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Sub-acute toxicity profile of methanolic leaf extract of *Securidaca longipedunculata* in rats

Sadiq, F. U[*1]., Abalaka, M.E[1]. and Babayi, H[1].
*,[1]Department of Microbiology, School of Life Sciences,
Federal University of Technology, Minna, Niger State, Nigeria.
E-mail: fawziyyahsadi@gmail.com

Abstract
This study investigates the toxicological profile of *Securidaca longipedunculata*in rats. Sub-acute toxicity study was conducted by oral administration of the extracts to rats at daily doses of 25, 50 and 100mg/kg body weight for 28 days. Methanol leaf extract of *S. longipedunculata* caused significant ($p< 0.05$) increase in serum urea, creatinine, sodium & proteins but significantly ($p< 0.05$) decreased the serum alkaline phosphatase (ALP) and cholesterol concentration when compared with the controls. However, there was no significant ($p> 0.05$) difference in serum aspartate transaminase (AST), alanine transaminase (ALT), potassium, triglyceride albumin and bilirubin concentration when compared with control. Jobelyn and dexamethazone caused significant ($p< 0.05$) increase in serum AST, urea, triglycerides, sodium and protein. Dexamethazone caused significant increase ($p<0.05$) in bilirubin, cholesterol, and a decrease in serum ALP and creatinine concentration when compared with the control. The extract also had no significant ($p>0.05$) effect on hematological parameters except for a significant increase ($p<0.05$) in white blood cells when compared with the normal control. The plant extracts have shown no serious adverse effect on hematological and biochemical parameters. Thus, *S. longipedunculata* methanol leaf extract could be considered as a natural source of antibiotics for therapeutic purposes.
Keywords:dexamethasone, therapeutic, hematological, *Securidaca, longipedunculata*

INTRODUCTION

Many plant products contain active chemical compounds such as tannins, flavonoids, alkaloids, phenols, saponins, essential oils and other aromatic compounds, which have antimicrobial and physiologically active principles that are useful to both man and animals (Talib and Mahasneh, 2010). These plant products have proved useful both in their crude and pure forms in traditional practice for the treatment of various ailments.

Though effective, the practice has however remained crude because doses are mostly not quantified and dosage prescription is usually in form of aqueous decoctions and unduly bulky powders (Abalaka *et al*., 2011). Even with the extensive usage of herbal drugs, less than ten percent of herbal products in the world market are standardized to known active components (Sahoo and Manchikanti, 2013). Lack of specific evaluation on toxicity of herbal drugs could lead to serious complications (Yakubu*et al*., 2012).

The growing interest in herbal medicine therefore demands toxicity risk assessment of the various indigenous preparations used in the treatment of diseases. *S.longipedunculata*(violet tree) is an important plant specie with potential benefits in the treatment of various diseases including those caused by microorganisms (Kamba and Hassan, 2010; Auwal*et al*., 2012). Though extracts from this species are suggested to have little toxicity at low concentrations (Kamba and Hassan, 2010; Auwal*et al*., 2012), further efforts are required to investigate the potential toxicity of *S. longipedunculata*. Therefore, the study is designed to evaluate the toxicity of *S. longipedunculata* in rats.

MATERIALS AND METHODS

Toxicological evaluation of crude methanol leafextract of *S. longipedunculata*

Healthy albino rats of average weight 120-150g were purchased from Department of Biochemistry, Federal University of Technology, Minna, Niger State, Nigeria. The rats were kept in clean plastic cages and were allowed access to rat pellets and water.Theywere maintained under standard laboratory conditions in the laboratory and the cages were cleaned and disinfected regularly.The study was carried out according to the Guidelines for the Care and the Use of Laboratory Animals of the Institute of Laboratory Animal Resources, Commission of Life Sciences, National Research Council, USA (ILAS, 1997). The studies included the determination of LD_{50}, evaluation of the effects of the extract on hematological and plasma biochemical parameters.

Acute toxicity study (LD_{50})

The acute toxicity study was conducted as described by Aniague*t al*. (2004). The acute toxicity study was conducted to observe the range of toxicity so the proper dose level could be established. The study was conducted in two phases. In the first phase, nine rats were divided into 3 groups of 3 rats each. Groups 1, 2 and 3 animals were given 10, 500 and 1000mg/kg body weight of the *S. longipedunculata* methanol leaf (Lm) extract respectively. In the second phase, the experiment was set up like the first phase but with the oral administration of 1600, 2900 and 5000mg/kg body weight of the Lmextract to groups 1, 2, and 3 with each group containing three rats each. In both phases of the experiment, the animals were observed 24 hourly for 14 days for physiological changes. The volume of extract to be administered based on the weight of the rat was calculated with the formula below;

$$\text{Volume } (cm^3) = \frac{\text{Weight of animal (g) x Dose to administer (mg)}}{\text{Concentration (mg/ml) } f} * 100g$$

Sub-chronic toxicity study

This study was carried out according to the method employed by Aniague*t al*. (2004).Thirty wistar rats (30) were selected for the sub-chronic toxicity study. They were divided into six groups of five rats each. Three groups were given 25, 50 and 100 mg/kgbw of crude methanol leaf extract orally for 28 days, while the 4th group served as immune suppressant group which was administered with dexamethazone dose (3 mg/kgbw). The 5th served as immune stimulant group administered with jobelyn dose (4.17 mg/kgbw), while the 6th wascontrol and were only fed with water. The rats were weighed before the commencement of treatment. Thereafter, they were weighed weekly throughout the duration of the study. At the end of the study, the animals were sacrificed.

Determination of weekly body weight and relative organ weight

The body weights of the rats were taken weeklyin the course of the experiment and after the experiment. The weight gains were computed as follows:

$$\text{Weight gain} = \text{Final weight of rat (g)} - \text{Initial weight of rat (g)}$$

The relative organ weight (ROW) was calculated as follows:

$$\text{ROW} = \frac{\text{Absolute Organ Weight (kg)}}{\text{Body Weight of Rat on Sacrifice Day (kg)}} * \frac{100}{1}$$

Collection of blood sample and isolation of the tissues from rat

Blood samples were collected from each of the sacrificed animals. Briefly, the animals were anaesthetized with diethyl ether. The jugular vein was carefully cut to obtain blood, which was collected into heparinised and EDTA bottles for biochemical and haematological parameters respectively. For obtaining the plasma sample necessary to analyse the biochemical parameters, the blood collected into heparinised or non-EDTA bottles were centrifuged at 3000 revolutions per minute (rpm) for 15 minutes. The plasma samples were collected and kept in a freezer until they were analyzed for the biochemical parameters. The blood samples collected into EDTA bottles were analyzed immediately for haematological indices viathe automated hematologic analyzer (model number: SYSMEX KX21), a product of SYSMEX Corporation, Japan. The methods described by To (2002) were adopted for the analysis.

The sacrificed animals were also dissected and their organs (kidney, liver, heart and spleen) were collected, washed in normal saline, weighed and fixed in 10% formalin solution in order to assess the general toxicity of the extract. The relative organ weights were later computed and recorded.

Estimation of liver function indices

The effect of the Lm extract on plasma biochemical parameters including (alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), total cholesterol (TC), high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, triglycerides (TG), urea and creatinine levels were determined using commercial kits obtained from Radox laboratory, UK.

RESULTS

Acute oraltoxicity (LD_{50})

The result presented in Table 1 shows the acute toxicity profile of methanol leaf extract of *Securidaca longipedunculata* in rats. No death was recorded up to the doses of 5000 mg/kgbw. Thus, the LD_{50} is greater than 5000 mg/kgbw in rats. Oral administration of the extract at 1600mg/kgbw was accompanied with general calmness and the animals were devoid of any unusual behaviour or activity. However, abnormal signs such as slight irritability and poor feeding began to manifest at a dose of 2900mg/ kgbw.

Table 1: Acute oral toxicity profile of methanolic leaf extract (Lm) of *Securidacalongipedunculata*in Rats

Dose (mg/kgbw)	Observations	Mortality
10	Animals showed no apparent change in appearance and activity.	$0/_3$
100	Animals were calm and devoid of unusual reactions	$0/_3$
1000	Animals showed no apparent changes in appearance and activity.	$0/_3$
1600	Animals showed no apparent changes in appearance and activity	$0/_3$
2900	Animals had sustained agitation, decreased feed intake and intense skin redness	$0/_3$
5000	Animals had intense skin redness and disorientation.	$0/_3$

mg/kgbw: milligram per kilogram body weight

Effect of methanolic leaf extract of *S. longipedunculata* on liver function indices in rats

Table 2 shows the effect of the methanol leaf extract (25mg/kgbw, 50mg/kgbw and 100mg/kgbw) on liver function indices (ASP, ALP, ALT, Protein, Albumin, Bilirubin) in rats. The methanol leaf extract of *S. longipedunculata* caused significant ($p< 0.05$) decrease in the serum ALP levels whencompared with the control rats. There was no significant ($p> 0.05$) difference in serum AST and ALT levels in rat administered with Lm extract of *S. longipedunculata* (25, 50 and 100 mg/kg bw) when compared with control. However, Jobelyn and dexamethazonecaused significant ($p< 0.05$) increase in serum AST, when compared with the control while dexamethazone caused significant decrease ($p<0.05$) in ALP levels when compared with the control rats.

The Lm extract of *S. longipedunculata* caused significant ($p< 0.05$) increase in serum proteins whencompared with the control rats. However, there was no significant ($p> 0.05$) difference in serum albumin and bilirubin concentration in rat administered with Lm extract of *S. longipedunculata* (25, 50 and 100 mg/kg b.wt) when compared with control. Jobelyn and dexamethazone also caused significant ($p< 0.05$) increase in serum protein when compared with the control. Dexamethazone caused further increase ($p<0.05$) in bilirubin concentration when compared with the control.

Effect of methanolic leaf extractof *S. longipedunculata* on kidney function indices in rats

Table 3 shows the effects of methanolic leaf extract of *S. longipedunculata*at 25mg/kgbw, 50mg/kgbw and 100mg/kgbw on kidney function indices (urea, creatinine, sodium and potassium ions) in rats following oral administration for 28 days. The methanol leaf extract of *S. longipedunculata* caused significant ($p< 0.05$) increase in serum urea and creatinine concentration whencompared with the control rats. Jobelyn and dexamethazone caused significant ($p< 0.05$) increase in urea concentrations when compared with the control.

However, dexamethazone caused a decrease ($p<0.05$) in creatinine concentration when compared with the control. The Lm extract of *S. longipedunculata* caused significant ($p< 0.05$) increase in serum sodium. However, there was no significant ($p> 0.05$) difference in serum potassium concentration in rat administered withLm extract of *S. longipedunculata* (25, 50 and 100 mg/kg bw) when compared with control. Jobelyn and dexamethazonealso significantly ($p< 0.05$) increased the serum sodium concentrations when compared with the control.

Table 2: Effect of methanolic leaf extract of *S. longipedunculata* on the liver function indices in rats

	Treatment (mg/kgbw)					
Liver function indices	25	50	100	Dexamethaz. (3)	Jobelyn (4.17)	Control
AST (U/L)	7.00±2.55^{c}	7.90±0.99^{c}	7.80±0.85^{c}	14.4±0.00^{b}	19.90±2.40^{a}	6.90±0.42^{c}
ALT (U/L)	113.40±3.11^{a}	107.50±2.12^{a}	106.40±1.13^{a}	104.60±1.41^{a}	109.40±0.00^{a}	108.55±1.34^{a}
ALP (U/L)	55.75±1.06^{b}	53.75±1.77^{b}	35.00±3.54^{c}	57.50±3.54^{b}	55.00±0.00^{b}	85.00±3.54^{a}
Protein (g/dl)	21.85±4.03^{a}	13.30±2.69^{b}	14.25±6.72^{b}	14.25±1.34^{b}	19.00±2.69^{ab}	8.55±1.34^{c}
Albumin (mmol/l)	3.80±1.13^{a}	2.55±0.21^{a}	2.75±0.49^{a}	2.80±0.57^{a}	3.85±1.20^{a}	2.60±0.28^{a}
Bilirubin (mmol/l)	4.58±1.01^{b}	3.84±0.34^{b}	5.33±3.10^{a}	3.09±0.26^{b}	4.85±1.24^{b}	3.84±0.41^{b}

Values are mean ± SD of three determinants. Values with different superscripts across the same row are significantly different from each other at P<0.05.

Table 3 Effect of methanolic leaf extract of *S. longipedunculata*on the kidney function indices in rats

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	Treatment (mg/kgbw)					
Kidney Function Indices	25	50	100	Dexamethaz. (3)	Jobelyn (4.17)	Control
Urea (mg/dl)	44.27±3.19^{d}	46.36±2.56^{cd}	53.43±1.99^{b}	66.62±4.36^{a}	51.76±2.17^{bc}	36.89±0.00^{c}
Creatine (mmol/l)	3.15±0.49^{a}	3.50±0.00^{a}	3.30±0.28^{a}	0.50±0.00^{c}	1.70±0.28^{b}	1.50±0.00^{b}
Sodium (mmol/l)	156.65±2.33^{a}	151.65±2.33^{a}	134.15±1.20^{ab}	142.45±1.20^{a}	144.10±3.54^{a}	116.60±0.00^{b}
Potassium (mmol/l)	2.65±0.21a	2.85±0.07a	2.30±0.28a	2.40±0.00a	2.35±0.07a	2.15±0.07a

Values are mean ± SD of three determinants. Values with different superscriptsacross the same row are significantly different from each other at P<0.05.

Effect of methanolic leaf extract of *S. longipedunculata* on lipid profile in rats

Table 4 shows the effect of the extract on lipid profile of rats after 28 days exposure. Lm extract of *S. longipedunculata* caused no significant (p< 0.05) alteration to the concentration of serum triglycerides but a significant (p< 0.05) decrease in the serum cholesterol concentration was observed whencompared with the control rats.Jobelyn and dexamethazonecaused significant (p< 0.05) increase in serum triglyceride concentrations when compared with the control. Dexamethazonealso caused further increase (p<0.05) in cholesterol when compared with the control.

Haematological parameters

Effect of sub-chronic administration of methanol leaf extract of *S. longipedunculata*on hematological parameters in rats is shown in Table 5. Methanol leaf extract of *S. longipedunculata* had no significant (p>0.05) effect on red blood cells (RBC), haemoglobin (Hb), packed cell volume (PCV), mean corpuscular haemoglobin concentration (MCHC), mean corpuscular hemoglobin (MCH), mean cell volume (MCV) and differential counts when compared with the normal control. However, groups of rat administered with methanol leaf extract of *S. longipedunculata* at doses of 50 and 100 mg/kg as well as those treated with dexamethazone had significantly higher (p<0.05) WBC when compared with the normal control.

Table 4 Effect of methanolic leaf extractof *S. longipedunculata*on the lipids profile in rats

	Treatment (mg/kgbw)					
Lipid Profile	25	50	100	Dexamethaz. (3)	Jobelyn (4.17)	Control
Cholesterol	55.45±2.33^{b}	52.35±0.72^{b}	55.25±12.79^{b}	38.00±0.00^{c}	89.75±1.34^{a}	91.60±5.09^{a}
Triglycerides	180.35±6.01^{c}	184.40±0.85^{c}	213.80±2.12^{b}	234.00±5.66^{a}	234.55±6.44^{a}	166.50±3.82^{d}

Values are mean ± SD of three determinants. Values with different superscripts across the same row are significantly different from each other at P<0.05.

Table 5: Effect of methanolic leaf extractof *S. longipedunculata*on hematological parameters in rats

	Treatment (mg/kgbw)					
Kidney Function Indices	25	50	100	Dexamethaz. (3)	Jobelyn (4.17)	Control
HB (g/L)	14.25±1.20[a]	15.25±0.49[a]	13.50±1.13[a]	14.90±0.57[a]	14.20±1.27[a]	13.65±0.35[a]
PCV (%)	43.50±2.12[a]	45.50±0.71[a]	41.50±4.95[a]	44.50±0.71[a]	43.00±5.66[a]	43.00±0.00[a]
MCV (FL)	54.50±4.95[a]	49.50±0.71[a]	52.00±0.00[a]	48.00±1.41[a]	48.50±0.71[a]	54.50±4.95[a]
MCH (pg)	19.00±2.83[a]	17.50±2.12[a]	17.50±0.71[a]	16.00±0.00[a]	21.00±7.71[a]	17.50±0.71[a]
MCHC (g/l)	34.50±2.12[a]	35.00±2.83[a]	33.00±1.41[a]	33.50±0.71[a]	45.50±13.44[a]	31.50±0.71[a]
RBC (x 10^{12})	7.75±0.35[b]	7.00±0.85[b]	7.95±0.92[b]	7.20±0.42[b]	9.55±0.07[a]	7.95±0.64[b]
TWBC (x10^{12})	4.00±1.41[b]	17.40±2.40[a]	10.60±7.64[a]	9.70±0.42[a]	5.50±2.40[b]	5.65±0.49[b]
Neutrophil (%)	20.00±0.00[a]	21.50±26.16[a]	9.00±1.41[a]	12.00±2.83[a]	31.00±28.28[a]	38.50±12.02[a]
Lymphocyte (%)	47.50±3.54[a]	56.50±24.75[a]	64.50±4.95[a]	53.50±9.19[a]	38.50±17.68[a]	34.00±12.73[a]
Monocyte (%)	32.50±3.54[a]	22.00±1.41[a]	26.50±3.54[a]	34.50±6.36[a]	30.50±10.61[a]	27.50±0.71[a]
Eosinophil (%)	32.50±3.54[a]	22.00±1.41[a]	26.50±3.54[a]	34.50±6.36[a]	30.50±10.61[a]	27.50±0.71[a]
RDWt (μm)	17.95±1.06[a]	17.95±0.78[a]	18.60±0.57[a]	18.20±0.28[a]	17.30±1.40[a]	18.15±0.21[a]

Values are in means ± SD of three determinants. Values with the same superscriptsacross the same row are not significantly different ($P \geq 0.05$).

MCV: Mean corpuscular volume
HB: Haemoglobin count
MCH: Mean corpuscular haemoglobin
MCHC: Mean corpuscular haemoglobin concentration
µg /kgbw: Microgram per kilogram body weight
RBC: Red blood cell count
pg: Picogram
PCV: Packed cell volume
g/dl: gram per deciliter
FL: Femtoliterr
TWBC:Total White Blood Cells
RDWt: Red Cell Distribution width

Effect of of methanolic leaf extractof *S.longipedunculata* on the body weight of rats

Table 6 shows the weekly effect of oral administration of methanolic leaf extract of *S. longipedunculata* on the body weight of rats. Significant and progressive increase in weight was observed on all the experimental rats throughout the 28 days of extract administration. However, the weight gain was significantly ($p<0.05$) lower in rats administered with dexamethazone when compared with the control and other experimental groups.

Effect of methanolic leaf extract of *S.longipedunculata*on relative organ weights of rats.

Table 7 shows the effect of sub-chronic administration of methanol leaf extract of *S. longipedunculata* on relative organ weights of rats. The computed weight of the kidneys, spleen and liver were not altered by all the doses of the extract and the standard drugs; dexamethazone and jobelyn. However, dexamethazone caused significant ($p<0.05$) decrease in relative weights of spleen and heart when compared with the control.

Table 6: Effect of methanolic leaf extract of *S. longipedunculata* on body weight gain in rats

Treatment(mg/kgbw)	Weeks					Weight
	0	1	2	3	4	gain
25	159.00±7.00 [a]	168.67±3.79[bc]	186.00±2.65[b]	190.33±2.87[c]	197.67±56.98[ab]	38.67
50	163.00±7.00 [a]	174.00±2.00[bc]	190.33±2.08[b]	203.67±6.11[b]	209.00±6.24[b]	46.00
100	155.00±4.58 [a]	176.00±2.00[b]	192.00±6.56[b]	194.33±6.66[c]	197.00±14.79[ab]	42.00
Dexamethazone(3)	163.00±2.65 [a]	166.33±2.89[c]	171.67±4.04 [a]	174.00±3.61 [a]	184.33±4.51 [a]	21.33
Jobelyn (4.17)	142.33±5.86[a]	172.67±9.45[bc]	184.33±4.16[b]	191.00±5.29[c]	187.67±0.58[ab]	45.67
Control	153.33±1.53 [a]	184.67±4.16 [a]	203.67±5.51 [a]	215.67±4.62 [a]	197.67±8.33 [a]	44.34

Values are in means ± SD of three determinants. Values with the same superscript along the same column are not significantly different ($P \geq 0.05$).

Table 7: Effect of methanolic leaf extract of *S. longipedunculata*on relative organ weight of rats

Treatment (mg/kgbw)	Liver	Spleen	Kidney	Heart
25	3.13±0.96[a]	0.25±0.03[a]	0.58±0.24[a]	0.29±0.18[a]
50	3.24±0.64[a]	0.26±0.04[a]	0.62±0.18[a]	0.29±0.04[a]
100	3.42±0.67[a]	0.26±0.03[a]	0.60±0.00[a]	0.24±0.09[a]
Dexamethazone (3)	2.49±1.05[a]	0.18±0.01[b]	0.43±0.16[a]	0.16±0.06[b]
Jobelyn (4.17)	2.95±1.14[a]	0.26±0.04[a]	0.58±0.16[a]	0.26±0.08[a]
Control	2.27±0.28[a]	0.17±0.03[b]	0.35±0.05[a]	0.22±0.05[a]

Values are in means ± SD of three determinants. Values with the same superscript along the same column are not significantly different ($P \geq 0.05$).

DISCUSSION

About 80% of the world's population is thought to depend chiefly on traditional medicine for their primary health care needs. Emphases have however been laid that safety should be the overriding criteria in the selection of natural medicine for use in health care (WHO, 2010). In this study, the acute lethal treatment with leaf extract of *S. longipedunculata* showed that the extract did not cause any mortality even at the highest dose (5000 mg/kgbw) tested. The LD_{50} is greater than 5000mg/kg body weight, which is thought to be safe as suggested by Lorke (1983). This result suggests that the methanol leaf extract of *S. longipedunculata* is relatively non-toxic (Lorke, 1983). This is expected considering that the plant is edible. The non-lethal effects produced with the high dose of this extract are an indication that the methanol leaves extract of *S. longipedunculata is* relatively safe on acute oral exposure. These findings are in conformity with those reported by Donald *et al*. (2011); Auwal*et al*. (2012) on phytochemical composition and acute toxicity of root bark extracts of *S. longipedunculata*. However, Agbajeand Adekoya(2012) demonstrated LD_{50} at a dose of 3162.27 mg/kgbw after oral administration of *S. longipedunculata* root extracts.

Assessment of haematological parameters can be used to determine the extent of deleterious effect of foreign compounds including plant extract on the blood (Lawal*et al*., 2015a). It can also be used to explain blood-relating functions of a chemical compound including those contained in plant extracts (Bashir *et al*., 2015). Non-significant ($P > 0.05$) effect of the extract at various doses (25mg/kgbw, 50mg/kgbw and 100mg/kgbw) on the RBC and indices relating to it (Hb, PCV, MCV, MCH and MCHC) throughout the experimental period indicated that these parameters were not affected. This might be an indication that there was no destruction of matured RBC's and no change in the rate of production of erythrocytes (erythropoiesis) (Berinyu*et al*., 2015). It might also indicate that the extract did not exhibit erythropoeitin potential, the humoral regulator of RBC production (Shittu*et al*., 2015a). The lack of significant effect ($P > 0.05$) on the RBC and Hb also implies that the oxygen-carrying capacity of the blood was not hindered. The blood indices MCV, MCH and MCHC have a particular importance in diagnosis of anaemia in most animals. The non-significant ($P > 0.05$) effects on these indices suggested that there was no effect on the average size of RBC (microcytes) and in the haemoglobin weight per RBC. This implies that the extract did not possess any potential of inducing anaemia throughout the 28 days period of administration. However, the significant increase($P < 0.05$) in WBC following the administration of the extract for 28 days indicated a boost in the immune system since increase in WBC increases the immunological action of the body (Akanji *et al*., 2013). The results of the present study correspond with the findings of Abalaka *et al*., (2009) who reported that no doses related changes in the haematological and biochemical parameters in rats exposed to *Momordica charantia* (100mg/kgbw, 500mg/kgbw, 800 mg/kgbw)

except that there is a slight increase in the mean counts of white blood cells (WBC).

Serum biochemical parameters are valuable tools for assessing the integrity and functionality of organs as well as risk assessment, pathological condition and general health status of the body (Lawal *et al.*, 2016). Alkaline phosphatase (ALP) is a 'marker' enzyme for the plasma membrane and endoplasmic reticulum; it is therefore an ectoenzyme of the plasma membrane and it is often used to assess the integrity of the plasma membrane (Shittu *et al.*, 2015). The reduction in alkaline phosphatase activities following the administration of methanol leaves extract of *S. longipedunculata* might be adduced to either loss of membrane components (including ALP) into the extracellular fluid (Yakubu *et al.*, 2013), inactivation of the enzyme molecule *in situ* (Akanji *et al.*, 2013), or inhibition of the enzyme activity at the cellular/molecular level.

It may also be due to a reduction in concentration or total absence of specific phospholipids required by this memebrane-bound enzyme to express its full activity (Das *et al.*, 2015). The reduction in ALP activity from the tissues could be attributable to disruption of the ordered lipid-bilayer of the membrane structure leading to escape of detectable quantity of ALP out of the cell into the extracellular fluid (Muhammad *et al.*, 2015). Such reduction in the tissues' ALP activities could hinder adequate transportation of required ions or molecules across their cell membrane and this may lead to starvation of the cells (Shittu*et al.*, 2015a). Reduction in ALP activities as observed in this study might also adversely affect other metabolic processes where the enzyme is involved such as the synthesis of nuclear proteins, nucleic acids and phospholipids as well as in the cleavage of phosphate esters (Nwaka *et al.*, 2015).

AST and ALT are biomarkers of hepatic integrity and to a certain level can be used to assess the extent of hepatocellular damage, the ALT activities however, give more valuable information relevant to the integrity of the hepatocyte than AST (Yakubu and Musa, 2012). The non-significant ($P > 0.05$) effect of the extract at various doses (25mg/kgbw, 50mg/kgbw and 100mg/kgbw) on the serum AST and ALT throughout the experimental period indicated that these enzyme activities were not affected. This might be an indication that there were no leakages of the enzymes from liver to the serum. However, serum AST activities was significantly ($P < 0.05$) raised in rats dosed withdexamethazone for 4 weeks when compared with the control rats. The chemical constituents of the dexamethazone may have altered the enzyme activity or increased the amounts of important molecules needed for the optimum activities of the enzyme (Lawal*et al.*, 2015b). Such increase in AST activities will however, adversely affect the metabolism of amino acid and carbohydrate with consequent effect on ATP generation (Adeyemi*et al.*, 2015). It appears that the dexamethazone might have selectively affected the transaminases since ALT activities in the serum of the animals were not altered. This may be connected to the earlier mentioned selective toxicity of chemical compounds on the body system (Lawal *et al.*, 2016).

The concentration of the proteins, bilirubin and albumin in the serum could indicate the state of the liver and ascertain types of liver damage (Ashafa *et al.*, 2015). The observed increase in serum proteins in rats dosed with methanol leaf extract of *S. longipedunculata* might be attributed to dehydration. It might also be due to increased rate of hepatic synthesis of protein without proportionate increase in the rate of its elimination. Consequently, the amino acid pool may no longer be maintained within normal limits.

Bilirubin is the major breakdown product that results from the destruction of old red blood cells. It is removed from the blood by the liver, chemically modified by a process called conjugation (formation of bilirubin), secreted into the bile, passed into the intestine and to some extent, reabsorbed from the intestine (Yakubu*et al.*, 2005). The non-significant ($P > 0.05$) effect of the extract at various doses (25mg/kgbw, 50mg/kgbw and 100mg/kgbw) on the serum bilirubin and albumin was an indication that there was no impairment in the liver function with respect to the serum bilirubin and albumin. However, the significant ($p<0.05$) increase in bilirubin concentration in rat-administered dexamethazone when compared with the control group indicates hepatic impairment (Guyton and Hall, 2001).

Sodium and potassium are electrolytes that can be used to assess renal function. The significant ($P > 0.05$) increase in the serum sodium ions following the chronic administration of extract of *S. longipedunculata* at various doses could be an indication of tubular and glomerular dysfunctions. Constancy of endogenous creatinine production and its release into the body fluids makes creatinine a useful endogenous substance whose clearance may be measured as an indication of glomerular filteration rate. The significant ($P > 0.05$) increase in the serum urea and creatinine concentration following the extract administration of the extract at various doses may be attributed to impairment in the functional capacity of the nephron. This is an

indication of abnormality in the physiological excretion of urea and creatinine caused by a non-renal factor, which is the extract in this study. However, previous study has indicated that the kidney has the potential of recovering from the assault caused by administration of plant extract (Yakubu*et al.*, 2008).

Organ-body weight ratio is a marker of cell constriction and inflammation (Shittu*et al.*, 2015b). The lack of significant ($P > 0.05$) change in the size of the organs relative to the entire weight of the animalssuggests that the plant extract did not cause inflammation or constriction in the cells of the various organs investigated (Berinyuy*et al.*, 2015). However, the significant ($P < 0.05$) decrease in the weight of the heart caused by the dexamethazone administration for 28 days might probably be attributable to the organs constriction (Yakubu and Musa, 2012).

CONCLUSION

Toxicological study, revealed that the plant extract has no serious adverse effect on hematological and biochemical parameters, however the mild alteration in some biochemical parameters following administration of extracts could be attributed to immunological response of the animals induced by the constituents of the extract.

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