normal architecture with no pathology while the 2000 mg/kg body weight treatment showing interrupted architecture, severe inflammation, glomerulosclerosis and distended Bowman's capsule



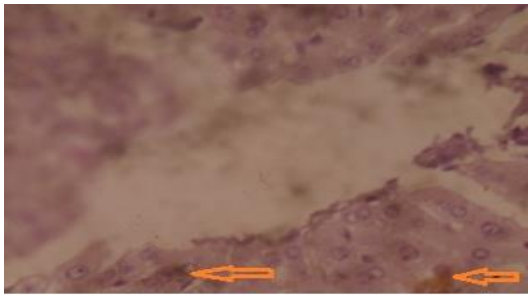
G



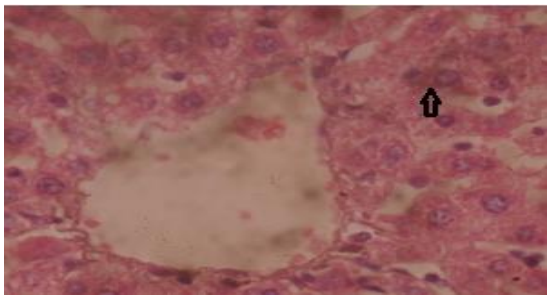
H

Plate 4: Histological presentation histology of the liver of untreated control wistar albino rat G and at 1000 mg/kg body weight rat H, magnification x10. Liver of the control showing normal

central vein, cords of hepatocytes with no pathology which received distilled water and feed for three days. H orally administered 1000 mg/kg body weight of aqueous extract of the aerial parts of *Euphorbia heterophylla* shows distended central vein, hepatic cords, with fewer normal kuffer cells

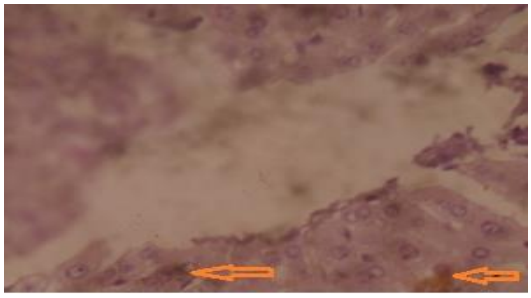


I

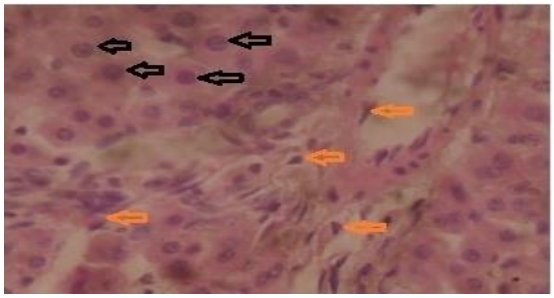


J

Plate 5: Histological presentation histology of the liver of untreated control wistar albino rat I and at 1500 mg/kg body weight rat J, magnification x10. Liver of the control showing normal central vein, cords of hepatocytes with no pathology which received distilled water and feed for three days. While J treated with 1500 mg/kg showing histology of the liver of rat administered 1500mg/kg body weight of aqueous extract of the aerial parts of *Euphorbia heterophylla* for seven days showing inflamed hepatic cords, inflamed kufer cell with higher level of hepatocellular necrosis.



K



L

Plate 6: Histological presentation histology of the liver of untreated control wistar albino rat I and at 2000mg/kg body weight rat J, magnification x10. Liver of the control showing normal central vein, cords of hepatocytes with no pathology which received distilled water and feed for three days. While L orally administered with 2000 mg/kg body weight of aqueous extract of the aerial parts of *Euphorbia heterophylla* with increased inflammation, rupture Central vein, severe hepatocellular necrosis.

CONCLUSION

Exposure of wistar albino rats to aqueous extract of the aerial parts of *Euphorbia heterophylla* resulted in elevated levels of the plasma haematological parameters, electrolytes, liver enzyme activities and improvement on the architecture of both the kidney and liver on histological examination.. Altered kidney and liver architecture occurred for 2000 mg/kg treatment which is mainly due toxicity of the extract which also led to increased sleep rate, urination and salivation. However, doses at 500 and 1000 mg/kg body weight were safe for treatment.

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CONFLICT OF INTEREST

The authors declare that they do not have any conflicts of interest with the content of this article.

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