African Journal of Biotechnology Vol. 8 (8), pp. 1425-1430, 20 April, 2009
Available online at http://www.academicjournals.org/AJB
ISSN 1684–5315 © 2009 Academic Journals

Full Length Research Paper

Effects of aqueous extract from the leaves of *Chrysocoma ciliata* L. on some biochemical parameters of Wistar rats

A. O. T. Ashafa, M. T. Yakubu, D. S. Grierson and A. J. Afolayan*

Department of Botany, University of Fort Hare, Alice 5700, South Africa.

Accepted 9 February, 2009

The effect of oral administration of aqueous extract of *Chrysocoma ciliata* leaves at 50, 100, 200 and 400 mg/kg body weight for 14 days on some biochemical parameters of male rats was investigated. The extract did not have any significant effect ($p > 0.05$) on the serum concentrations of sodium, potassium, chloride, urea, calcium, albumin, magnesium, inorganic phosphorus, uric acid, globulin and total protein as well as the red blood cell (RBC), hemoglobin (Hb), packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC) and red cell distribution width (RCW). While the WBC was reduced at 50 and 100 mg/kg body weight, the 200 and 400 mg/kg body weight increased the blood parameter. The 50, 100 and 200 decreased the MCV. The doses increased the levels of large unstained cells (LUC), neutrophils, eosinophils, serum alkaline phosphatase, gamma glutamyl transferase, alanine and aspartate aminotransaminases whereas the lymphocytes, basophils, serum total and conjugated bilirubin were decreased in the animals. The platelet levels fluctuated throughout the experimental period. The level of the monocyte was only increased at 100 mg/kg body weight of the extract. The 50, 100 and 200 mg/kg body weight of the extract decreased the serum cholesterol concentration in the animals, whereas the 400 mg/kg body weight increased the lipid parameter. Similarly, the 50, 100 and 200 mg/kg body weight also decreased the serum triacylglycerol of the animals. The HDL-C, LDL-C and atherogenic index compared favourably with the control. While there was no significant change at all the doses investigated in the kidney and heart-body weight ratios, the extract at 50 and 400 mg/kg body weight increased the liver-body weight ratio. In contrast, the 50, 100 and 200 mg/kg body weight decreased the testes-body weight ratio. The parameter and dose specific effect of the extract on the biochemical parameters suggest selective toxicity.

Key words: *Chrysocoma ciliata,* function indices, serum lipids, haematological parameters, selective toxicity.

INTRODUCTION

Chrysocoma ciliata otherwise known as bitterbos or bitter cowcurd (English), *kaalsiektebos* (Afrikaans) and *Ihbosisi* (Xhosa), is a dense, rounded shrub growing up to 0.5 m in height. It is indigenous to Southern Africa, usually becoming invasive in overgrazed parts of the karoo and poorly managed velds (Van Wyk et al., 2002). The yellowish green leaves which are small and needle shaped are sticky to touch. The plant has been reported to cause kaalsiekte (alopecia or hair loss) in lambs and lakseersiekte (purging disease) in adult animals (Tokarina et al., 1986; Van Wyk et al., 2002). Information obtained on the ethnomedical uses of the plant from some herb sellers and herbalists in Alice, South Africa include relief of headache, menstrual and stomach pains. It is also used in boosting fertility in women.

Many plants have been reported to be toxic to both human and livestocks. For example, *Vernonia molissima*, *Datura stramonium* and *Solanum aculeastrum* have been implicated as nephrotoxic and hepatotoxic agents in livestock and humans (Ertekin et al., 2005; Koduru et al., 2006). Similarly, stem sample of *Fadogia agrestis* have

*Corresponding author. E-mail: Aafolayan@ufh.ac.za. Tel: +27822022167. Fax: +27866282295.

also been reported to exhibit localized systemic toxicity on haematological indices in rats (Yakubu et al., 2007), while *Allium ascalonium* Bory and Chaub have been shown to decrease most of the parameters relating to red blood cells and also increased most of those relating to white blood cells (Owoyele et al., 2004). However, to the best of our knowledge, there is dearth of information on the effect of *C. ciliata* leaf extract on some biochemical parameters of liver and kidney damage, serum lipids and haematological parameters of rats. Therefore, this study was aimed at providing information on the effect of the aqueous extract of this herb on biochemical parameters of rats in order to evaluate the safety or toxicological potentials of the extract.

MATERIALS AND METHODS

Plant material and authentication

The plant was collected in March, 2008 from a single population of *C. ciliata* growing within the premises of Alice campus of the University of Fort Hare, South Africa. It was authenticated by Mr Tony Dold of the Selmar Schonland Herbarium, Rhodes University, South Africa. A voucher specimen (AshMed.2008/1) was prepared and deposited in the Giffen Herbarium of University of Fort Hare.

Preparation of extract

The leaves of *C. ciliata* were carefully rinsed under running tap water, oven dried at 40°C and pulverized. Powdered plant material (150 g) was extracted in distilled water at room temperature for 48 h on an orbital shaker (Stuart Scientific Orbital Shaker, UK). The extract was filtered through Whatman no. 1 filter paper and freeze-dried using Savant Refrigerated Vapor Trap, (RVT4104, USA). This was reconstituted in distilled water to give the required doses of 50, 100, 200 and 400 mg/kg body weight used in this study.

Experimental animals

Twenty male Wistar rats weighing between 200 and 230 g were obtained from the Animal House of the Agricultural and Rural Development Research Institute (ARDRI), University of Fort Hare. The rats were housed in polypropylene 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 maintained on Balance Trusty Chunks (Pioneer Foods (Pty) Ltd, Huquenot, South Africa) and tap water *ad libitum.* The study was carried out following the approval of the ethical committee on animal use and care of the University of Fort Hare, South Africa.

Animal grouping and extract administration

The animals were grouped into four consisting of five rats each. Group A (control) received orally, 0.5 ml of distilled water for 14 days while groups B, C and D were treated like the control except that they received 50, 100, 200 and 400 mg/kg body weight of the extract. The distilled water and the extract were administered daily between 1000 – 1030 h using metal oropharyngeal cannula.

Assay kits and chemical reagents

The assay kits for cholesterol, triacylglycerol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), creatinine, urea, calcium, sodium, magnesium, potassium, inorganic phosphorus, albumin, bilirubin, alkaline phosphatase, gamma glutamyl transferase, alanine and aspartate aminotransferases were obtained from Roche Diagnostic GmbH, Mannhein, Germany.

Preparation of serum

The procedure described by Yakubu et al. (2005) was used in the preparation of serum. Briefly, under ether anaesthesia, the neck area of the rats was quickly shaved to expose the jugular veins. The veins after being slightly displaced (to prevent blood contamination by interstitial fluid) were sharply cut with sterile scapel blade and an aliquot (2 ml) of the blood was collected into EDTA sample bottles (BD Diagnostics, Preanalytical Systems, Midrand, USA) for the haematological analysis. Another 5 ml of the blood was allowed to clot for 10 min at room temperature and then centrifuged at 1282 g x 5 min using Hermle Bench Top Centrifuge (Model Hermle, Z300, Hamburg, Germany). The sera were later aspirated with Pasteur pipettes into sample bottles and used within 12 h of preparation for the determination of the biochemical parameters. The liver, kidney, heart and testes were thereafter removed from the animals, freed of surrounding tissues and fats, blotted in tissue paper and thereafter weighed for the determination of the organ-body weight ratio as described by Yakubu et al. (2008).

Determination of biochemical parameters

Adopting the method of Tietz et al. (1994), the levels of creatinine, uric acid, calcium, magnesium, chloride, sodium and potassium ions, phosphorus and urea were determined in the serum. Cholesterol, LDL-C, HDL-C, triacylglycerol, albumin, bilirubin (total and conjugated), total protein, alkaline phosphatase, gamma glutamyl transferase, alanine and aspartate aminotransferases were determined in the serum using assay kits from Roche Diagnostics, GmbH, Mannhein, Germany on Roche modular (model P800) Mannhein, Germany. While the globulin content in the serum was obtained using an expression given by Tietz et al. (1994), the atherogenic index was computed as described by Panagiotakos et al. (2003). The Advia 2120 (Bayer, Germany) was used for the determination of hematological parameters.

Statistical analysis

Data were expressed as means of five replicates ± SD. They were subjected to one way ANOVA and means were separated by the Duncan Multiple Range Test. Percentage data were transformed to arcsine before analysis. Significant levels were tested at $P < 0.05$.

RESULTS

The aqueous extract of *C. ciliata* at all the doses tested did not have any significant effect on the RBC, Hb, PCV, MCH, MCHC and RCW. While the WBC was reduced at 50 and 100 mg/kg body weight of the extract, the 200 and 400 mg/kg body weight increased the blood parameter. The 50, 100 and 200 decreased the MCV. Whereas all the doses investigated increased the levels of LUC, neutrophils and eosinophils in the animals, the lympho-cytes and basophils were decreased throughout the

Table 1. Effects of aqueous extract of *C. ciliata* leaf on the haematological parameters of Wistar rats. n = 5, $\overline{X}$ ± S.D.

Haematological parameters	Extract (mg/kg body weight)				
	Control	50	100	200	400
WBC (x 10^9/l)	15.69 ± 5.25^a	11.47 ± 5.25^b	13.28 ± 3.44^c	21.06 ± 5.62^d	19.96 ± 3.62^d
RBC (x 10^{12}/l)	8.18 ± 0.51^a	8.58 ± 0.79^a	8.69 ± 0.38^a	8.36 ± 0.49^a	8.19 ± 0.39^a
Hb (g/dl)	15.47 ± 0.80^a	15.63 ± 0.78^a	15.55 ± 0.63^a	15.43 ± 0.62^a	15.63 ± 0.63^a
PCV (l /l)	0.50 ± 0.02^a	0.50 ± 0.03^a	0.49 ± 0.01^a	0.51 ± 0.03^a	0.48 ± 0.02^a
MCV (fl)	60.30 ± 1.28^a	57.50 ± 1.74^b	55.70 ± 1.90^b	52.98 ± 1.31^c	60.35 ± 1.78^a
MCH (pg)	18.93 ± 0.54^a	18.28 ± 0.75^a	17.95 ± 0.50^a	18.15 ± 0.73^a	18.53 ± 0.36^a
MCHC (g/dL)	33.88 ± 5.04^a	31.75 ± 0.62^a	32.23 ± 1.32^a	32.30 ± 0.72^a	30.73 ± 0.83^a
RCDW (%)	13.08 ± 0.31^a	13.07 ± 0.19^a	13.05 ± 0.47^a	13.02 ± 0.59^a	13.05 ± 0.48^a
Platelet (x10^9/l)	846.25 ± 7.47^a	786.25 ± 4.76^b	933 .00 ± 5.68^c	859.50 ± 8.66^a	789.00 ± 9.0.3^b
Neutrophils (%)	4.90 ± 0.80^a	7.50 ± 0.03^b	10.5 ± 0.98^b	6.07 ± 0.11^b	6.20 ± 0.56^b
Monocytes (%)	33.33 ± 2.42^a	32.93 ± 2.95^a	46.2 ± 3.76^b	29.7 ± 5.06^a	34.38 ± 1.21^a
Lymphocytes (%)	53.50 ± 4.84^a	46.05 ± 2.84^b	23.60 ± 1.64^c	28.70 ± 2.38^d	35.38 ± 2. 81^e
LUC (%)	8.13 ± 0.57^a	9.83 ± 0.45^b	11.33 ± 1.97^c	11.15 ± 0.06^c	11.40 ± 0.75^c
Eosinophils (%)	2.30 ± 0.07^a	3.07 ± 0.06^b	2.98 ± 0.03^b	5.35 ± 0.07^c	5.80 ± 0.05^c
Basophils (%)	0.93 ± 0.02^a	0.55 ± 0.04^b	0.65 ± 0.01^b	0.65 ± 0.06^b	0.63 ± 0.04^b

Means with the same superscript across the rows for each parameter are not significantly different (P > 0.05). WBC, white blood cell; RBC, red blood cell; PCV, packed cell volume; Hb, hemoglobin; MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration; LUC, large unstained cells; RCDW, Red cell distribution width.

experimental period. The platelet levels fluctuated throughout the experimental period. The level of the monocyte was only increased at 100 mg/kg body weight of the extract (Table 1).

The extract at all the doses (50, 100, 200 and 400 mg/kg body weight) did not produce any significant effect on the serum concentrations of sodium, potassium, chloride, urea, calcium, albumin, magnesium, inorganic phosphorus, uric acid, globulin and total protein of the animals. Creatinine level increased significantly only at 100 mg/kg body weight. The extract reduced the concentrations of total and conjugated bilirubin in the serum of the animals. Generally, the extract at all the doses increased the activity of alkaline phosphatase, gamma glutamyl transferase, alanine and aspartate aminotransaminases in the serum (Table 2).

The 50, 100 and 200 mg/kg body weight of the extract decreased the serum cholesterol concentration in the animals whereas the 400 mg/kg body weight increased the lipid parameter. Similarly, the 50, 100 and 200 mg/kg body weight also decreased the serum triacylglycerol of the animals. The HDL-C, LDL-C and atherogenic index were not significantly different when compared with the control (Table 3).

While there was no significant change at all the doses investigated in the kidney and heart-body weight ratios, the extract at 50 and 400 mg/kg body weight increased the liver-body weight ratio. In contrast, the 50, 100 and 200 mg/kg body weight decreased the testes-body weight ratio (Figure 1).

DISCUSSION

The various biochemical parameters investigated in this study are useful indices of evaluating the toxicity of plant extract in animals (Yakubu et al., 2003, 2007, 2008). Assessment of haematological parameters can be used to determine the extent of deleterious effect of extracts on the blood of an animal. It can also be used to explain blood relating functions of a plant extract or its products (Yakubu et al., 2007). Such analysis is relevant to risk evaluation as changes in the haematological system have higher predictive value for human toxicity, when the data are translated from animal studies (Olson et al., 2000). The non-significant effect of the extract on the RBC may be an indication that the balance between the rate of production and destruction of the blood corpuscles (erythropoiesis) was not altered. MCHC, MCH and MCV relates to individual red blood cells while Hb, RBC, PCV, LUC and RCDW are associated with the total population of red blood cells. Therefore, the absence of significant effect of the extract on RBC, Hb, PCV, MCH, MCHC and RCDW could mean that neither the incorporation of haemoglobin into red blood cells nor the morphology and osmotic fragility of the red blood cells was altered (Adebayo et al., 2005). The decreased MCV and the elevated levels of LUC by the extract further suggest selective toxicity of the extract and or its components. The significant increase in the neutrophils by the extract could possibly suggest enhancement in the ability of the blood component to phagocytose. Lymphocytes are the

Table 2. Effect of administration of *C. ciliata* leaf extract on liver and kidney function parameters of Wistar rats. n = 5, $\overline{X}$ ± S.D.

Parameters	Extract (mg/kg body weight)				
	Control	50	100	200	400
Sodium (mmol/l)	138.25 ± 2.06^a	140.25 ± 1.89^a	140.00 ± 2.16^a	138.75 ± 1.25^a	138.75 ± 2.62^a
Potassium (mmol/l)	5.28 ± 0.83^a	5.28 ± 0.60^a	5.20 ± 0.24^a	5.38 ± 0.06^a	5.30 ± 0.65^c
Chloride (mmol/ l)	101.00 ± 0.00^a	103.00 ± 2.65^a	103.00 ± 2.83^a	102.00 ± 1.00^a	102.00 ± 0.58^a
Urea (mmol/l)	6.23 ± 0.34^a	6.05 ± 0.57^a	6.00 ± 0.29^a	6.25 ± 0.45^a	6.38 ± 0.83^a
Creatinine (mmol/l)	47.75 ± 5.50^a	48.50 ± 5.80^a	54.00 ± 7.11^b	48.00 ± 4.08^a	48.25 ± 3.77^a
Calcium (mmol/l)	2.38 ± 0.05^a	2.33 ± 0.16^a	2.36 ± 0.06^a	2.27 ± 0.09^a	2.38 ± 0.09^a
Albumin (mmol/l)	17.00 ± 1.08^a	15.75 ± 4.43^a	17.25 ± 1.26^a	16.25 ± 3.59^a	16.50 ± 0.58^a
Magnesium (mmol/l)	1.12 ± 0.12^a	1.11 ± 0.13^a	1.10 ± 0.05^a	1.09 ± 0.09^a	1.13 ± 0.09^a
Inorganic Phosphorus (mmol/l)	2.70 ± 0.18^a	2.63 ± 0.48^a	2.68 ± 0.26^a	2.62 ± 0.21^a	2.65 ± 0.12^a
Uric acid (mmol/l)	0.15 ± 0.05^a	0.14 ± 0.02^a	0.14 ± 0.04^a	0.16 ± 0.03^a	0.15 ± 0.02^a
Total bilirubin (µmol/l)	14.00 ± 1.00^a	9.75 ± 0.42^b	8.00 ± 0.71^b	9.75 ± 0.77^b	9.00 ± 0.16^b
Conjugated bilirubin (µmol/l)	5.25 ± 0.11^a	3.00 ± 0.16^b	3.00 ± 0.81^b	3.25 ± 0.95^b	3.50 ± 0.29^b
Globulin (mmol/l)	53.75 ±2.01^a	55.50 ±0.40^a	54.00 ±0.45^a	54.00 ± 0.25^a	53.50 ±0.77^a
Total protein (g/l)	70.75 ±3.14^a	71.25 ± 3.30^a	71.25 ± 2.62^a	70.25 ± 3.05^a	70.00 ± 1.82^a
Alkaline phosphatase (U/L)	316.75 ± 7.22^a	354.25 ± 8.00^b	390.00 ± 7.30^c	418.00 ± 7.64^d	513.25 ± 6.82^e
γ- Glutamyl transferase (U/L)	5.50 ± 0.10^a	9.75 ± 0.50^b	9.25 ± 0.50^b	7.50 ± 0.00^c	8.25 ± 0.50^b
Alanine aminotransaminase (U/L)	68.25 ± 3.14^a	83.25 ± 3.47^b	98.25 ± 2.80^c	84.50 ± 3.51^b	103.75 ± 4.64^c
Aspartate aminotransaminase (U/L)	216.67 ± 8.22^a	317.33 ± 6.30^b	394.75 ± 6.17^c	313.75 ± 4.15^b	429.00 ± 5.23^d

Means with the same superscript across the row for each parameter are not significantly different (P > 0.05).

Table 3. Effect of *C. ciliata* leaf extract on serum lipid profile of Wistar rats. n = 5, $\overline{X}$ ± S.D.

Extract (mg/kg body weight)					
Parameters	Control	50	100	200	400
Cholesterol (mmol/l)	1.35 ± 0.03^a	1.18 ± 0.06^b	1.08 ± 0.07^b	1.08 ± 0.04^b	1.43 ± 0.07^c
TAG (mmol/l)	1.75 ± 0.19^a	1.40 ± 0.13^b	1.43 ± 0.20^b	1.28 ± 0.07^c	1.78 ± 0.03^a
HDL-C (mmol/ l)	0.93 ± 0.09^a	0.90 ± 0.06^a	0.95 ± 0.03^a	0.90 ± 0.04^a	0.91 ± 0.01^a
LDL-C (mmol /l)	0.76 ± 0.05^a	0.71 ± 0.07^a	0.74 ± 0.03^a	0.75 ± 0.03^a	0.75 ± 0.04^a
Atherogenic index (LDL-C/HDL-C)	0.82	0.79	0.78	0.78	0.82

Means with the same superscript across the rows for each parameter are not significantly different (P > 0.05).

main effector cells of the immune system (McKnight et al., 1999). The reduction in the lymphocytes in this study may affect the effector cells of the immune system. Similarly, decreased levels of eosinophils and basophils observed in this study could be an indication of adverse effect on the immune system. The non-definite effect of the extract on the platelets can be attributed to adaptation by the animals to the effect of the extract. Since monocytes have been shown to increase in cases of infection, the increase in monocytes at 100 mg/kg body weight of the extract observed in this study could be as result of selective and dose specific effect of the extract on the immune system of the animals. All these alterations suggest selective toxicity of the extract on the haematological parameters investigated in this study.

The biochemical indices monitored in the serum such as the electrolytes and other secretory substances of the liver and kidney can be used as 'markers' for assessing the functional capacities of the organs (Yakubu et al., 2003). These parameters of organ function if altered will impair the normal functioning of the organs. The absence of significant effect on the serum concentrations of sodium, potassium, chloride, urea, calcium, albumin, magnesium, inorganic phosphorus, uric acid, globulin and total protein of the animals suggest that the secretory ability and normal functioning of these organs in relations to these parameters were unaffected. Creatinine is the major catabolic products of the muscle. The dose-specific increase in creatinine suggests selective toxicity of the extract. Bilirubin, a metabolic breakdown product of heme derived from senescent red blood cells, is also one of the most commonly used liver function tests. The reduction in

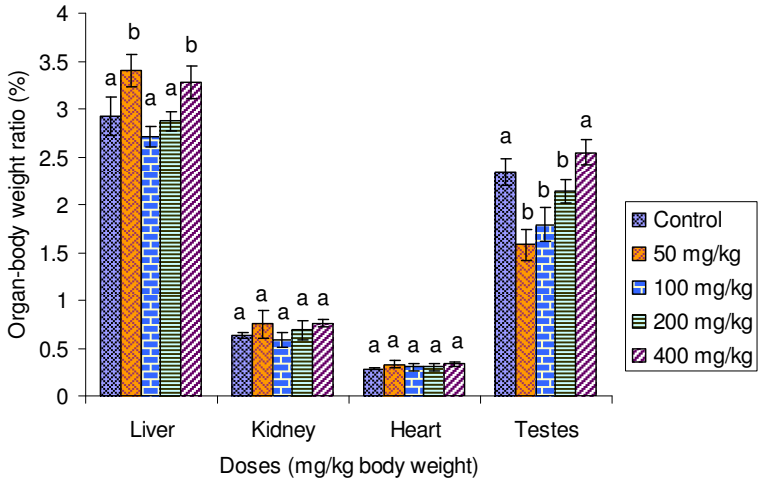

Figure 1. Effect of aqueous extract of *C. ciliata* on organ-body weight ratio of Wistar rats.

the total and conjugated bilirubin could be adduced to impairment in the secretory function of these proteins. It may also adversely affect the functional activity of the liver.

Alkaline phosphatase (ALP) is a 'marker' enzyme of damage for the plasma membrane and endoplasmic reticulum (Wright and Plummer, 1974; Shahjahan et al., 2004). It is frequently used to assess the integrity of the plasma membrane (Akanji et al., 1993). Similarly, γ-glutamyl transferase is a membrane bound enzyme which catalyses the transfer of γ-glutamyl group between peptides and amino acids (Tate and Ross, 1977). Enzymes from diseased or damaged tissues may become recognizable in the serum presumably by leakage through altered cell membrane of the rat organs (Akanji and Ngaha, 1989). The increase in serum ALP and GGT activities following the oral administration of the extract implies damage to the plasma membrane (Yakubu et al., 2003). Such increase in the activities of the enzymes suggests disruption of the ordered lipid-bilayer of the membrane structure of the affected organs. Alanine and aspartate aminotransaminases are cytosolic enzymes that can be used to assess damage to the liver and heart (Chapatwala et al., 1982). The increase in the serum enzymes is quite understandable since disruption of the plasma membrane of the organs of the animals will be accompanied by leakage of these cytosolic enzymes into the serum, hence, the observed increase in the level of the enzymes in the serum (Akanji and Yakubu, 2000).

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 heart to atherosclerosis and its associated coronary heart diseases (Yakubu et al., 2008). High blood cholesterol concentrations are an important risk factor for cardiovascular disease (Abolaji et al., 2007). Therefore, the reduced levels of serum cholesterol at 50, 100 and 200 mg/kg body weight of the extract may be clinically beneficial to the animals as the extract is unlikely to be associated with cardiovascular risk at these doses. Similarly, the decreased levels of serum triacylglycerol by the extract may be explained by a reduced lipolysis (Yakubu et al., 2008). The absence of significant effect on the HDL-C, LDL-C and atherogenic index may be an indication that the extract may not predispose the animals to atherosclerosis and coronary heart diseases (Philip, 1995; Jackson, 1996; Mayes, 1996; Panagiotakos et al., 2003).

According to Moore and Dalley (1999), an increase in organ-body weight ratio is an indication of inflammation while a decrease may be due to cell constriction. The increase in the liver-body weight ratio observed with the extract at 50 and 400 mg/kg body weight may be due to increase in functional ability of the organ while a decrease in the testes-body weight ratio may be adduced to cellular constriction. The absence of significant effect on the kidney and heart-body weight ratios of the animals is an indication that the extract did not adversely affected the size of these organs in relation to the weight of the animals.

Our study has shown that the aqueous extract of *C. ciliata* leaves is capable of producing alterations on some biochemical parameters investigated. These alterations are dose and parameter specific. Therefore, the extract from this herb may not be completely safe for oral remedies.

ACKNOWLEDGEMENTS

We appreciate the support from National Research Foundation of South Africa and Govan Mbeki Research and Development Centre of the University of Fort Hare.

REFERENCES

Abolaji AO, Adebayo AH, Odesanmi OS (2007). Effect of ethanolic extract of *Parinari polyandra* (Rosaceae) on serum lipid profile and some electrolytes in pregnant rabbits. Res. J. Med. Plants 1: 121-127.

Adebayo JO, ,Adesokan AA, Olatunji LA, Buoro DO, Soladoye AO (2005). Effect of Ethanolic extract of *Bougainvillea spectabilis* leaves on haematological and serum lipid variables in rats. Biochem. 17: 45.

Akanji MA, Ngaha EO (1989). Effect of repeated administration of berenil on urinary excretion with corresponding tissue pattern in rats. Pharmacol. Toxicol. 64: 272-275.

Akanji MA, Olagoke OA, Oloyede OB (1993).Effect of chronic consumption of metabisulphite on the integrity of the kidney cellular system. Toxicol. 81: 173-179.

Akanji MA, Yakubu MT (2000). α-Tocopherol protects against metabisulphite-induced tissue damage in rats. Niger. J. Biochem. Mol. Biol. 15: 179-183.

Chapatwala K, Boykin MA, Rajanna B (1982). Effect of inraperitoneally injected cadmium on renal and hepatic glycogenic emzymes in the rat. Drug. Chem. Toxicol. 5: 305-317.

Ertekin V, Selimoglu MA, Altinkaynak S (2005). A combination of unusual presentations Of *Datura stramonium* intoxication in a child: Rhabdomyolysis and fulminant hepatitius. J. Emerg. Med. 28: 227-228.

Jackson J (1996). Diet and Health: Implication for reducing chronic disease risks. National Research Council. National Academic Press, Washington DC.

Koduru S, Grierson DS, Afolayan AJ (2006). Antimicrobial activity of *Solanum aculeastrum*. Pharm. Biol. 44: 283-286.

Mayes PA (1996). Lipid transport and storage. In: Harper's biochemistry. Murray RK, Granner DK, Mayes PA, Rodwell VW (Eds), 24th ed. Prentice Hall International, Inc., USA, pp. 254- 255.

McKnight DC, Mills RG, Bray JJ, Crag PA (1999). Human Physiology, 4th ed. Churchill Livingstone, pp. 290- 294.

Moore KL, Dalley AF (1999). Clinical Oriented Anatomy (4th Edition). Lippincot Williams and Williams; a Woller Klumner Corporation, Philadelphia. pp. 263-271.

Olson H, Betton G, Robinson D, Thomas K, Monro A, Kolaja G, Lilly P, Sanders J, Sipes G, Bracken W, Dorato M, Deun KV, Smith P, Berger B, Heller A (2000). Concordance of toxicity of pharma-ceuticals in humans and in animals. Regul. Toxicol. Pharmacol. 32: 56-67.

Owoyele BV, Alabi OT, Adebayo JO, Soladoye AO, Abioye AIR, Jimoh SA (2004). Haematologivcal evaluation of Ethanolic extract of *Allium ascalonium* in male albino rats. Fitoterapia. 75: 322-326.

Panagiotakos B, Pitsavos C, Skoumas J, Chrysohoou C, Toutouza M, Stefanadis CI, Toutouzas PK (2003). Importance of LDL/HDL ratio as a predicator for coronary heart disease events in patients with heterozygous familial hypercholesterolemia: A 15 year follow-up (1987-2002). Curr. Med. Res. Opin., 19: 89-94.

Phillip DM (1995). Plasma enzyme in diagnosis. In: Clinical chemistry in diagnosis and Treatment, 6th ed. Arnold Publishers, London.p.303-307.

Shahjahan M, Sabitha KE, Jamu M, Shyamala-Dev CS (2004). Effect of *Solanum trilobatum* against carbon tetrachloride induced hepatic damage in albino rats. Indian J. Med. Res. 120: 194-198.

Tate SS, Rose ME (1977). Human kidney γ-glutamyl transpeptidase: catalytic properties,subunit, structure and localization of the γ-glutamyl binding site on the large subunit. J. Biol. Chem. 252: 6042-6045.

Tietz NW, Prude EL, Sirgard-Anderson O (1994). Tietz Textbook of clinical chemistry. 2nd edition, W.B. Saunders Company, London. p. 1354.

Tokarnia CB, Do bereiner J, Amorin PR, Gava A (1986). Consorte L B, Intoxicac¸a˜o experimental por *Vernonia molissima* (Compositae) em coelhos. *Pesquisa* Veterina´ria Brasileira, 6: 5.

Van Wyk BE,Van Heerden F, Van Oudsthoorn B (2002). Poisonous Plants of South Africa. Pretoria Briza Publications. pp. 66-67.

Wright PJ, Plummer DT (1974). The use of urinary enzyme measurement to detect renal damage caused by nephrotoxic compounds. Biochem Pharmacol. 23: 65-73.

Yakubu MT, Akanji MA, Oladiji AT (2007). Haematological evaluation in male albino rats following chronic administration of aqueous extract of *Fadogia agrestis* stem. Pharmacog. Mag. 3: 34.

Yakubu MT, Akanji MA, Oladiji AT (2008). Alterations in serum lipid profile of male rats by oral administration of aqueous extract of *Fadogia argrestis* stem. Res. J. Med. Plant. 2: 66-73.

Yakubu MT, Akanji MA, Oladiji AT (2005). Aphrodisiac potentials of the aqueous extract of *Fadogia argresits* (Schweinf. Ex Hiern) stem in male albino rats. Asian J.Adrol.7: 399-404.

Yakubu MT, Bilbis LS, Lawal M, Akanji MA (2003). Evaluation of selected parameters of rat Liver and kidney function following repeated administration of yohimbine. Biochemistry, 15: 50-56.