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Toxicity profile of aqueous extract of *Cassia alata* flower in Wistar rats

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Abstract

The aqueous extract of *Cassia alata* (Linn.) flower has been used to treat various ailments in folklore medicine in various parts of Africa. Toxicological evaluation of C. alata extract flower was determined in Wistar rats at doses of 100, 400 and 800 mg/kg by oral administration for 4 weeks and the effect on anthropometric, haematological, biochemical and histopathological parameters were assessed. The extract significantly ($P<0.05$) increased the lymphocytes, monocytes, granulocytes and platelets counts at doses of 400 and 800 mg/kg in the female rats. There were no significant differences ($P>0.05$) in the lipid profile, biochemical parameters, body weight and relative organ weight in the treated rats compared to the control. Examination of histological sections of the liver, lung, kidney, spleen and heart did not show any remarkable changes or gross pathological changes during the post mortem examination of the animals at all doses compared with the control. The results obtained in this study suggest that the aqueous extract of *C. alata* flower is relatively safe when administered orally in rats.

Keywords: *Cassia alata*; Toxicity; Liver function; Renal function; Haematology

INTRODUCTION

The use of plants as effective sources of both traditional and modern medicine has led to an increased focus on plant research and in certain African countries, up to 90% of the population still relies exclusively on plants as a source of medicines (Isaac *et al.*, 2011). Researchers are continuously engaged in toxicological assessments of different medicinal plants in order to ascertain their safety in humans and ensure their continued use. Although medicinal plants are assumed to be safe, some of them can potentially be toxic, causing fatal reactions and sometimes death, this singular fact underscores the need for safety assessment evaluation of the myriad of medicinal plants (Nasri and Hedayatollah, 2013).

Cassia alata Linn a native to South America has now naturalized in many tropical countries in Africa including Nigeria. It is commonly known as "Rai dore" in Hausa, "Asuwon oyinbo" in Yoruba, "Omirima" in Igbo and "Whu shil-shili" in Kilba. It is an erect tropical perennial herb which belongs to the family Fabaceae. Several parts of *Cassia alata* have been used in traditional medicine. Anti-allergic activity of *Cassia alata* has been recently been reported (Singh *et al.,* 2012). The plant possesses laxative, anti-inflammatory, anti-mutagenic, analgesic, and antimicrobial properties (Khan *et al.,* 2001; Villasenor *et al.*, 2002; Somchit *et al.,* 2003;

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Hennebelle *et al*., 2009). Chemical analyses of extracts from *Cassia alata* yielded constituents as phenolics, fatty acids, terpenoids, and anthraquinones (Khare, 2007; Liu *et al.,* 2009). The seeds are used as a coffee substitute and reportedly have antiasthmatic effect (Malgras, 1992). The roots of *Cassia alata* have been used in the Southern Nigeria, as an abortifacient by women (Tologbonse *et al.,* 2015). A report on the decoction of flowers, bark and wood indicate their use in treating skin diseases such as pruritus, eczema, itching, bronchitis and asthma (Kirtikar and Basu, 1975).

Antimicrobial activity of the aqueous extract of *Cassia alata* flower has also been reported (Abubacker *et al.,* 2008; Selvi *et al.,* 2012). A study indicated significantly reduction in hematological indices and weight loss after administration of aqueous leaf extract of *Cassia alata* for14 days in male albino rats (Sodipo *et al.,* 1998). In another toxicity study (Yagi *et al.,* 1998), rats fed with 2% or 10% dried ground leaves of *Cassia alata* in their chow or 100 ml ethanol extract in their daily drinking water showed marked elevation in renal and liver function when compared to control after 4 weeks.

Although several studies have been done on the flower extract of this plant, information is scanty in literature addressing the toxicity effect of the aqueous extract of *Cassia alata* flower in the same manner as it is claimed to be used in the management of several diseases in the folklore medicine of Nigeria. In this study, we have evaluated the toxicity profile of the flower extract orally in rats of both sexes for four weeks to justify these claims.

EXPERIMENTAL

Plant materials. Fresh flowers of *Cassia alata* were collected from its natural habitat at Nassarawa state, Nigeria in the month of June, 2015. They were identified and authenticated by Mr. Ibrahim Muazzam of the Nigerian Institute of Pharmaceutical research (NIPRID), Abuja where a voucher specimen number NIPRID/H/6781 was deposited in their herbarium.

Animals. Albino Wistar rats of either sex (150-180 g) were used for this study. The animals were obtained from Animal House, Department of Pharmacology and Toxicology, University of Benin, Nigeria. The animals were fed with standard pelletized feed (Ewu Feeds and Flour Mills Limited, Ewu, Edo state, Nigeria) and had free access to drinking water. The animals were acclimatized for two weeks and were exposed to natural lighting conditions, at normal room temperature. The study was carried out following the approval from the Ethics Committee on the Use and Care of Animals of the University of Benin, Benin City, Nigeria.

Preparation of extracts. The flowers were air dried for about two weeks and pulverized by a mechanical grinder. The powdered plant material (200 g) was boiled with 2L of distilled water for 30 min. The aqueous extract was filtered and concentrated to dryness using a rotary evaporator (yield = 18%). The dried extract was stored in clean glass containers in the refrigerator at 4 ^{o}C until used. This was later reconstituted to give the required doses of 100, 400 and 800 mg/kg body weight used in the present study.

Animal grouping and extract administration. Forty Wistar rats, of either sex, were randomly grouped into four (A-D) of ten animals each. Each group had five males and five females. Group A (control) were orally administered with 4 ml/kg of distilled water on daily basis for 4 weeks. Animals in Groups B-D were orally administered the extract at 100, 400 and 800 mg/kg daily for 4 weeks. Thereafter, body weights of the animals were taken at 7 day intervals for 4 weeks.

Preparation of serum and isolation of organs. After 4 weeks of extract

administration, the animals were humanely sacrificed by chloroform anaesthetization and blood samples were withdrawn by cardiac puncture with a 21G needle mounted on a 10 ml syringe. An aliquot of blood was collected into sample bottles containing EDTA for the haematological analysis. The remainder (5 mL) was centrifuged at 2500rpm for 5 min. The serum obtained was used for the various biochemical assays. The rats were further dissected and the liver, kidney, heart, lungs and spleen excised, freed of fat, blotted with clean tissue paper and then weighed. The relative organ weight of each organ to their body weights was determined (Yakubu *et al.*, 2008).

Determination of biochemical parameters. The Automated Haematologic Analyzer (Diatron® Abacus junior hematology analyzer) was used in the determination of the red blood cell count (RBC), packed cell volume (PCV), haemoglobin concentration (Hb), platelet count (PLT), erythrocyte indices, total white blood cell counts and its differentials using whole blood. Biochemical analyses were performed after the blood samples without anticoagulant were centrifuged at 3000 rpm for 10 min to obtain plasma or serum, respectively. Plasma was used to determine glucose, and the serum for other biochemical parameters: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total protein, creatinine, urea, bilirubin, globulin, total triglycerides, total cholesterol, high density lipoproteins and low density lipoproteins. These were evaluated with standardized diagnostic kits (Randox® by Randox laboratories Ltd., UK) using a spectrophotometer (INICO® 1200). Serum electrolytes, such as sodium and potassium, were measured by an ion-autoanalyser (Flame Photometer).

Histopathology. Liver, kidney, spleen, lungs, heart were fixed immediately in 10% formo-saline and the tissues were embedded in paraffin and then sectioned, stained with hematoxylin and eosin and were examined under light microscope. Histopathological evaluations were performed by a pathologist. Photomicrographs of the microscopic sections were taken with the help of a photomicroscope (Motic, Canada) provided with Motic Images Plus 2.0 software.

Statistical analysis. Data were expressed as the mean ± SEM. The data were analysed using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test. Statistical analysis was performed using GraphPad Prism V. 6.01 where $p<0.05$ was considered statistically significant

RESULTS

The aqueous extract of *Cassia alata* flower at all doses (100, 400 and 800 mg/kg) investigated in the present study did not significantly ($P>0.05$) alter the red blood cells (RBC), packed cell volume (PCV), mean corpuscular volume (MCV), haemoglobin (Hb), mean corpuscular haemoglobin concentration (MCHC), mean platelet volume (MPV). However, the lymphocytes, monocytes, granulocytes and platelets were significantly increased ($P<0.05$) at doses of 400 and 800 mg/kg of the extract in table 1.

As shown in table 2 and table 3, the aqueous extract of *Cassia alata* flower at all doses did not significantly affect the biochemical parameters and the lipid profile of the animals after 4 weeks of administration of the extract when compared with the control animals and between the sexes.

The body weight gain of the animals during the period of treatments was similar among the animals treated with aqueous extract of *Cassia alata* or vehicle in table 4. The values of relative weight (%) of heart, lungs liver, kidneys and spleen from animals treated for 28 days with aqueous extract of *Cassia alata* or vehicle are presented in table 5. Significant statistical differences were not

observed in the relative weight of these organs among any of the groups.

There were no gross pathological changes observed on organs during the post mortem examination of the animals from either group. Examination of histological sections of the liver, lung, kidney, spleen and heart found no remarkable changes other than mild caused mild follicular activation in the spleen and in heart, mild vascular intima erosion (figure 1).

Table 1. Effect of aqueous extract of *C. alata* flower on some haematological parameters of Wistar rats.

Sex	Parameters	Treatment groups (mg/kg)			
		Control	100	400	800
Male	RBC ($x10^6$/µl)	7.61±0.33	7.44 ±0.69	7.21 ±0.11	7.89±0.42
	Hb (g/dl)	13.50±0.54	13.12±1.16	12.93±0.11	14.44±0.60
	HCT (%)	41.02±0.42	42.91±2.82	42.05±4.28	42.20±3.17
	WBC ($x10^3$/µl)	2.18±0.29	2.82±0.43	2.34±0.61	2.92±0.70
	PLT ($x10^3$/µl)	465.20±21.16	562.00 ±52.2	526.20±48.49	588.00±50.44
	MPV(fL)	4.28±0.63	4.74±0.17	4.96±0.19	4.86±0.09
	LY($x10^3$/ul)	2.08±0.29	2.62±2.80	2.14±0.58	2.21±0.433
	MO($x10^3$/ul)	0.02±0.02	0.10±0.03	0.11±0.03*	0.50±0.23*
	GR($x10^3$/ul)	0.04±0.02	0.08±0.02	0.12±0.08*	0.24±0.17*
	MCV (fL)	48.3±2.03	53.20±0.44	48.11±0.23	58.01±2.20
	MCH (pg)	18.38±0.08	17.66±0.45	17.34±0.16	17.72±0.23
	MCHC (g/dl)	36.82±0.35	30.44±0.82	32.06±0.24	31.78±0.27
	RDWc (%)	15.22±0.15	18.46±1.66	17.62±1.65	15.24±0.26
	PDW (%)	30.54±1.78	28.79±0.67	30.55±1.63	28.84±0.29
Female	RBC ($x10^6$/µl)	7.22±0.21	7.87±0.76	7.04±0.11	8.20±0.07
	Hb (g/dl)	13.50±0.41	13.85±1.32	12.70±0.18	15.10±0.15
	HCT (%)	37.72±1.03	40.00±0.69	39.90±0.40	42.00±1.78
	WBC ($x10^3$/µl)	1.07±0.68	1.92±0.17	1.88±0.42	3.68±0.56*
	PLT ($x10^3$/µl)	497.72±43.86	576.21±19.66	487.00±37.26	626.20±14.83*
	MPV(fL)	5.50±0.14	4.74±0.10	4.90±0.10	4.64±0.17
	LY($x10^3$/ul)	1.68±0.34	1.76±0.22	1.46±0.30	3.18±0.54*
	MO($x10^3$/ul)	0.03±0.03	0.06±0.04	0.20±0.18*	0.63±0.09*
	GR($x10^3$/ul)	0.12±0.01	0.10±0.05	0.18±0.15	0.24±0.07
	MCV (fL)	52.20±0.73	56.50±1.25	56.80±0.93	55.51±0.67
	MCH (pg)	18.70±0.32	17.81±0.31	17.9±0.25	17.7±0.11
	MCHC (g/dl)	35.8±0.25	31.58±0.63	31.7±0.29	31.68±0.29
	RDWc (%)	14.8±0.34	18.82±3.82	15.32±0.22	15.38±0.37
	PDW (%)	34.92±3.17	27.84±0.25	29.04±0.49	28.08±0.28

Values are expressed as mean ± SEM (n = 10). Hb = Hemoglobin; HCT = Hematocrit; RBC = red blood cells; WBC = white blood cells; PLT = platelets; MPV = mean platelet volume; GR = granulocytes count; MO = monocytes/ eosinophils; LY = lymphocytes; MCV = mean corpuscular volume; MCHC = mean corpuscular hemoglobin concentration; MCH = mean corpuscular hemoglobin; RDWc = red cell distribution width; PDW = platelet distribution width. Control group received 4ml/kg distilled water. *P<0.05 compared with control.

Table 2. Effect of aqueous extract of *C. alata* flower on some biochemical parameters of Wistar rats.

Sex	Parameters	Treatment groups (mg/kg)			
		Control	100	400	800
Male	Creatinine (mg/dl)	0.86±0.02	0.80±0.01	0.86±0.02	0.74±0.04
	Urea (mg/dl)	46.20±4.15	50.64±1.89	48.81±1.02	49.22 ±2.18
	HCO_3 (mMol/L)	21.62±1.52	21.40±3.05	22.01±1.0	20.40±2.07
	Na (mEq/L)	142.60±1.55	142.83±1.92	140.60±0.89	143.8±1.30
	K (mmol/L)	4.44±0.26	5.06±0.78	4.56±0.15	4.94±0.35
	Cl (mmol/L)	101.81±1.3	102.80±1.3	102.62±1.52	103.43±1.34
	TP (mg/dl)	6.84±0.19	6.24±0.09	6.24±0.09	6.58±0.20
	ALB (mg/dl)	4.02±0.06	3.78±0.05	4.02±0.08	2.54±0.21
	GLO (G/dl)	2.84±0.17	2.46±0.12	2.32±0.11	2.54±021
	TB (mg/dl)	0.58±0.07	0.56±0.05	0.62±0.02	0.64±0.04
	CB (mg/dl)	0.24±0.02	0.24±0.04	0.24±0.02	0.03±0.03
	ALP (IU/L)	19.60±0.24	27.21±4.27	29.22±2.89	33.20±5.78
	AST (IU/L)	100.42±5.92	113.29±3.56	109.42±3.44	110.20±6.99
	ALT (IU/L)	20.00±1.26	23.80±0.96	18.62±1.21	20.05±1.22
	Glucose (mg/dl)	87.40±4.37	75.21±6.27	81.61±9.3	71.60±5.1
Female	Creatinine (mg/dl)	0.74±0.02	0.82±0.04	0.64±0.07	0.80±0.03
	Urea (mg/dl)	48.20±1.11	48.52±3.73	46.40±3.57	47.00±2.21
	HCO_3 (mMol/L)	22.24±2.86	21.52±1.8367	22.60±0.89	18.61±3.36
	Na (mEq/L)	143.64±1.14	143.22±1.48	141.40±1.34	143.10±1.30
	K (mmol/L)	4.50±0.35	4.64±0.30	4.42±0.55	5.14±0.74
	Cl (mmol/L)	105.80±1.48	104.11±2.12	102.40±1.34	104.44±1.67
	TP (mg/dl)	6.98±0.25	6.62±0.18	6.76±0.19	6.24±0.20
	ALB (mg/dl)	3.92±0.14	3.72±0.06	3.76±0.05	3.78±0.09
	GLO (G/dl)	2.96±0.22	3.12±0.12	3.10±0.10	2.46±0.17
	TB (mg/dl)	0.58±0.04	0.05±0.04	0.54±0.04	0.64±0.02
	CB (mg/dl)	0.24±0.02	0.22±0.04	0.24±0.05	0.28±0.04
	ALP (IU/L)	22.8±0.86	20.20±0.06	24.20±0.05	0.28±0.04
	AST (IU/L)	110.24±3.38	112.82±4.21	108.88±2.69	109.40±2.38
	ALT (IU/L)	21.00±0.15	22.00±1.26	25.00±1.55	21.00±0.84
	Glucose (mg/dl)	96.80±8.73	100.24±5.58	85.80±4.374	114.41±9.92

Values are expressed as mean ± SEM (n = 10); Control group received 4 ml/kg distilled water. ALP, Alkaline Phosphatase; AST, Aspartate transaminase; ALT, Alanine transaminase; TB, Total Bilirubin; CB, conjugated Bilirubin; GLO, globulin.

Table 3. Effect of administration of aqueous extract of *C. alata* flower on the lipid profile of Wistar rats.

Sex	Parameters	Treatment groups (mg/kg)			
		Control	100	400	800
Male	TCHOL (mg/dl)	65.20±2.51	61.21±2.40	68.26±1.85	66.40±1.34
	TG (mg/dl)	52.81±7.08	51.24±3.89	62.60±3.58	54.21±4.55
	HDL (mg/dl)	46.84±1.65	43.08±2.56	48.40±2.04	48.61±2.42
	LDL (mg/dl)	7.80±0.97	7.22±1.019	7.42±1.12	7.00±1.92
Female	TCHOL (mg/dl)	65.40±1.50	69.40±1.29	64.16±3.06	60.88±0.80
	TG (mg/dl)	62.21±4.32	69.60±4.89	61.40±5.54	54.20±5.29
	HDL (mg/dl)	46.22±0.73	47.61±1.44	44.22±2.24	42.41±1.50
	LDL (mg/dl)	8.10±0.55	8.02±1.46	8.40±1.62	7.60±1.44

Values are expressed as mean ± SEM (n = 10); Control group received 4 ml/kg distilled water.
TCHOL, total cholesterol; TG, triglycerides; HDL, high density lipoproteins; LDL, low density lipoproteins.

Table 4. Effect of administration of aqueous extract of *C. alata* flower on the body weights of Wistar rats

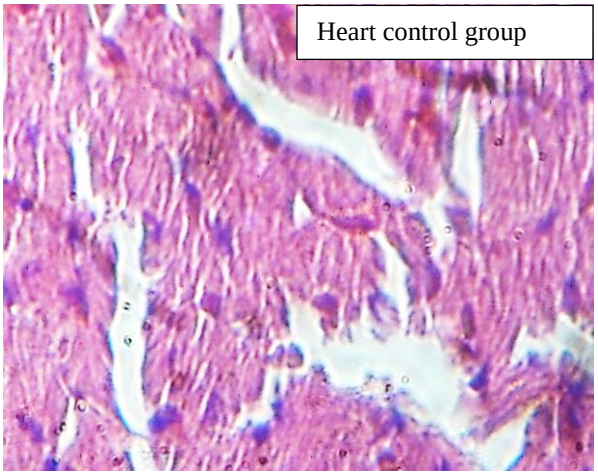
Sex	Groups	Days				
		0	7	14	21	28
Male	Control	129.00±5.10	163.00±3.74	167.10±2.55	178.00±3.39	186.60±2.86
	100 mg/kg	130.10±7.42	154.20±7.65	170.25±6.52	164.10±5.79	181.00±6.18
	400 mg/kg	134.00±3.67	152.20±4.64	165.00±6.32	174.00±7.31	174.60±4.91
	800 mg/kg	136.10±5.79	148.00±3.39	166.10±4.85	176.30±4.85	182.20±6.41
Female	Control	122.20±3.39	150.10±4.74	155.00±6.12	162.00±5.60	152.20±6.11
	100 mg/kg	132.00±3.74	148.45±3.39	155.75±6.12	156.20±4.00	161.10±4.08
	400 mg/kg	123.24±4.06	141.00±6.20	143.00±4.90	145.01±5.83	148.60±6.52
	800 mg/kg	122.40±3.39	138.60±4.06	139.00±4.85	146.52±5.34	142.80±3.10

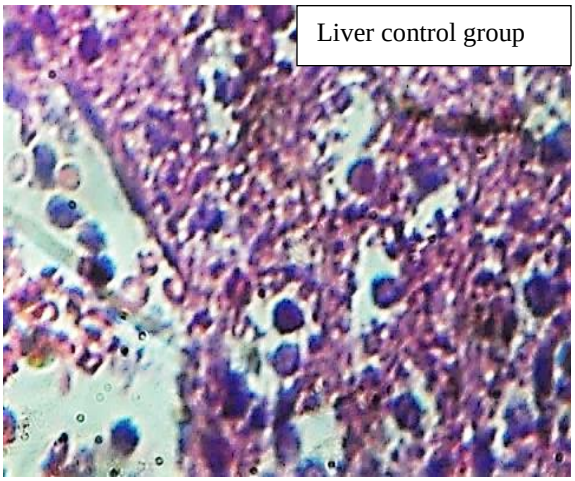
Values are expressed as mean ± SEM (n = 10)

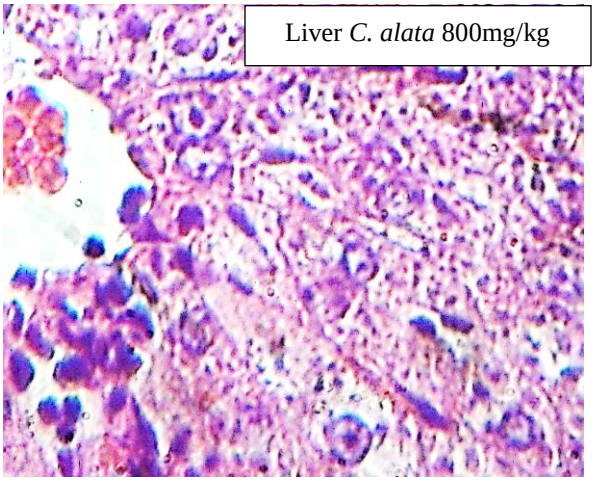
Table 5. Effect of administration of aqueous extract of *C. alata* flower on the relative organ weight of Wistar rats

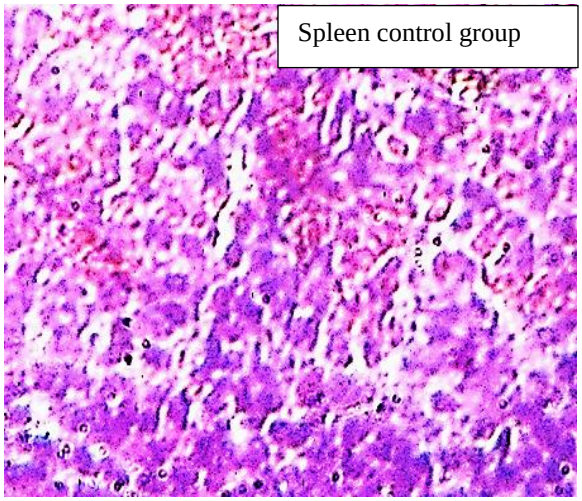
Sex	Parameters	Treatment groups (mg/kg)			
		Control	100	400	800
Male	Spleen (%)	0.31±0.02	0.44±0.07	0.36±0.02	0.33±0.01
	Lungs (%)	0.75±0.01	0.81±0.02	0.77±0.01	0.71±0.01
	Liver (%)	3.53±0.04	4.14±0.01	4.04±0.07	3.23±0.02
	Heart (%)	0.30±0.04	0.42±0.02	0.39±0.01	0.33±0.03
	Kidney (%)	0.32±0.09	0.31±0.09	0.52±0.04	0.40±0.01
Female	Spleen (%)	0.35±0.04	0.41±0.01	0.40±0.03	0.40±0.02
	Lungs (%)	0.91±0.01	0.81±0.05	0.90±0.09	0.92±0.04
	Liver (%)	3.03±0.01	4.51±0.05	4.10±0.02	4.34±0.01
	Heart (%)	0.31±0.06	0.38±0.03	0.30±0.05	0.34±0.02
	Kidney (%)	0.33±0.01	0.37±0.09	0.47±0.02	0.42±0.02

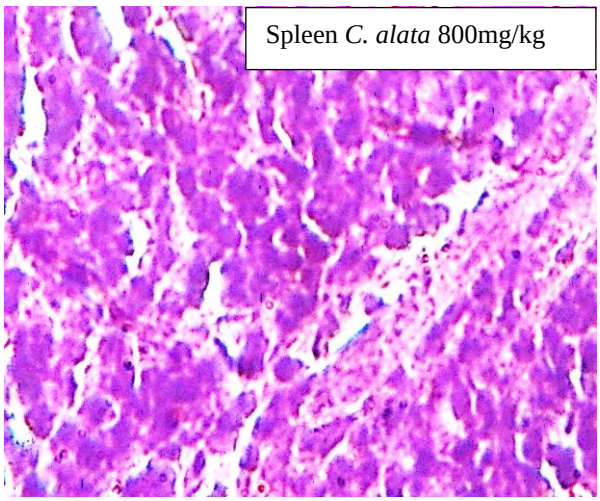
Values are expressed as mean ± SEM (n = 10)




Liver control group


Liver *C. alata* 800mg/kg


Spleen control group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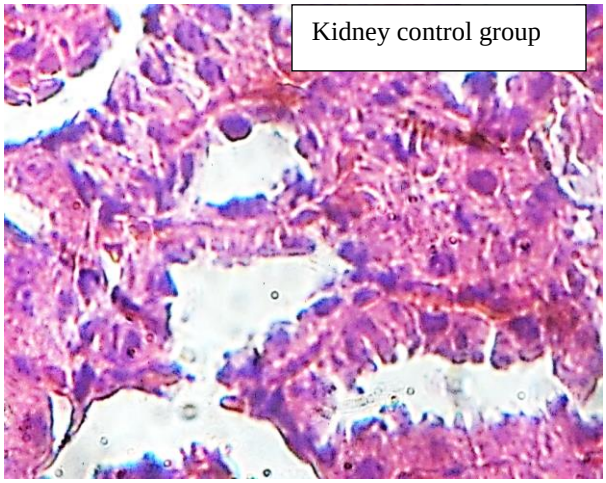
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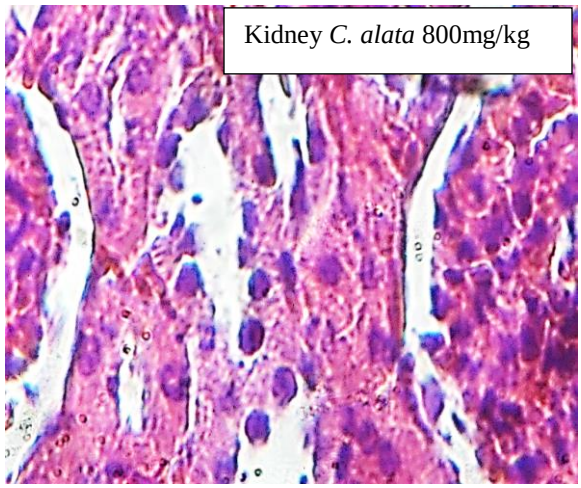
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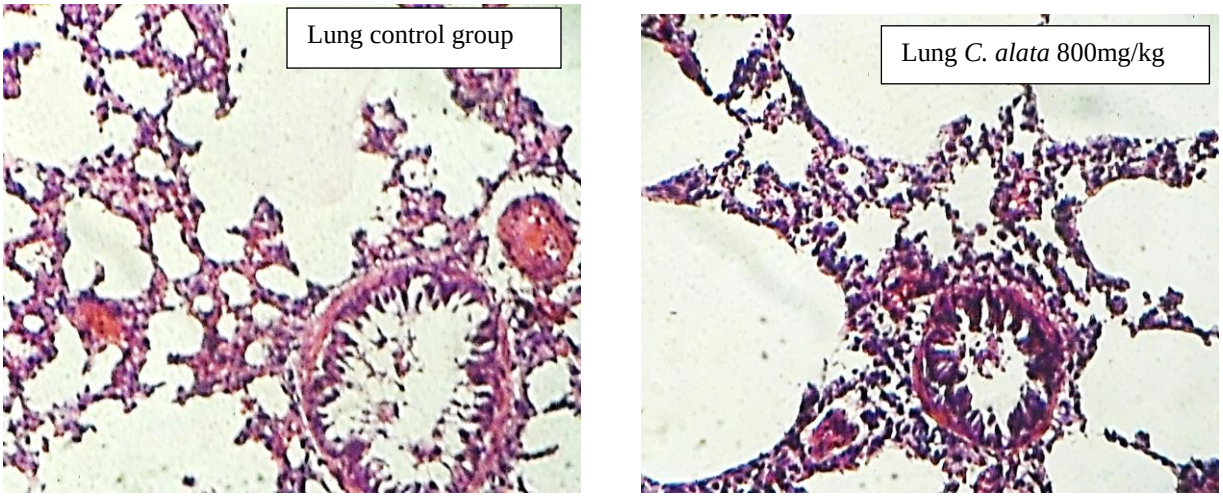

Figure1. Photomicrographs of heart, liver, spleen, kidney and lungs histopathology from representative male Wistar rats treated with vehicle (control group) or the highest dosage of *C. alata.* On the right the heart (x400), liver (x400), spleen(x400), kidney (x400) and lung (x100) of the vehicle group are represented, and on the right the same organs of the group (800 mg/kg) are represented. Hematoxylin and eosin stain.

DISCUSSION

Animal toxicity studies are commonly used to assess potential health risk in humans caused by intrinsic adverse effects of chemical compounds/plant extracts (Klaassen and Eaton, 1991; Afolayan and Yakubu, 2009; Oyedemi *et al*., 2010). These adverse effects may manifest as significant alterations in the levels of biomolecules such as enzymes and metabolic products, normal functioning and histomorphology of the organs (Yakubu *et al.*, 2009). Although there are many traditional herbal medicines available, only a few have been verified by clinical trials, hence their efficacy and safety are still questioned by consumers (Cheng *et al.*, 2009). Evaluation of haematological parameters can be used to determine the extent of the damaging effect of foreign compounds including plant extracts on the blood constituents of an animal. Such toxicity testing is relevant to risk evaluation as changes in the haematological system have higher predictive value for human toxicity, when data are translated from animal studies (Olson *et al.*, 2000).

In the present study, *Cassia alata* flower extract significantly increased white blood cells and the differential leukocytes counts in the test animals at the highest dose. These results suggest that the extract may have immunological properties, by stimulating increased production of white blood cells, thereby boosting the defense system of the animals. This report corroborates the histological report of the spleen showing mild follicular activation. The study also revealed a significant increase in platelet count in the female animals which may enhance blood clotting time in the animal. However, the values were still within the normal range (Mitruka and Rawnsley, 1977; Palmeiro *et al.*, 2003).

Serum enzyme activities are used as indicators of chemical-induced liver damage (Drotman and Lawhorn, 1978). These enzymes are mainly localized in the cytoplasm and any damage in hepatic cells may result in alteration in the serum level of the enzymes. Thus, the changes in activity and concentration of tumor marker enzymes like AST, ALT and ALP in tissue such as liver could reflect the state of hepatotoxicity (Vinitha *et al.*, 1995). In this study, results showed no significant increase ($P<0.05$) in the liver enzymes of the treated groups when compared with the control, thus suggesting that administration of *Cassia alata* flower

extract has no hepatotoxic effects in rats after treatment for 4 weeks.

Evaluation of serum proteins such as albumin and globulin are good criteria for assessing the secretory ability/functional capacity of the liver (Naganna, 1989). The extract did not have any effect on the albumin and total protein in the serum of animals at all the doses investigated, this could imply that the synthetic and secretory functions of the liver with respect to these proteins were not affected.

Renal function values are usually used to assess the normal functioning of different parts of the nephrons (Abolaji *et al.*, 2007). The serum concentrations of electrolytes could give an insight into the effect of the plant extract on the tubular and or glomerular part of the kidney. Therefore, the non-significant effect of *Cassia alata* flower extract on the renal function indices may indicate that the normal homeostasis of the ions at the tubular and glomerular levels were not affected by the plant extract. However, these results are in contrast to previous studies (Sodipo *et al.*, 1998; Yagi *et al.*, 1998), which revealed the significant elevation of hepatic and renal makers after administration of *Cassia alata* leaf extract. The reason for the discrepancies may be due to the fact that the toxic principles in the leaf extract of *Cassia alata* may be different from that of the flower extract.

Lipid profile is used to access the risk of cardiovascular disease and it is usually altered in various disease states such as diabetes (Betteridge, 1994). Except for the HDL cholesterol, high level of all lipids in the blood is arguably a high risk factor in the onset of cardiovascular disorders. High serum concentrations of triglycerides and LDLs have been reported to cause atherosclerosis and coronary heart diseases (Eisenhaver *et al.*, 1998). Exposure of the animals to *Cassia alata* flower extract after 4 weeks did not significantly alter the lipid profile of the animals. The lipid profile values were considerably similar between both sexes and within the normal range. Generally, changes in body and internal organ weights are indications of adverse side effects of drugs/chemical.

Weight loss is a simple and sensitive index of toxicity after exposure to toxic substance (Teo *et al.*, 2005). There were no significant changes in the body weights and relative organ weights of the animals throughout the course of extract administration in all the doses compared with the control animals. This observation may indicate that the extract did not alter the metabolic processes of the treated animals which may subsequently affect the hormones and body weight (Cajuday and Poscidio, 2010).

Histopathology of various organs revealed no gross abnormality or pathologic effect on the heart, lungs, kidneys, liver and spleen by the extract at all doses administered compared to the control. The mild interstitial congestion and mild portal congestion (at all doses) seen with the kidney and liver respectively could not be adduced to the extract and was not pathologic but may however indicate chronic inflammation, which is a protective response of the tissues (Igbe *et al.*, 2013). This suggests a relative lack of toxicity by the plant extract.

Conclusion. The repeated-dose oral toxicity study showed no serious signs or significant changes in haematological, biochemical, and histopathological parameters, or other remarkable effects in the rats. These toxicity studies suggest that the *Cassia alata* flower extract is relatively safe when administered orally to rodents.

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