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TOXICOLOGICAL EVALUATION OF AQUEOUS LEAF EXTRACT OF *SENNA ALATA* IN PREGNANT WISTAR RATS

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ABSTRACT

Objective: Aqueous leaf extract of *Senna alata* at 250, 500 and 1000 mg/kg body weight was evaluated for toxicity in pregnant Wistar rats. **Methods:** Pregnant rats were grouped into four (A, B, C and D) of five animals each such that rats in groups A, B, C and D received 0.5 ml of distilled water, 250, 500 and 1000 mg/kg body weight of the extract respectively, from days 10-18 post-coitus. **Results:** The extract reduced ($P<0.05$) the activities of alkaline phosphatase, aspartate transaminase, alanine transaminase and gamma glutamyl transferase in the liver and kidney of the animals with increases in heart and serum enzymes. The levels of haematological parameters, serum albumin, globulin, creatinine, sodium, calcium, chloride ions, blood urea nitrogen (BUN): creatinine ratio, total cholesterol, triacylglycerol, low- and high-density lipoprotein cholesterol were decreased by the extract while those of urea, uric acid, serum total bilirubin, phosphate, potassium, calcium and atherogenic index increased significantly. The myocardial fibres were normal in the heart while there was varying degree of necrosis of the tubular epithelial cells in the kidney and hepatic degeneration in the liver. **Conclusion:** The extract caused both functional and structural toxicities and therefore not safe for consumption during pregnancy.

Keywords: *Senna alata*, Fabaceae, Pregnancy, Functional toxicity, Structural toxicity, Biomarkers

INTRODUCTION

Senna alata (Linn) Roxb. (=*Cassia alata* Linn) which belongs to the Fabaceae family (subfamily Caesalpiniaceae) is often variously called Ringworm Bush, Candlebra Bush, Empress Candle Plant and Ringworm Tree (English), asunwon oyinbo (Yoruba-Western Nigeria) and nelkhi or okpo (Igbo-Eastern Nigeria).[1] It is native to Mexico and grows in forest areas of West Africa. *S. alata* is an erect, tropical, annual herb of 0.15 m high with bilateral, leathery compound leaves (50-80 cm long) that fold together in the dark. The fruit is a straight pod of about 25 cm long.[2] The seeds are small and square in shape while the inflorescence looks like a yellow candle. The root, stem, stem bark and leaves have been separately claimed to be used to manage hepatitis, scabies, pruritis, jaundice, gastroenteritis, ringworm, ulcer, eczema, burns, wound, skin and upper respiratory tract infection, diarrhoea, constipation, food poisoning and poisonous bites.[3,4] The leaves have been implicated to be used as abortifacient and to hasten labour.[1]

S. alata have been scientifically evaluated for a variety of pharmacological activities such as antibacterial, antifungal, antiparasitic, laxative, antidiabetic, anti-inflammatory, analgesic and abortifacient.[5-12] The toxicological studies available in the open scientific literature on *S. alata* thus far have used normal mice and rats as models.[13, 14] Since the extract have been reported to possess abortifacient activity in pregnant rats, there is also the need to investigate the toxic implications of the same doses of extract in pregnant rats. Therefore, the present study was aimed at providing information on the effect of aqueous leaf extract of *S. alata* on some functional indices of the liver, heart and kidney of pregnant Wistar rats. We also investigated the haematological and lipid profile as well as the histoarchitectural changes in the selected organs of the pregnant animals following the administration of the extract on days 10-18 post-coitus.

MATERIALS AND METHODS

Materials

Plant materials

The plant sample, obtained from herb sellers at a market (Oja tuntun) in Ilorin, Nigeria was authenticated at the Forestry Research Institute of Nigeria, Jericho, Ibadan, Nigeria. A voucher specimen (FHI 10845) was deposited at the Herbarium of the Institute.

Assay kits and other reagents

The assay kits for urea, creatinine and uric acid were products of Quinica Clinical Aplicada, S.A Amosta, Spain, while those for albumin, bilirubin, globulin, aspartate transaminase (AST), alanine transaminase (ALT), γ-glutamyl transferase (GGT), sodium, potassium, calcium, chloride, phosphate, cholesterol, triacylglycerol, low- and high- density lipoprotein cholesterol were products of Randox Laboratories, Ltd, United Kingdom. Para-nitrophenyl phosphate was a product of Sigma-Aldrich Chemical, United Kingdom. All other reagents used were of analytical grade and were prepared in glass-distilled water.

Laboratory animals

Forty rats *(Rattus norvegicus)* made up of equal number of males (184.80 ± 4.16 g) and females (163.65 ± 3.11 g) were obtained from the Animal Breeding Unit of the Department of Biochemistry, University of Ilorin, Ilorin, Nigeria. The animals, housed in aluminium cages that were placed in well-ventilated room conditions (temperature: 22 ± 3ºC; 12 h light-dark cycle; humidity: 45%-50%) were also supplied with rat pellets (Bendel Feeds and Flour Mill, Ewu, Edo, Nigeria) and water *ad libitum*.

Preparation of aqueous leaf extract

The leaves of *Senna alata* were oven-dried at 40^0C for 72 h to a constant weight using Uniscope SM9053 Laboratory Oven, (Surgifriend Medicals, Essex, England). The dried leaves were then pulverized with an electric blender (Crown Star Blender CS- 242B, Trident (H.K.) Ltd, China) from which 100 g each was extracted in 1000 ml of cold distilled water for 48 hours with constant shaking. This was later filtered with Whatmann No. 1 filter paper and thereafter lyophilized (Micromodulyo Freeze Dryer, FS400-05, USA) to give a yield of 16.50 g which was reconstituted in distilled water to give the required doses of 250, 500 and 1 000 mg/kg body weight used in this study. The doses were as used previously in our study on the abortifacient activity of the aqueous leaf extract of *S. alata* in pregnant rats.[12]

Animal grouping and extract administration

Female rats were paired overnight with the male rats in ratio 1:1 in aluminium cages that made the animals have free access to food and water. The day when vaginal plug and spermatozoa (detected with the aid of light microscope) appeared in the vaginal smear was considered as day zero of pregnancy. Pregnancy was also confirmed with the aid of pregnancy strip dipped into their urine. The pregnant animals were thereafter completely randomized into four groups (A, B, C and D) of five animals each. The distilled water and the extracts were administered orally to the various groups of animals on days 10 to 18 (organogenetic period) post coitus on daily basis, using oropharyngeal cannula as follows: Group A (control) received 0.5 ml of distilled water while animals in Groups B, C and D, were treated in the same manner as the control except that they received equal volume of the extract containing 250, 500 and 1000 mg/kg body weight respectively. The animals were humanely handled according to the guidelines of National Institute of Health on the Care and Use of Laboratory Animals.[15] This study was carried out following approval from the Ethical Committee on Animal Use and Care of the Department of Biochemistry, University of Ilorin, Ilorin, Nigeria (Ref: UIL/BCH/EC/2008/001).

Preparation of serum and tissue supernatants

The animals were anaesthetized in a glass jar containing cotton wool soaked in diethyl ether. The unconscious rat was quickly removed and the neck area cleared of fur. The jugular veins were cut and blood was collected into the test tubes. The blood samples were allowed to clot at room temperature for 10 min after which they were centrifuged at 894 *g* x 10 min. The resulting serum was collected using Pasteur pipette and kept frozen overnight before being used for the biochemical analyses. The animals were thereafter dissected; the liver, heart and kidney removed and cleaned of blood by blotting in tissue paper. The kidneys were decapsulated after which the organs of interest were weighed separately and homogenized in ice-cold 0.25M sucrose solution (1:5 w/v). The homogenates were centrifuged at 1398 *g* x 15 min to obtain the supernatant, which were then used within 24 hours for the biochemical analyses.

Determination of biochemical and haematological parameters

The procedures adopted for the biochemical parameters were as described for alkaline phosphatase[16], aspartate and alanine transaminases[17], gamma glutamyl transferase[18], total protein[19], bilirubin[20], albumin[21], urea[22], creatinine[23], calcium, phosphate, uric acid, globulin, potassium, sodium and chloride ions[24]. The blood urea nitrogen (BUN): creatinine ratio was computed as the ratio of serum urea to creatinine. The lipids assayed included total cholesterol[25], low density lipoprotein-cholesterol[26], high density lipoprotein-cholesterol[27], triglycerides[28] and atherogenic index[29]. The organ-body weight ratio was computed using the expression of Yakubu *et al*[30]. The haematological parameters of haemoglobin (Hb), packed cell volume (PCV), red blood cells (RBC), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), white blood cells (WBC), platelets, neutrophils and lymphocytes were analysed using Haematologic Analyzer, Sysmex, KX-21, Japan by adopting the principles described by Dacie and Lewis[31].

Histological examination

Tissue sections of the liver, heart and left kidney of the animals were prepared using the procedures described by Drury and Wallington[32] and Krause[33]. The tissues were stained with hematoxylin/eosin (H&E) and photomicrographs captured at x 400 with a Canon PowerShot A560 Digital Camera, Canon USA Inc., NY, USA.

Statistical analysis

Data were expressed as the means ± SEM of five replicates. Significant differences were determined using a one-way analysis of variance and Duncan Multiple Range Test at $P<0.05$.

RESULTS

The extract significantly ($P<0.05$) decreased the activities of ALP, GGT, AST and ALT in the liver and kidney of the animals (Tables 1-4). In contrast, the activities of these enzymes were increased ($P<0.05$) by all the doses of the extract in the heart and serum of the animals (Tables 1-4).

The extract also decreased ($P<0.05$) the concentrations of albumin, globulin, creatinine, sodium, calcium and chloride ion in the serum of the animals whereas the total bilirubin, urea, uric acid, potassium and phosphate increased ($P<0.05$) (Tables 5 and 6). The computed blood urea nitrogen: creatinine ratio in the extract treated animals was lower than the distilled water treated control rats (Table 6).

In addition, all the doses of the extract significantly ($P<0.05$) reduced the serum concentrations of total cholesterol, triglycerides, low- and high- density lipoprotein cholesterols whereas the computed atherogenic index increased significantly ($P<0.05$) (Table 7).

The extract at the doses of 250, 500 and 1000 mg/kg body weight selectively affected the haematological parameters. For example, all the doses of the extract decreased ($P<0.05$) the levels of Hb, PCV, RBC, MCV, MCH, MCHC whereas the WBC, platelets, neutrophils and lymphocytes increased significantly ($P<0.05$) (Table 8).

While the computed heart-body weight ratio was not significantly altered ($P>0.05$), the extract decreased ($P<0.05$) the liver- and kidney-body weight ratios. Furthermore, compared with their respective controls (Plates 1a, 2a and 3a), the extract did not produce any histoarchitectural change in the heart of the animals as the myocardial fibres were normal (Plates 1b, c and d). In contrast, the hepatic degeneration ranged from mild to severe with the lymphocytes extending into the lobule in the liver (Plates 2b, c and d) whereas in the kidney, the glomerulus were normal with necrosis of tubular epithelial cells and inflammatory cells within the interstitum (Plates 3b, c and d).

DISCUSSION

Aqueous leaf extract of *S. alata* has been acclaimed in folk medicine of Nigeria to be used as an abortifacient and to 'wash the uterus'. This claim however has been substantiated by adequate scientific data.[12] Previous report by Yakubu *et al*[12] focussed only on maternal and fetal outcomes without reporting on the safety of the extract in other tissues of the pregnant rats. Therefore, the present study discusses the implications of aqueous leaf extract of *S. alata* on selected markers of damage and histology of the liver, kidney and heart as well as lipid and haematological profile of pregnant rats while adopting the same dose regimen (250, 500 and 1000 mg/kg

body weight) used previously in the abortifacient study.

ALP, GGT, AST and ALT are important markers of damage to the plasma membrane and cytosol.[34, 35] The reduction in the activities of ALP in the liver and kidney as well as GGT of the animals which was accompanied with corresponding increase in the serum enzymes suggest permeability changes arising from damage to the cell membrane of the organs. The elevated serum GGT, a more effective indicator of hepatobilliary toxicity than the ALP[36] further corroborates the hepatoxicity of the extract. Thus, it is not surprising to have reduction in the AST and ALT of the tissues since damage to plasma membrane will consequentially lead to leakage of the cytosolic content, in this instance, the AST and ALT. These alterations suggest that the extract is hepato- and nephrotoxic. In contrast, the increase in the activity of ALP, GGT, AST and ALT in the heart of the animals could be due to enhanced synthesis of these enzymes. The reason for the different pattern of toxicity pattern by the extract on these tissues is not immediately known but may be due to the differences in the drug-metabolizing enzymes of the tissues. The changes in the activities of the enzymes will have consequential effects on the metabolic processes that depend on the enzymes.

The extract exhibited selective systemic toxicity on the haematological parameters investigated as evidenced by the decrease in red blood cells and factors relating to it (haemoglobin, packed cell volume, mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration) and increase in white blood cells and those factors relating to it (platelets, neutrophils and platelets). The decrease in RBC and factors relating to it may be an indication that the balance between the rate of production and destruction has been altered. It may also be that the individual and total population of the red blood cells have been adversely affected. The findings in this study are similar to that reported earlier by Adebayo *et al*[37] on *Bougainvillea spectabilis* leaves. Furthermore, the increase in WBC and factors relating to it suggest that the immune system has been challenged by the extract. These are indications of selective systemic toxicity of the plant extract.

Albumin and globulin are useful indicators of synthetic function of the liver whereas bilirubin could be used to assess excretory function of the organ. The decrease in both the albumin and globulin by the extract in the present study may suggest diminished synthetic function of the liver arising probably from hepatocellular injury[38], increased catabolism, abnormal distribution and abnormal or excessive loss. The obtained elevated levels of bilirubin further support hepatotoxicity of the extract arising from an effect on the normal excretory function of the liver of the pregnant animals.

Changes in the serum concentrations of creatinine, urea, uric acid and electrolytes such as Na^+, Ca^{2+}, K^+, PO_4^{2-} and Cl^- are indicators of renal function at the tubular and glomerular levels. The reduced levels of serum creatinine by the extract suggest glomerular dysfunction[39] while similar reduction in the levels of Na^+, Ca^{2+} and Cl^- indicates decreased tubular reabsorption.[40] Furthermore, the increased levels of serum urea and uric acid implies that there was reduction in the glomerular filtration rate of the kidney while the increase in the levels of K^+, and PO_4^{2-} suggest tubular damage since the ions are reabsorbed at the distal tubules of the kidney. All these

are indications of renal dysfunction arising probably from interference with metabolic process of the metabolite, inefficient filtration by the kidney and obstruction of lower urinary tract, impaired glomerular and tubular reabsorption or excretion of these ions. This therefore implies impairment or interference in the normal excretory and reabsorptive functions of the kidney. The serum BUN: creatinine ratio measures the amount of nitrogen in the blood, and can also indicate dysfunction by either the liver or kidney since urea is produced by the liver and excreted by the kidney. Therefore, the low values of computed serum BUN: creatinine ratio compared to the control suggests that the elevated urea in the serum of the animals is a consequence of liver dysfunction.

Changes in the levels of cholesterol, TAG, HDL-C and LDL-C in the serum of the animals can serve as useful indicators of altered lipid metabolism and pre-disposition of the animals to cardiovascular risk.[41] The extract affected the metabolism of lipid in the pregnant animals probably by impairing the normal biosynthesis of cholesterol and enhancing lipolysis. The significant decrease in LDL-C is understandable since there is a direct relationship between cholesterol and LDL-C.[41] This trend was supported in the present study where both the cholesterol and LDL-C of the serum of pregnant rats were decreased by the extract of *S. alata* leaves. Furthermore, the reduction in the serum content of HDL-C, the medium by which cholesterol from peripheral tissues is transported to the liver to reduce the amount stored in the tissue and the possibility of developing atherosclerotic plague, may not be clinically beneficial as it may predispose the animals to cardiovascular risk. This is corroborated by the elevated computed atherogenic index, an index of atherosclerosis and its associated heart diseases.[42]

Organ-body ratio can be used to indicate swelling, atrophy and hypertrophy.[43] The decrease in the liver- and kidney-body weight ratios may be a manifestation of the moderate to severe hepatic degeneration and extensive degeneration of tubular epithelial cells revealed by histological examination in the present study. In contrast, the absence of significant changes in the heart-body weight ratio was also corroborated by lack of visible histoarchitectural changes since the myocardial fibres were normal. The nephrotoxicity and hepatotoxicity of the aqueous leaf extract of *S. alata* at the doses of 250-1000 mg/kg body weight were corroborated by histoarchitectural alterations in the kidney and liver of the pregnant animals. Therefore, the toxicological impact of the aqueous leaf extract of *S. alata* in the present study was both functional and structural in the liver and kidney whereas it was only functional in the heart of the animals. The disparity in the histological results of the organs may be attributed to direct involvement of the liver and kidney in the detoxification and eventual elimination of the extract.

In conclusion, aqueous leaf extract of *S. alata* pose toxicological risk to the organs of pregnant rats investigated in the present study. Therefore, the extract may cause structural and functional dysfunctions in the liver and kidney while the toxicological impact is restricted to functional dysfunction in the heart of the pregnant animals. The extract could predispose the pregnant animals to systemic toxicity and cardiovascular risk.

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Table 1: Alkaline phosphatase activity of selected tissues of pregnant rats administered with aqueous leaf extract of *S. alata*

Doses	Alakline phosphatase activity (nm/min/mg protein)			
	Liver	**Kidney**	**Heart**	**Serum**
Control (Distilled water)	3.85 ± 0.07^{a}	22.18 ± 1.65^{a}	4.76 ± 0.11^{a}	0.41 ± 0.02^{a}
250 mg/kg body weight	2.02 ± 0.06^{b}	12.00 ± 0.82^{b}	6.76 ± 0.24^{b}	0.78 ± 0.01^{b}
500 mg/kg body weight	1.48 ± 0.02^{c}	10.50 ± 0.12^{b}	7.81 ± 0.03^{b}	1.02 ± 0.03^{c}
1000 mg/kg body weight	0.92 ± 0.05^{d}	11.52 ± 0.05^{b}	9.02 ± 0.06^{c}	1.41 ± 0.02^{d}

Values are means ± SD of five determinations
Test values carrying superscripts different from the control are significantly different ($P<0.05$).

Table 2: Gamma glutamyl transferase activity of selected tissues of pregnant rats administered with aqueous leaf extract of *S. alata*

Doses	Gamma glutamyl transferase activity (U/L)			
	Liver	**Kidney**	**Heart**	**Serum**
Control (Distilled water)	39.52 ± 3.01^{a}	27.83 ± 5.52^{a}	12.28 ± 1.48^{a}	4.41 ± 0.02^{a}
250 mg/kg body weight	22.05 ± 2.18^{b}	19.46 ± 0.52^{b}	17.26 ± 1.05^{b}	6.11 ± 0.14^{b}
500 mg/kg body weight	11.77 ± 0.28^{c}	12.06 ± 0.16^{c}	25.63 ± 1.44^{c}	8.76 ± 0.86^{c}
1000 mg/kg body weight	10.59 ± 0.32^{c}	8.14 ± 1.01^{d}	38.41 ± 3.01^{d}	8.62 ± 0.73^{c}

Values are means ± SD of five determinations
Test values carrying superscripts different from the control are significantly different ($P<0.05$).

Table 3: Alanine transaminase activity of selected tissues of pregnant rats administered with aqueous leaf extract of *S. alata*

Doses	Alanine transaminase activity (U/L)			
	Liver	Kidney	Heart	Serum
Control (Distilled water)	350.00 ± 13.32[a]	128.46 ±5.61[a]	132.28 ±6.16[a]	32.14 ± 3.11[a]
250 mg/kg body weight	220.00 ± 7.96[b]	88.66 ±6.21[b]	151.50 ±1.64[b]	57.21 ± 4.11[b]
500 mg/kg body weight	139.41 ± 7.48[c]	62.14 ±5.72[c]	190.03 ±6.71[c]	68.00 ± 3.01[c]
1000 mg/kg body weight	140.19 ± 5.09[c]	45.82 ±4.72[d]	191.70 ±6.00[c]	88.51 ± 4.27[d]

Values are means ± SD of five determinations
Test values carrying superscripts different from the control are significantly different (P<0.05).

Table 4: Aspartate transaminase activity of selected tissues of pregnant rats administered with aqueous leaf extract of *S. alata*

Doses	Aspartate transaminase activity (U/L)			
	Liver	Kidney	Heart	Serum
Control (Distilled water)	1010.02 ± 15.73[a]	880.09 ±12.44[a]	32.22 ±4.10[a]	17.28 ± 2.00[a]
250 mg/kg body weight	750.00 ± 10.95[b]	510.32 ±21.91[b]	49.10 ±3.88[b]	27.21 ± 2.11[b]
500 mg/kg body weight	7493.33 ± 10.41[c]	460.22 ±11.11[c]	62.86 ±6.58[c]	38.10 ± 3.58[c]
1000 mg/kg body weight	465.28 ± 8.43[d]	307.86 ±8.09[d]	64.01 ±8.62[c]	40.00 ± 2.08[c]

Values are means ± SD of five determinations
Test values carrying superscripts different from the control are significantly different (P<0.05).

Table 5: Serum liver function indices of pregnant rats administered with aqueous leaf extract of *S. alata*

Indices	Extract (mg/kg body weight)			
	Control	250	500	1000
Albumin (g/L)	39.00 ± 1.09[a]	22.00 ±0.89[b]	21.33 ±1.37[b]	14.08 ± 0.89[c]
Globulin (g/L)	17.50 ± 0.55[a]	14.00 ±1.03[b]	13.50 ±0.25[b]	9.18 ± 0.89[c]
Total bilirubin (g/L)	15.00 ± 0.45[a]	20.22 ±1.25[b]	22.05 ±0.67[c]	24.49 ± 0.59[d]

Values are means ± SD of five determinations
Test values carrying superscripts different from the control are significantly different ($P<0.05$).

Table 6: Serum kidney function indices of pregnant rats administered with aqueous leaf extract of *S. alata*

Indices	Extract (mg/kg body weight)			
	Control	250	500	1000
Urea (mmol/L)	0.70 ± 0.01[a]	1.20 ±0.22[b]	1.15 ±0.05[c]	1.05 ± 0.05[d]
Creatinine (mmol/L)	19.00 ± 0.91[a]	14.00 ±0.19[b]	12.50 ±0.55[c]	11.50 ± 0.05[c]
Blood urea nitrogen (BUN):creatinine ratio	1: 27	1:12	1:11	1:11
Uric acid (mmol/L)	$0.03x\ 10^{-1} \pm 0.79 \times 10^{-3a}$	$0.05 \times 10^{-1} \pm 0.89 \times 10^{-3b}$	$0.06 \times 10^{-1} \pm 0.89 \times 10^{-3b}$	$0.05 \times 10^{-1} \pm 0.52 \times 10^{-3b}$
Sodium ion (mmol/L)	77.50 ± 2.73[a]	68.50 ±2.73[b]	69.00 ± 2.68[b]	67.00 ± 1.79[b]
Potassium ion (mmol/L)	1.45 ± 0.01[a]	1.57 ±0.04[b]	1.70 ±0.09[c]	1.73 ± 0.14[c]
Calcium ion (mmol/L)	1.28 ± 0.24[a]	1.05 ±0.02[b]	1.00 ±0.06[b]	0.95 ± 0.01[b]
Chloride ion (mmol/L)	0.51 ± 0.01[a]	0.50 ±0.00[a]	0.44 ±0.01[b]	0.26 ± 0.02[c]
Phosphate ion (mmol/L)	0.51 ± 0.01[a]	1.50 ±0.02[b]	0.89 ±0.01[c]	0.98 ± 0.01[c]

Values are means ± SD of five determinations
Test values carrying superscripts different from the control are significantly different ($P<0.05$).

Table 7: Serum lipid profile of pregnant rats administered with aqueous leaf extract of *S. alata*

Indices	Extract (mg/kg body weight)			
	Control	**250**	**500**	**1000**
Total cholesterol (mmol/L)	2.13 ± 0.14^{a}	1.20 ± 0.11^{b}	1.09 ± 0.09^{c}	0.57 ± 0.04^{d}
Triglyceride (mmol/L)	0.59 ± 0.91^{a}	0.38 ± 0.05^{b}	0.34 ± 0.06^{b}	0.30 ± 0.02^{c}
Low-density lipoprotein cholesterol (mmol/L)	1.02 ± 0.08^{a}	0.81 ± 0.04^{b}	0.62 ± 0.07^{c}	0.51 ± 0.06^{d}
High-density lipoprotein cholesterol (mmol/L)	2.83 ± 0.23^{a}	1.30 ± 0.09^{b}	1.10 ± 0.13^{c}	0.77 ± 0.19^{d}
Atherogenic index (LDLC/HDLC	0.36 ± 0.13^{a}	0.62 ± 0.04^{b}	0.56 ± 0.14^{c}	0.66 ± 0.02^{c}

Values are means ± SD of five determinations
Test values carrying superscripts different from the control are significantly different ($P<0.05$).

Table 8: Haematological parameters of pregnant rats administered with aqueous leaf extract of *S. alata*

Treatment	Doses (mg/kg body weight	Hb (g/dl)	PCV (%)	RBC (x 10^{12}/l)	MCV (fl)	MCH (pg)	MCHC (g/dl)	WBC (x 10^{9}/l)	PLAT (x 10^{9}/l)	NEUT (%)	LYMP (%)
Distilled water	Control	18.65 ± 2.05[a]	53.33 ± 2.02[a]	4.25 ± 0.63[a]	132.33 ± 7.57[a]	37.33 ± 3.50[a]	32.67 ± 2.08[a]	7.77 ± 0.50[a]	841.00 ± 11.01[a]	10.00 ± 0.71[a]	90.02 ± 8.72[a]
	250	15.50 ± 2.81[b]	48.33 ± 2.31[b]	3.37 ± 0.75[b]	112.33 ± 4.97[b]	23.00 ± 0.53[b]	24.00 ± 0.20[b]	9.53 ± 0.41[b]	1013.33 ± 17.03[b]	13.10 ± 0.20[b]	106.00 ± 2.80[b]
Extract	500	12.90 ± 1.13[c]	41.67 ± 2.89[c]	3.28 ± 0.37[b]	113.67 ± 6.11[b]	20.33 ± 2.52[b]	22.67 ± 0.58[b]	10.53 ± 0.15[b]	980.60 ± 18.85[b]	13.67 ± 0.02[b]	127.08 ± 7.02[c]
	1000	11.70 ± 1.28[d]	31.00 ± 2.65[d]	3.27 ± 0.55[b]	103.00 ± 4.27[c]	16.67 ± 2.29[c]	17.67 ± 0.13[c]	13.40 ± 0.84[c]	1210.00 ± 16.37[c]	16.33 ± 1.06[a]	122.67 ± 6.06[c]

Values are means ± SD of five determinations

Test values carrying superscripts different from the control are significantly different ($P<0.05$).

Table 9: Organ body weight ratio of pregnant rats administered with aqueous leaf extract of *S. alata*

Doses	Organ body weight ratio (%)		
	Liver	Kidney	Heart
Control (Distilled water)	4.69 ± 0.24[a]	0.63 ± 0.09[a]	0.36 ± 0.03[a]
250 mg/kg body weight	3.93 ± 0.32[b]	0.54 ± 0.05[b]	0.34 ± 0.04[a]
500 mg/kg body weight	3.66 ± 0.63[c]	0.55 ± 0.03[b]	0.35 ± 0.03[a]
1000 mg/kg body weight	3.69 ± 0.31[c]	0.54 ± 0.04[b]	0.35 ± 0.02[c]

Values are means ± SD of five determinations
Test values carrying superscripts different from the control are significantly different (P<0.05).

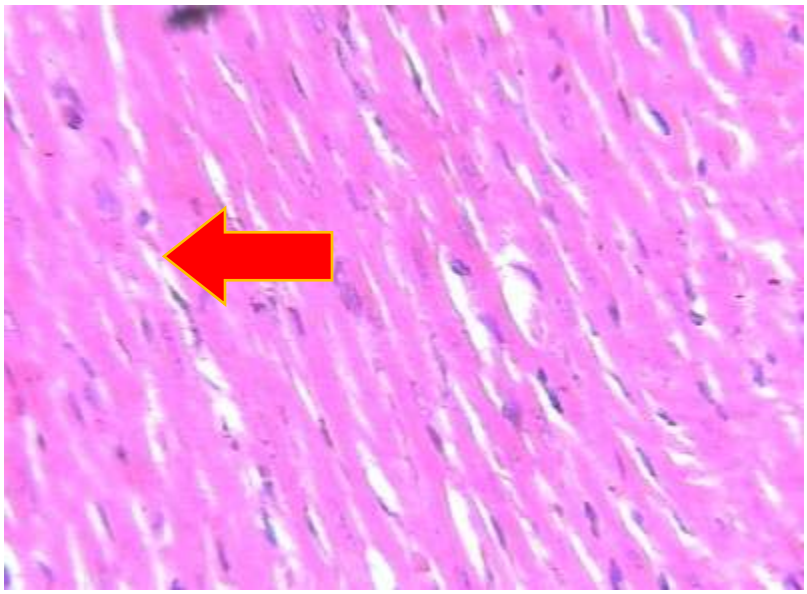

Plate 1a: Photomicrograph of the heart of pregnant rat orally administered with distilled water on days 10-18 post coitus. The arrow shows normal myocardial fibres (x400) (H & E).

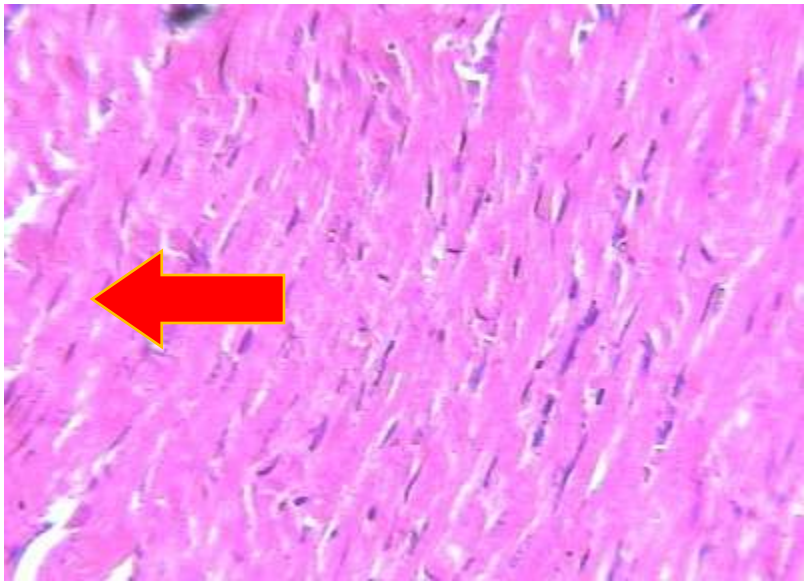

Plate 1b: Photomicrograph of the heart of pregnant rat orally administered with 250 mg/kg body weight of aqueous leaf extract of *S. alata* on days 10-18 post coitus. The arrow shows normal myocardial fibres (x400) (H & E).

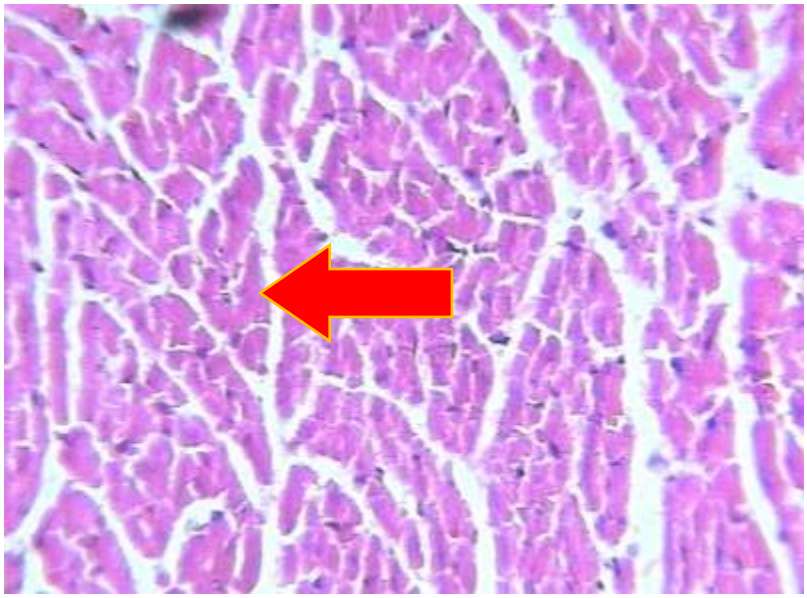

Plate 1c: Photomicrograph of the heart of pregnant rat orally administered with 500 mg/kg body weight of aqueous leaf extract of *S. alata* on days 10-18 post coitus. The arrow shows normal myocardial fibres (x400) (H & E).

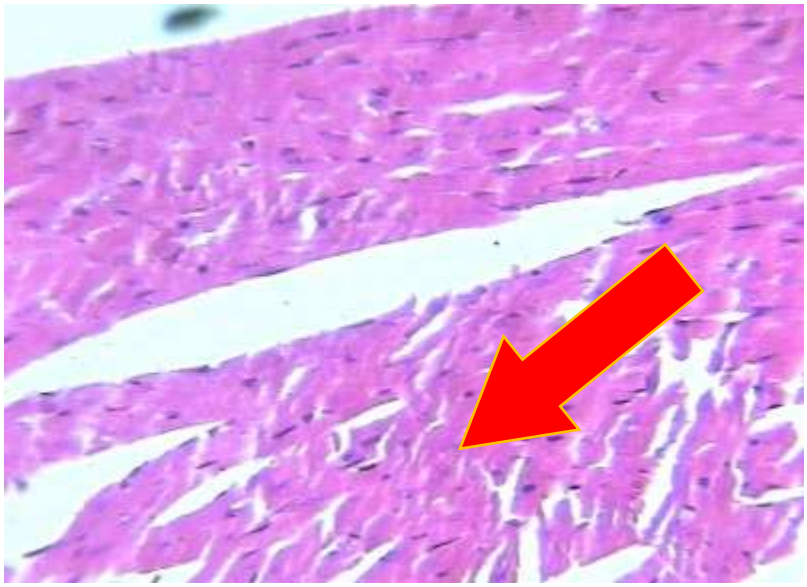

Plate 1d: Photomicrograph of the heart of pregnant rat orally administered with 1000 mg/kg body weight of aqueous leaf extract of *S. alata* on days 10-18 post coitus. The arrow shows normal myocardial fibres (x400) (H & E).

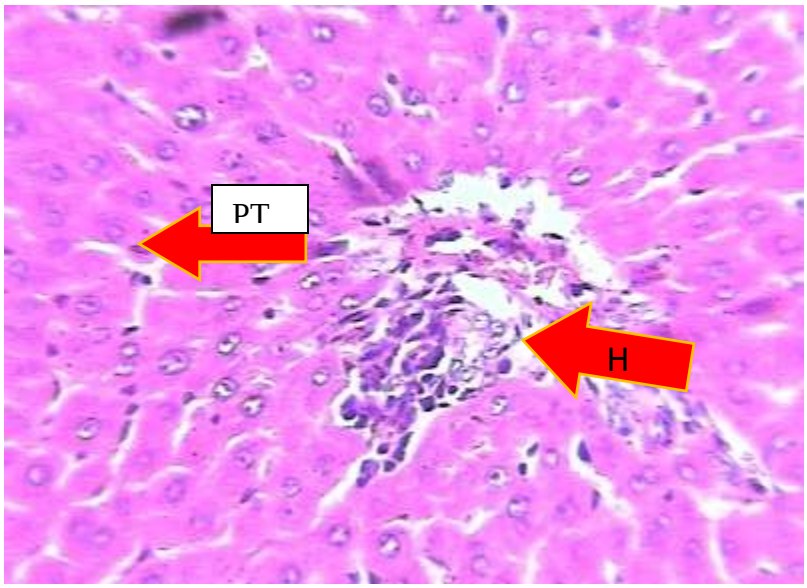

Plate 2a: Photomicrograph of the liver of pregnant rat orally administered with distilled water on days 10-18 post coitus. The arrows shows portal tract (PT) containing few lymphocytes and normal hepatocytes (H) with no degenerative changes (x400) (H & E).

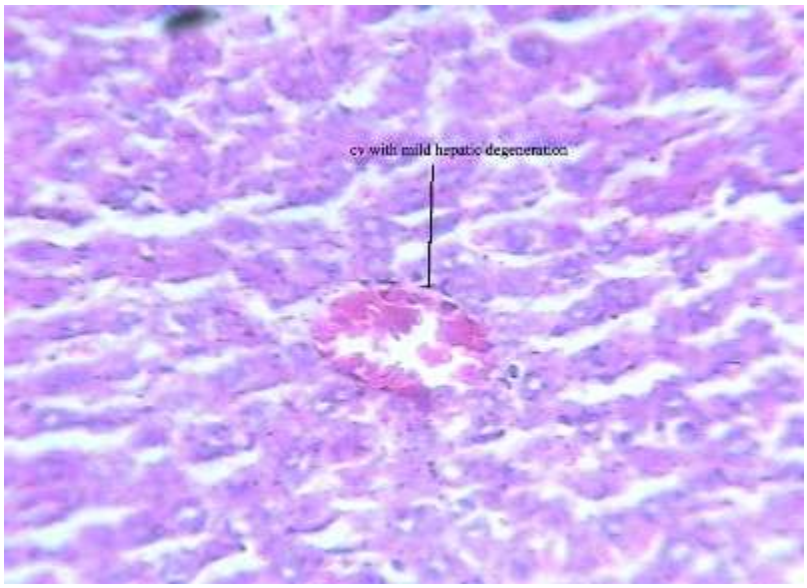

Plate 2b: Photomicrograph of the liver of pregnant rat orally administered with 250 mg/kg body weight of aqueous leaf extract of *S. alata* on days 10-18 post coitus. There was mild to moderate hepatic degeneration (x400) (H & E).

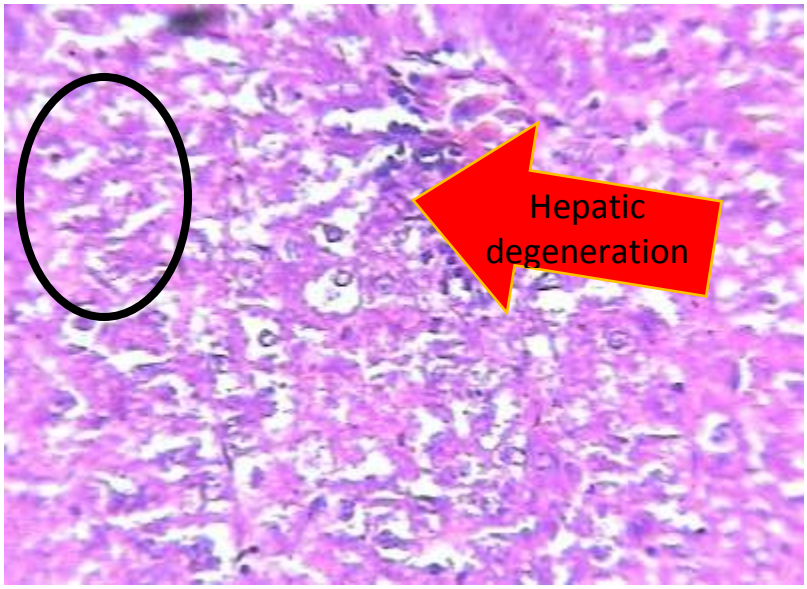

Plate 2c: Photomicrograph of the liver of pregnant rat orally administered with 500 mg/kg body weight of aqueous leaf extract of *S. alata* on days 10-18 post coitus. The circled spot shows portal tract with lymphocytes extending into the lobule. The arrow shows severe degeneration of the hepatocytes (x400) (H & E).

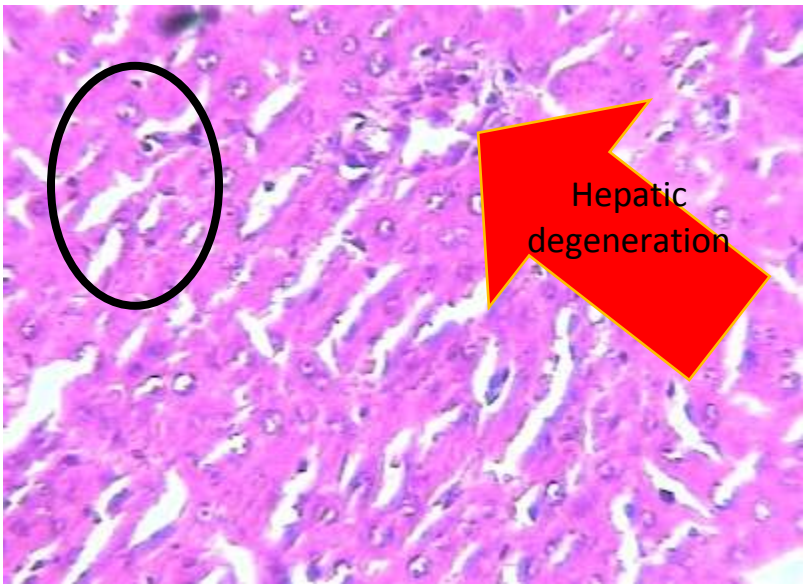

Plate 2d: Photomicrograph of the liver of pregnant rat orally administered with 1000 mg/kg body weight of aqueous leaf extract of *S. alata* on days 10-18 post coitus. The circled spot shows portal tract with lymphocytes extending into the lobule. The arrow indicates severe degeneration of the hepatocytes (x400) (H & E).

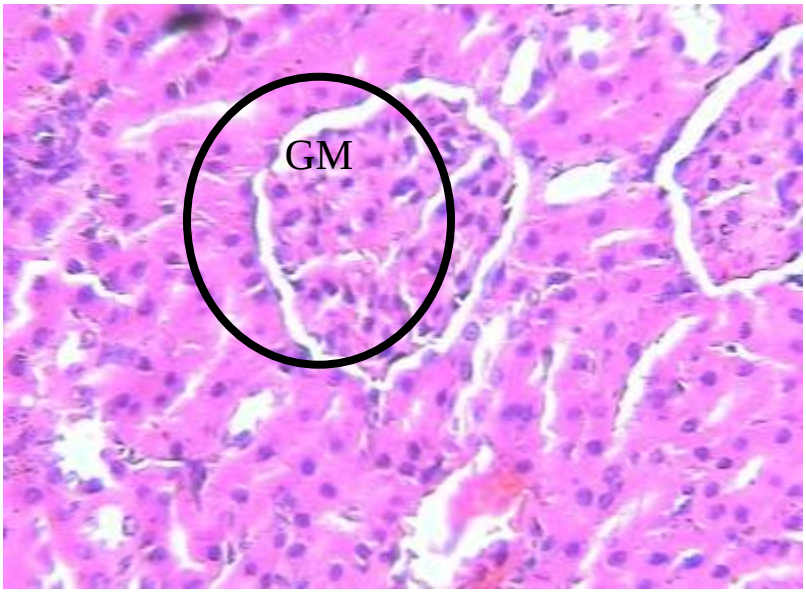

Plate 3a: Photomicrograph of the kidney of pregnant rat orally administered with distilled water on days 10-18 post coitus. The circled spot shows normal glomeruli (GM) and tubules (x400) (H & E).

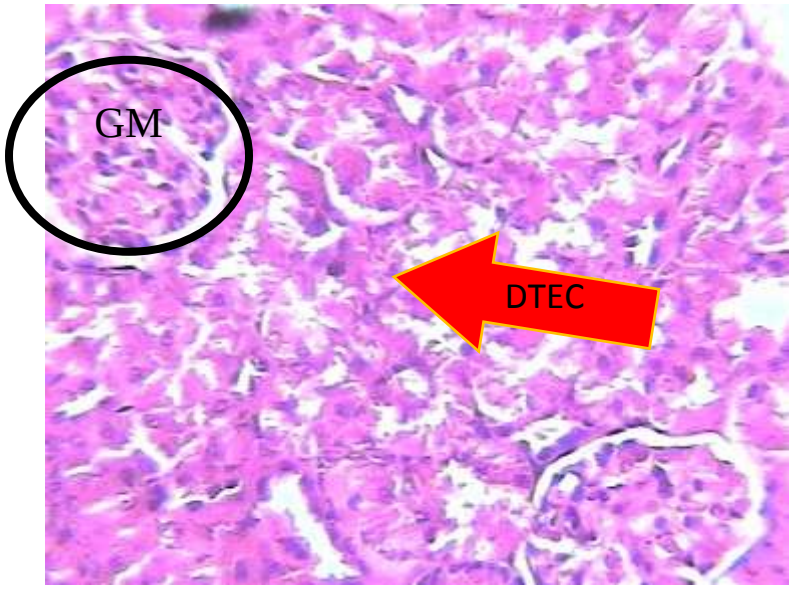

Plate 3b: Photomicrograph of the kidney of pregnant rat orally administered with 250 mg/kg body weight of aqueous leaf extract of *S. alata* on days 10-18 post coitus. The circled spot shows normal glomeruli (GM) while the arrow indicates degenerated tubular epithelial cells (DTEC) (x400) (H & E).

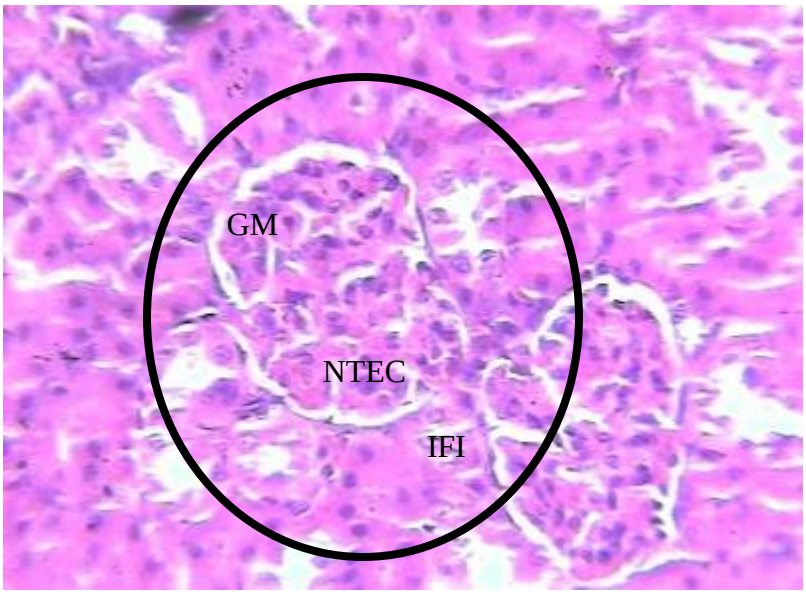

Plate 3c: Photomicrograph of the kidney of pregnant rat orally administered with 500 mg/kg body weight of aqueous leaf extract of *S. alata* on days 10-18 post coitus. The circled spot shows normal glomeruli (GM) with varying degree of necrosis of tubular epithelial cells (NTEC) and inflammatory cells within the interstitum (IFI) (x400) (H & E).

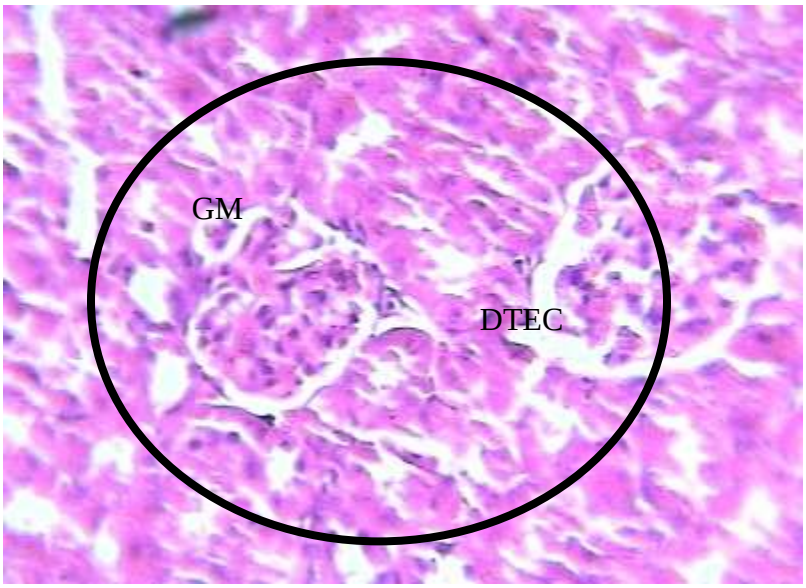

Plate 3d: Photomicrograph of the kidney of pregnant rat orally administered with 500 mg/kg body weight of aqueous leaf extract of *S. alata* on days 10-18 post coitus. The circled spot shows normal glomeruli (GM) and extensive degeneration of tubular epithelial cells (DTEC) (x400) (H & E).