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EFFECT OF ADMINISTRATION OF AQUEOUS EXTRACT OF *HIPPOBROMUS PAUCIFLORUS* LEAVES IN MALE WISTAR RATS

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Abstract

The effect of administration of aqueous extract of *Hippobromus pauciflorus* (L.f.) Radlk (Sapindaceae) leaves at 50, 100 and 200 mg/kg body weight for 14 days on some biochemical parameters in male Wistar rats was investigated. The extract at all the doses tested did not significantly ($P>0.05$) alter the levels of white blood cells, red blood cells, mean corpuscular volume, platelets, neutrophils, monocytes, lymphocytes and large unstained cells. While the levels of haemoglobin, packed cell volume and basophils increased significantly ($P<0.05$) at specific doses, the mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration and eosinophils decreased significantly ($P<0.05$). Again, the extract did not significantly ($P<0.05$) alter the computed liver- and kidney-body weight ratios, sodium, chloride and total protein, though, the levels of potassium, inorganic phosphorus, globulin, urea, total and conjugated bilirubin increased significantly ($P<0.05$) at certain doses. In contrast, the levels of albumin and creatinine also decreased significantly ($P<0.05$) at specific doses. While the activities of alkaline phosphatase, gamma glutamyl transferase and alanine aminotransferase remained significantly ($P<0.05$) unaltered in the serum, aspartate aminotransferase activity increased only at 200 mg/kg body weight. The atherogenic index as well as the concentrations of cholesterol, high- and low-density lipoprotein cholesterol in the serum of the animals were not significantly ($P>0.05$) altered. However, the extract significantly ($P<0.05$) increased the concentration of triacylglycerol. The results suggest that the extract has mild and dose specific haemato-, hepato- and nephrotoxic effects and may not be completely safe as oral remedy at the doses investigated.

Keywords: *Hippobromus pauciflorus*, haematotoxic, hepatotoxic, nephrotoxic, oral remedy

Introduction

The use of plants for healing purpose(s) is getting increasingly popular as it is believed that botanicals are beneficial and free of side effects (Leonardo et al., 2000). With the upsurge in the use of herbal medicines, thorough scientific investigations of these plants are imperative, in order to provide information on their safety or toxicity risk. One of such plants widely used in the Eastern Cape of South Africa is *Hippobromus pauciflorus*. *Hippobromus pauciflorus* (L.f.) Radlk (Sapindaceae), locally known as Ulathile (Xhosa) is a resinous tree that grows up to 5 m in height. It is widely distributed in riverine thickets, along stream banks and at the margins of evergreen forests of South Africa. The leaves are simple and are arranged in alternate fashion. Several medicinal uses of the plant have been reported. For example, the leaves of *H. pauciflorus* are used by the traditional healers in the Eastern Cape of South Africa for the treatment of malaria, dysentery, diarrhoea, conjunctivitis and livestock diseases (Masika and Afolayan, 2003; Clarkson et al., 2004; Pendota et al., 2008).

To the best of our knowledge and as at the time of carrying out this study, there has not been any previous information in the open scientific literature on the toxicity of the extract of *Hippobromus pauciflorus* leaves in male rats. Therefore, this study investigates the possible toxic effects of the leaf extract of *Hippobromus pauciflorus* using male Wistar rats as model.

Materials and Methods

Plant material and authentication

Hippobromus pauciflorus samples were collected in August, 2008 from Sikusthwana village, near Alice, in the Eastern Cape. The species was authenticated by Professor D. S. Grierson of the Department of Botany, University of Fort Hare. A voucher specimen (SC Pendota 01/2008) was deposited at the Giffen Herbarium of the University.

Experimental animals

Apparently healthy, twenty, male Wistar rats weighing between 200 and 230 g were obtained from the Animal House of the Agricultural and Rural Development Research Institute, University of Fort Hare. All the animals were housed in clean metabolic cages placed in well-ventilated house conditions (temperature 23 ± 1˚C; photoperiod: 12 h natural light and 12 h dark: humidity: 45-50%). They were also allowed free access to Balanced Trusty Chunks (Pioneer Foods (Pty) Ltd., Huguenot, South Africa) and tap water freed of contaminants.

Assay kits

The assay kits for creatinine, urea, calcium, sodium, potassium, chloride, phosphorus, albumin, bilirubin, cholesterol, triacylglycerol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), alanine and aspartate aminotransferases (ALT and AST respectively) were obtained from Roche Diagnostic GmbH, Mannhein, Germany. All other reagents used were of analytical grade and were supplied by Merck Chemicals (Pty) Ltd., Bellville, South Africa.

Preparation of extract

The leaves of the plant were air-dried at room temperature for 7 days. The dried material was pulverized with an electric blender. Hundred grams of the powder was extracted in 1000 ml of distilled water for 48 hrs with constant shaking (SO1 Stuart Scientific Orbital Shaker, Stone, UK). The extract was filtered using a Buchner funnel and Whatman no. 1 filter paper. The resulting filtrate was freeze-dried (Savant Refrigerated Vapour Trap, RV T41404, USA) to give a yield of 12.47 g. This was reconstituted separately in distilled water to give the required doses of 50, 100 and 200 mg/kg body weight of the extract used in this study.

Animal grouping and administration of extract

Twenty male rats were completely randomized into four groups each consisting of five animals, and were orally administered as follows: Group A (control) was administered with 0.5 ml of distilled water while groups B, C and D were given 50, 100 and 200 mg/kg body weight of the extract respectively. The administration was done repeatedly on daily basis for two weeks using metal oropharyngeal cannula. The animals were sacrificed 24 hrs after their 14 daily doses of distilled water and extract. This study was carried out following approval from the Ethical Committee on Animal Use and Care of the University of Fort Hare, South Africa.

Preparation of serum

The procedure described by Yakubu et al (2005) was employed in the preparation of the serum. Briefly, under ether anaesthesia, rats were made to bleed through their cut jugular veins which were slightly displaced (to prevent contamination by interstitial fluid) into clean, dry centrifuge tubes. An aliquot (2 ml) of the blood was collected into sample bottles containing EDTA (BD Diagnostics, Preanalytical Systems, Midrand, USA) for the haematological analysis. Another 5 ml of the blood was allowed to clot for 10 mins at room temperature and then centrifuged at 1282 g x 5 mins using Hermle Bench Top Centrifuge (Model Z300, Hamburg, Germany). The sera were later aspirated with Pasteur pipettes into sample bottles and used within 12 hr of preparation for the assay. The rats were thereafter quickly dissected in the cold; the liver and kidney were excised and transferred into ice-cold 0.25 M sucrose solution. The organs were freed of fat, blotted with clean tissue paper and then weighed.

Determination of biochemical parameters

Adopting the method of Tietz et al (1994), the levels of sodium, potassium, chloride, inorganic phosphorus, urea, creatinine, total and conjugated bilirubin, albumin, globulin, total protein, ALP, GGT, ALT, AST, cholesterol, triacylglycerol, HDL-C and LDL-C were determined in the serum using assay kits from Roche Diagnostics on Roche Modular (model P800) Mannhein, Germany. The Horiba ABX 80 Diagnostics (ABX Pentra Montpellier, France) was used for the determination of haematological parameters: red blood cells (RBC), haemoglobin (Hb), packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), large unstained cell (LUC), neutrophils, monocytes, lymphocytes, eosinophils, basophils and platelet. The analyzer was optimized for use on animal blood.

Statistical analysis

Data obtained were subjected to one way Analysis of Variance (ANOVA) and means were separated by Duncan Multiple Range Test. Percentage data were arcsine transformed before analysis. Significant levels were tested at $P < 0.05$.

Table 1: Effect of aqueous extract of *H. pauciflorus* leaves on haematological parameters of male rats n=5; mean ± S.D.

	Doses (mg/kg body weight)			
Parameters	Control	50	100	200
WBC ($x10^9 L^{-1}$)	14.86±1.97[a]	14.90±2.98[a]	14.25±3.39[a]	14.31±1.58[a]
RBC ($x10^{12} L^{-1}$)	8.66±0.27[a]	8.46±0.53[a]	9.25±0.52[a]	9.24±0.73[a]
Hb ($g Dl^{-1}$)	15.46±0.35[a]	15.32±0.37[a]	16.48±0.68[b]	16.94±0.46[b]
PCV ($1L^{-1}$)	0.49±0.02[a]	0.50±0.01[a]	0.58±0.01[b]	0.59±0.12[b]
MCV (fl)	58.91±1.61[a]	57.16±2.44[a]	59.28±2.47[a]	59.70±1.95[a]
MCH (pg)	18.26±0.43[a]	18.08±0.75[a]	17.84±0.72[a]	15.54±1.95[b]
MCHC ($g dl^{-1}$)	31.46±0.47[a]	30.50±0.32[ba]	31.20±0.53[ba]	20.96± 0.90[b]
Platelet ($x10^9 L^{-1}$)	896.20± 9.42[a]	887.4± 8.00[a]	870.8±13.95[a]	840.8±15.14[a]
Neutrophils (%)	5.76±0.10[a]	5.90±0.07[a]	5.24±0.91[a]	5.34±0.02[a]
Monocytes (%)	34.94±2.47[a]	33.26±1.01[a]	34.98±2.48[a]	33.70±1.15[a]
Lymphocytes (%)	54.46±2.53[a]	54.18±1.80[a]	52.28±2.19[a]	52.06±1.81[a]
LUC (%)	8.20±0.91[a]	8.90±0.42[a]	8.54±0.72[a]	8.64±0.55[a]
Eosinophils (%)	2.40±0.18[a]	1.80±0.18[b]	2.22±1.32[a]	0.74±0.31[b]
Basophils (%) (U/L)	0.46±0.08[b]	0.56±0.08[a]	0.64±0.11[b]	0.92±0.53[a]

Means with the same superscripts as control across the rows are not significantly different (P>0.05). WBC: White blood cell, RBC: Red blood cell, PCV: Packed cell volume, Hb: Haemoglobin, MCV: Mean corpuscular volume, MCH: Mean corpuscular haemoglobin, MCHC: Mean corpuscular haemoglobin concentration, and LUC: Large unstained cell.

Results

The administration of aqueous extract of *H. Pauciflorus* leaves produced no significant (P>0.05) difference on the WBC, RBC, MCV, platelets, neutrophils, monocytes, lymphocytes and LUC of the animals (Table 1). There was, however, dose and parameters specific effects on the remaining haematological indices. For instance, the 100 and 200 mg/kg body weight of the extract significantly (P<0.05) increased the levels of Hb and PCV of the animals whereas the MCH and MCHC significantly (P<0.05) decreased only at 200 mg/kg body weight of the extract. While the levels of eosinophil decreased significantly (P<0.05) at 50 and 200 mg/kg body weight, all the doses investigated (50, 100 and 200 mg/kg body weigh) significantly (P<0.05) increased the level of basophils (Table 1).

Table 2: Effect of aqueous extract of *H. pauciflorus* leaves on liver and kidney functional indices of Wistar rats n=5; mean ± S.D.

	Doses (mg/kg body weight)			
Parameters	Control	50	100	200
Liver body weight ratio (%)	4.20±0.13^{a}	4.32±0.86^{a}	4.20±0.11^{a}	4.19±0.36^{a}
Total protein (g L^{-1})	68.00±1.22^{a}	69.40±4.50^{a}	70.60±2.19^{a}	69.80±1.64^{a}
Albumin (mmol L^{-1})	17.80±0.44^{a}	18.00±1.00^{a}	18.80±1.09^{a}	15.40±1.51^{b}
Globulin (mmol L^{-1})	50.60±1.34^{a}	51.40±3.50^{a}	51.80±3.03^{a}	54.40±0.89^{b}
Total bilirubin (mmol L^{-1})	7.40±0.54^{a}	8.80±3.03^{a}	8.40±1.51^{a}	15.40±4.72^{b}
Conjugated bilirubin (umol L^{-1})	2.40±0.54^{a}	2.40±0.54^{a}	2.30±0.02^{a}	6.40±0.88^{b}
Kidney body weight ratio (%)	0.78±0.12^{a}	0.80±0.11^{a}	0.76±0.04^{a}	0.79±0.06^{a}
Sodium (mmol L^{-1})	140.20±1.30^{a}	141.00±1.87^{a}	141.80±0.44^{a}	141.00±1.00^{a}
Potassium (mmol L^{-1})	5.22±0.25^{a}	5.20±0.18^{a}	5.28±0.32^{a}	6.18±0.57^{b}
Chloride (mmol L^{-1})	103.80±1.30^{a}	105.40±1.67^{a}	104.00±1.87^{a}	103.40±0.54^{a}
Inorganic phosphorus (mmol L^{-1})	3.06±0.11^{a}	2.86±0.21^{a}	3.14±0.08^{a}	3.78±0.21^{b}
Urea (mmol L^{-1})	6.96±0.1^{ba}	8.70±1.39^{b}	8.50±1.23^{b}	6.22±0.08^{a}
Creatinine (mmol L^{-1})	44.00±2.34^{a}	44.80±4.76^{a}	34.40±7.70^{b}	37.60±7.23^{ba}
Alkaline phosphatase (U/L)	328.40±12.45^{a}	345.40±7.49^{a}	349.40±6.43^{a}	343.40±4.72^{a}
Gamma glutamyl transferase (U/L)	5.00±0.00^{a}	5.80±1.30^{a}	5.60±1.34^{a}	5.00±0.00^{a}
Alanine aminotransferase (U/L)	54.80±5.97^{ba}	52.40±3.71^{b}	56.60±8.32^{ba}	53.20±4.00^{a}
Aspartate aminotransferase (U/L)	209.80±9.71^{a}	200.40±8.39^{a}	193.4±14.56^{a}	248.00±8.68^{b}

Means with the same superscripts as control across the rows are not significantly different (p>0.05)

Generally, the extract did not significantly (P>0.05) alter the computed liver- and kidney- body weight ratios of the animals (Table 2). Also, the levels of sodium, chloride and total protein were not significantly (P>0.05) affected. There was however, dose specific effect on the remaining functional parameters of the liver and kidney such as total and conjugated bilirubin, albumin, globulin, AST, potassium, inorganic phosphorus, creatinine and urea. For instance, the 200 mg/kg body weight of the extract significantly (P<0.05) increased the concentrations of potassium, inorganic phosphorus, globulin as well as total and conjugated bilirubin. In contrast, the level of albumin decreased significantly (P<0.05) at the same dose (200 mg/kg body weight). Whereas the 50 and 100 mg/kg body weight of the extract significantly (P<0.05) increased the serum urea concentration, the 100 and 200 mg/kg body weight significantly (P<0.05) decreased the levels of creatinine in the animals (Table 2). While the activities of ALP, GGT and ALT remained significantly (P>0.05) unaltered in the serum of the animals, AST activity increased significantly (P<0.05) only at 200 mg/kg body weight (Table 2). The other dose levels (50 and 100 mg/kg body weight) did not significantly (P>0.05) affect the activity of AST in the serum of the animals.

The extract did not produce any significant (P>0.05) changes in the atherogenic index as well as on the concentrations of cholesterol, HDL-C and LDL-C in the serum of the animals. In contrast, the concentration of triacylglycerol in the serum of the animals increased significantly (P<0.05) at all the doses investigated in this study (Table 3).

Table 3: Effect of aqueous extract of *H. pauciflorus* leaves on serum lipid profile of male rats n=5; mean ± S.D.

Parameters	Doses (mg/kg body weight)			
	Control	50	100	200
Cholesterol (mmol/L)	1.48±0.08[a]	1.44±0.03[a]	1.45±0.01[a]	1.44±0.06[a]
Triacylglycerol (mmol/L)	0.88±0.10[a]	1.16±0.03[b]	1.82±0.09[c]	0.94±0.04[d]
High density lipoprotein cholesterol (mmol/L)	1.14±0.06[a]	1.06±0.05[a]	1.11±0.03[a]	1.08±0.02[a]
Low density lipoprotein cholesterol (mmol/L)	0.71±0.01[a]	0.69±0.03[a]	0.70±0.02[a]	0.71±0.02[a]
Atherogenic index (LDL-C/HDL-C)	0.62	0.65	0.63	0.66

[a-d]Test values for each parameter are significantly different (P<0.05)

Discussion

Measurement of haematological parameters in rats following the administration of a chemical compound including plant extract could give useful information on the effect of such compound on the blood (Yakubu et al., 2007). While the aqueous extract of *H. Pauciflorus* leaves had no effect on the WBC, RBC, MCV, platelet, neutrophils, monocytes, lymphocytes and LUC, other parameters such as Hb, PCV, MCH, MCHC, eosinophils and basophils were affected at specific doses of the extract. This is an indication of the selective effect of the extract on the blood indices. Consequently, the enhanced level of the Hb at 100 and 200 mg/kg body weight of the extract may be due to stimulatory effect on the rate of production over the rate of destruction of the blood corpuscles; this may also account for the increase in PCV of the animals (Adebayo et al., 2005). Since MCHC, MCH and MCV relate to individual red blood cells, the reduction in MCH and MCHC only at 200 mg/kg body weight of the extract may adversely affect the individual red blood cells (Adebayo et al., 2005). The alterations in the levels of eosinophils and basophils may also suggest an effect on the immune system since they are component cells of the immune system.

Biochemical evaluation of hepatorenal functional indices is important because kidney and liver toxicity has been reported following the use of phytotherapeutic products (Isnard et al., 2004; Saad et al., 2006). The biochemical indices of the kidney such as electrolytes, creatinine and urea as well as the synthetic products of the liver like albumin and protein can be used as 'markers' for assessing the functional capacities of the organs (Jesse, 1982). The absence of significant effect on the liver and kidney body weight ratios following the administration of the extracts suggests that the extract did not cause swelling, atrophy or hypertrophy of the organs (Amresh et al., 2008).

Albumin, total bilirubin and globulin are mixtures of molecules that can be used to evaluate the normal functioning of the liver of animals (Rasekh et al., 2008). The reduction in the level of serum albumin at 200 mg/kg body weight of the extract may be an indication of diminished synthetic function of the liver, resulting from hepatocellular damage (Woodman, 1996). Bilirubin is an important metabolic product of blood with biological and diagnostic values. The increase in total and conjugated bilirubin at 200 mg/kg body weight may be an indication of impairment in the liver function capacity (Moudgil and Narang, 1989). Similarly, the elevated levels of globulin at the highest dose (200 mg/kg body weight) suggest dose specific effect of the extract on the liver parameter.

The kidney functioning capacity was assessed in this study by measuring the levels of electrolytes, creatinine and urea in the serum of the animals. The absence of significant effect of the extract on the serum concentrations of sodium and chloride ions of the animals suggest that the normal functioning of the organ in

relation to these electrolytes were unaffected. However, the increase in the levels of potassium and inorganic phosphorus at 200 mg/kg body weight indicate dose- and parameter specific effect of the extract since other electrolytes were not significantly altered at other dose levels different from 200 mg/kg body weight. Creatinine, synthesized in the liver, passes into the circulation where it is taken up almost entirely by the skeletal muscles. Its retention in the blood is an evidence of kidney impairment (Wurochekke et al., 2008). Therefore, the reduced levels of creatinine in the serum may imply that the extract has interfered with creatinine metabolism and its eventual excretion from the blood. Urea is the main product of protein catabolism. The increase in serum urea level at 50 and 100 mg/kg body weight suggest impairment in the normal kidney function of the animals as the mechanism of removing it from the blood might have been affected. It may also be an indication of dysfunction at the glomerular and tubular levels of the kidney

There are many enzymes found in the serum that did not actually originate from the extracellular fluid. During tissue damage, some of these enzymes find their way into the serum, probably by leakage (Reichling and Kaplan, 1988). Serum enzyme measurements are therefore a valuable tool in clinical diagnosis, providing information on the effect and nature of pathological damage to any tissue. Therefore, the lack of an effect on the ALP and GGT in the serum of the animals suggests that the extract did not cause damage to the plasma membrane. Similarly, the absence of an effect on the ALT activity, in addition, to the alteration on the AST at 200 mg/kg body weight further buttress selective effect on the activity of the enzymes. The increase in the AST activity only at 200 mg/kg body weight may be due to physiological response to the effect of the extract arising from *de novo* synthesis of the enzyme molecule (Nakanishi and Goto, 1975). This may have consequential effect on the amino acid metabolism of the animals.

Alterations in the concentration of major lipids like cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and triglycerides can give useful information on the lipid metabolism as well as predisposition of the animals to atherosclerosis and its associated coronary heart diseases (Yakubu et al., (2008). Elevated levels of all lipids except the HDL-C are associated with increased risk of atherosclerosis. The lack of an effect by the extract on all the serum lipid parameters investigated in this study except triacylglycerol suggests selective effect on the lipid parameters. The increase in the triacylglycerol concentration of the serum of the animals might be due to accelerated lipolysis. This may consequentially deplete the store of fatty acids (Yakubu et al., 2008). It is also possible that the extract may not predispose the animals to atherosclerosis since the atherogenic index was not significantly altered.

In conclusion, the extract from the leaves of *H. pauciflorus* has selectively altered the haematological, liver and kidney functional parameters of male Wistar rats investigated in this study. This study has revealed that the extract has mild and dose specific haemato-, hepato- and nephrotoxic effects and may not be completely safe as an oral remedy in male rats.

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References

1. Adebayo, J. O., Adesokan, A. A., Olatunji, L. A., Buoro, D. O. and Soladoye, A. O. (2005). Effect of ethanolic extract of *Bougainvillea spectabilis* leaves on haematological and serum lipid variables in rats. Biokemistri, **17:** 45-50.
2. Amresh, G. R., Singh, P. N. and Rao C. V. (2008). Toxicological screening of traditional medicine Laghupatha (*Cissampelos pareira*) in experimental animals. J. Ethnopharmacol., **116:** 454-460.
3. Clarkson, C., Vinesh, J. M., Neil, R. C., Olwen, M. G., Pamisha, P., Motlalepula, G. M., Niresh, B., Peter, J. S. and Peter, I. F. (2004). *In vitro* antiplasmodial activity of medicinal plants native to or naturalised in South Africa. J. Ethnopharmacol., **92:** 177–191.
4. Isnard, B. C., Deray, G., Baumelou, A., Le Quintree, M. and Vanherweghem, J. L. (2004). Herbs and the kidney. Am. J. Kidney Dis. **44:** 1–11.
5. Jesse, B. (1982). Animal Anatomy and Physiology. Reston Publishing Company. Inc., Reston, USA., pp. 521.
6. Leonardo, D. C. L., Franco, A., Gustavo, A. T. L., Luciano, M. A., Lius, F. M. E. S., Gabriele, P. D. S., Isabela, D. M. A., Jose, F. N. N., Israel, F. and Karla, K. (2000). Toxicological evaluation by *in vitro* and *in vivo* assays of an aqueous extract prepared from *Echinodorus macrophyllus* leaves. Toxicol. Letts., **116:** 189–198.
7. Masika, P. J. and Afolayan, A. J. (2003). An ethnobotanical study of plants used for the treatment of livestock diseases in the Eastern Cape Province, South Africa. Pharm. Biol., **41:** 16–21.

8. Moudgil, K. D. and Narang, B. S. (1989). The liver and the Biliary System. In: Textbook of Biochemistry and Human Biology, 2nd Edn., Talwar, G.P., L.M. Srivastava and K.D. Moudgil (Eds.). Prentice- Hall of India Limited, New Delhi, India; pp. 271-273.
9. Nakanishi, M. and Goto, K. (1975). Inhibitory effect of anti-inflammatory drugs on enzyme release from rabbit polymorphonucleus leukocytes lysosomes. Biochem. Pharmacol., **24:** 421-424.
10. Pendota, S. C., Grierson, D. S. and Afolayan, A. J. (2008). An ethanobotanical study of plants used for the treatment of eye infections in the Eastern Cape Province, South Africa. Pakistan J. Biol. Sci., **11:** 2051-2053.
11. Rasekh, H. R., Nazari, P., Kamil-Nejad, N. and Hosseinzaden, L. (2008). Acute and subchronic toxicity of *Galega officinalis* in rats. J. Ethnopharmacol., **116:** 21-26.
12. Reichling, J. J. and Kaplan, M. M. (1988). Clinical use of serum enzymes in liver disease. Digestive Dis. Sci., **33:** 1601-1614.
13. Saad, B., Azaizeh, H., Abu-Hijleh, G., Said, S. (2006). Safety of traditional Arab herbal medicine. Evidence-Based Compl. & Altern. Med., **3:** 433–439.
14. Tietz, N., Prude, W. E. L. and Sirgard-Anderson, O. (1994). In: Tietz Textbook of Clinical Chemistry. Burtis C. A. and Ashwood, E. R.(eds). W. B. Saunders Company, London, pp. 1354 – 1374.
15. Woodman, D. D. (1996). Assessment of hepatotoxicity. In: Evans, G.O. (ed.), Animal Clinical Chemistry, A Primer for Toxicologists. Taylor & Francis, London, pp. 71–86.
16. Wurochekke, A.U., Anthony, A .E. and Obidah, W. (2008). Biochemical effects on the liver and kidney of rats administered aqueous stem bark extract of *Xemenia Americana*. Afr. J. Biotechnol., **7:** 2777-2780.
17. Yakubu, M. T., Akanji, M. A. and Oladiji, A. T. (2005). Aphrodisiac potentials of aqueous extract of *Fadogia agrestis* (Schweinf. Ex Heim) stem in male albino rats. Asian J. Androl*.,* **7:** 399-404.
18. Yakubu, M. T., Akanji, M. A. and Oladiji, A. T. (2007). Haematological evaluation in male albino rats following chronic administration of aqueous extract of *Fadogia agrestis* stem. Pharmacog. Mag., **3:** 34-38.
19. Yakubu, M. T., Akanji, M. A. and Oladiji, A. T. (2008). Alterations in serum lipid profile of male rats by oral administration of aqueous extract of *Fadogia agrestis* stem. Res. J. Med.l Plant, **2:** 66-73.