Original paper

Title: Toxicological evaluation of *Aloe barbadensis* root extracts in Wistar rats: Haematology and Lipid profile.

Running title: Effect of *Aloe barbadensis* root extract on Wistar rat's haematology and lipid profile.

ABSTRACT

A. barbadensis is a folkloric medicinal plant used for decades to treat several ailments such as intestinal ulcers, gynaecological problems, wound healing, ringworm and eczema. Other uses of *A. barbadensis* include impotence, low libido, appetite disorder, emmenagogue, pile, asthma, cough and jaundice. This study was aimed at determining the safety of the ethanol extract of *Aloe barbadensis* root using haematological, and lipid parameters. *A. barbadensis* root extract (100, 200 and 400 mg/kg) and control (distilled water-0.2mL/kg) were administered to sixty male Wistar rats (150-270 g body weights) for 14 days. The haematological parameters were determined using the collected whole blood and lipid profile assessed using the serum. The oral administration of the extract on red blood cells and white blood cells, as well as other haematological indices (haemoglobin, Platelets crit, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, granulocytes, lymphocytes, Platelets crit and monocytes), were significantly ($p<0.05$) not altered. A non-significant ($p>0.05$) effect of the extract on high-density lipoproteins (HDL) and low-density lipoproteins (LDL) was observed in the serum of the male rats. The results indicate that within the doses used in the study, the ethanol extract of *A. barbadensis* root is relatively non-toxic with no significant

localized toxicity. However, the root of *A. barbadensis* should be cautiously used because of its selective effect on some lipid parameters in the male rats.

Keywords: *Aloe barbadensis*; toxicity; ethanol extract; hematological parameters; lipid profile.

INTRODUCTION

Aloe barbadensis Mill. commonly called aloe vera, belongs to the family Xanthorrhoeaceae (APG, 2009). *A. barbadensis* is a succulent herb growing up to 1-4 feet tall with a short stem and white spots on the light green leaves. The leaves (20-50 cm long), 3-5 cm wide at the base, tapering to a pointed tip. *Aloe vera* possesses a shallow root (Ryczkowski, 2020) with a rhizome-root system (Rajeswari et al. 2012). The folk use the leaf juice to treat intestinal ulcers, catarrh and gynaecological problems (Idu et al. 2014). Similarly, fresh leaf juice is taken orally to treat stomach ulcers and heal wounds (Ross, 1999). Aloe vera leaf can be used to manage skin irritations such as ringworm and eczema when passed over low heat. The root of *A. barbadensis,* according to Adodo (2014), can be used to treat constipation and impotence. It is also used as a purgative, appetite-stimulant, emmenagogue and for managing colds, piles, asthma, cough and jaundice in ayurvedic formulation (Joseph and Raj, 2010). The root of *A. barbadensis* is popularly used to treat low libido, a common practice amongst the Ifa Nkari people of Akwa Ibom State, Nigeria (Erhabor et al. 2013).

It is important to note that *Aloe vera*, like other medicinal plants, deserves to be screened for safety. This becomes imperative following the immense traditional uses associated with different plant parts. Though, it is commonly believed that herbs are safe by Traditional medicine practitioners and other users of medicinal plants. This folk belief underscores the perception of the plant's natural origin (Afolayan and Yakubu, 2009). Despite this general belief, medicinal

plants possess active ingredients capable of having any form of detrimental effects on man and animals. This harmful effect can be on the cell (cytotoxicity), liver (hepatotoxicity), kidney (nephrotoxicity), blood (heamatotoxicity) or lipid (lipotoxicity).

Nevertheless, these injuries' occurrences depend on the number of chemicals absorbed (Betram, 1998). It is valid that appropriate scientific investigation of any medicinal plant's beneficial and harmful effects should be done (Idu et al. 2006). The toxic consequence of a drug in man has been reported to be akin to that of certain animals. Therefore, animal models are used in toxicological studies (Range et al. 1995). Validating any chemical substance or medicinal plant's toxicity has helped determine the upper limits of effective therapy (Sofowora, 1993).

Furthermore, the dearth of toxicological information on the root of *A. barbadensis* prodded this investigation. In this pre-clinical study, the toxicity evaluation of *A. barbadensis* root was limited to male Wistar rats' haematological and lipid profiles. The folkloric use of *A. barbadensis* root as an aphrodisiac in Nigeria (Erhabor and Idu, 2017) necessitated the use of male Wistar rats. Thus, this study was carried out to provide information on *A. barbadensis* root extract's toxicity in male rats.

MATERIALS AND METHODS

Collection and extraction of plant material

The fresh roots of *A. barbadensis* were collected in Okene settlement, Kogi State, Nigeria. The plant was identified by Mr. G. Ibhanesebhor, Herbarium Unit, Obafemi Awolowo University, Ile-Ife, Nigeria, with voucher number IFE17004, where it was deposited. Initially, the roots were rinsed in running water and placed on laboratory tables to dry at room

temperature. The roots were further dried in an oven set at 40 ºC for 10 minutes before grinding to powder. The fine powdered plant material (2kg) was extracted with 5L of ethanol using a soxhlet extractor. The extract was concentrated to dryness using a water bath (HH-S Water Bath; Searchtech Instruments) set at an average temperature of 50 ºC.

Animal grouping and administration of the extract

Sixty (60) healthy male Wistar rats (150-270 g body weight) were obtained from the animal breeding house of the Department of Anatomy, Faculty of Basic Medical Sciences, University of Benin, Nigeria, for this study. The animals were in the ventilated animal house of the Department of Animal and Environmental Biology, Faculty of Life Sciences, University of Benin, Nigeria, for acclimatization with optimum conditions (temperature, 25ºC; photoperiod, 12 hours of natural light and 12 hours of dark). The animals had unfettered access to water and standard commercial pellets. The ethical committee on experimental animal use and care of the Faculty of Life Sciences, University of Benin, Nigeria, reviewed and approved the protocol (LSC15101).

The 60 male rats were randomly placed into four groups (groups A, B, C and D) of 15 animals each and given treatment orally. Group A was administered the diluent (2 mL of distilled water), while groups B, C and D were given 100, 200 and 400 mg/kg body weight of *A. barbadensis* root extract using an orogastric tube. Five rats from all the groups were sacrificed after 1¼ hours of administering the respective doses of the extract on days 1, 7 and 14. The animals were handled following the international guiding principles for biomedical research involving animals as outlined by the Council for International Organization of Medical Sciences and the International Council for Laboratory Animal Science (CIOMS and ICLAS, 2012).

Preparation of serum

The modified procedure of Yakubu et al. (2005), was adopted in the preparation of the serum. Blood was collected from the Wistar rats on days 1, 7 and 14. Briefly, the rats' abdominal cavity was cut open under chloroform anesthesia to expose the internal organs with sterile forceps and scissors. After that, blood was collected through cardiac puncture using a 5 mL syringe and needle per animal into properly labelled clean non-coagulant sample bottles. The sample bottles were left at room temperature for 10 minutes to clot. An aliquot (2 mL) of the blood was collected into ethylenediaminetetraacetic acid (EDTA) sample bottles for the haematological analysis. The bottles were centrifuged at 3000 rpm for 10 minutes using a laboratory centrifuge. The collected sera were aspirated with Pasteur pipettes into clean, dry sample plain bottles and used within 12 hours of preparation for the lipid assays.

Haematological studies

The automated Sysmex KX-21 haematology analyzer (Sysmex Corporation, Kobe, Japan) was used to determine the number of red blood cells (RBC), haemoglobin (HGB), haematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC). Other haematological parameters assayed include red cell distribution width (RCDW), white blood cell (WBC), monocytes (MO), lymphocytes (LY), and platelets (PLT). Platelets crit (PCT), platelet density width (PDW), mean platelet volume (MPV) and granulocytes (GR).

Determination of lipid profile

The lipid profile of the serum was assayed by evaluating the total cholesterol, triglyceride (TRIG), high-density lipoproteins (HDL) and low-density lipoproteins (LDL). The total

cholesterol was determined using Trinder's earlier protocol (1969), while the amount of TRIG was done following Tietz's procedure (Tietz, 1990). The amount of high-density lipoproteins (HDL) and low-density lipoproteins (LDL) in serum was assessed by adopting the method described in the manufacturer's kits (Randox Laboratories Limited, UK).

Analysis of Data

Analyzed data were presented as mean ± SEM of the appropriate replicates. To compare means of different groups, One Way ANOVA was utilized and Duncan, multiple range tests done, to ascertain the differences among various means and the interaction between the variables using SPSS 15.0 computer software package. Differences at $P<0.05$ or $P<0.01$ were considered statistically significant.

RESULTS

Effect of *A. barbadensis* on Haematological parameters

Table 1 showed that most of the haematological parameters were not significantly affected by the extract's administration at the tested doses. The analyzed blood indices (HGB-haemaglobin, RBC-red blood cells count, MCH-mean corpuscular haemoglobin, RDW- red density width, GR- granulocytes count, LY(%)- lymphocytes, MO(%)- monocytes, PCT(%)-platelet crit, PDW(%)-platelet density width granulocyte) were not significantly affected by the administration of the extract on the respective days of treatment and across the days of testing too.

Table 1. Effect of administration of ethanol extract of *A. barbadensis* on haematological parameters of male rats

		Control(DW)	100mg/kg	200mg/kg	400mg/kg	P-value
GR (%)	Day 1	12±4.06	11.52±2.93	32.08±14.37	22.84±8.02	P>0.05
	Day 7	17.8±9.59	6.74±0.98	27.7±8.45	13.58±5.08	P>0.05
	Day 14	10.02±5.3	9.36±4.96	6.48±3.24	8.4±3.78	P>0.05
	P-Value	NS	NS	NS	NS	
HCT	Day 1	37.9±3.41	63.62±22.07	35.14±3.67	34.38$^{\#}$ ±5.18	P>0.05
	Day 7	45.88±4.24	50.46±2.78	46.88±2.82	57.66$^{\#\#}$ ±7.87	P>0.05
	Day 14	40.66±0.9	40.6±1.75	34.28±4.38	38.7$^{\#}$ ±4.55	P>0.05
	P-Value	NS	NS	NS	***P<0.05**	
HGB	Day 1	13.3±1.19	12.24±0.93	12.46±0.76	12.8±1.23	P>0.05
	Day 7	14.52±1.19	15±0.72	13.98±0.73	14.74±0.44	P>0.05
	Day 14	14.44±0.39	14.26±0.57	11.54±1.64	13.28±1.36	P>0.05
	P-Value	NS	NS	NS	NS	
LY%	Day 1	79.48±6.53	80.44±5.36	73.4±9.22	66.78±10.85	P>0.05
	Day 7	76.44±12.3	88.5±1.63	59.52±11.71	78.44±8.33	P>0.05
	Day 14	80.38±10.33	81.4±10.39	86.82±7.04	84.74±7.77	P>0.05
	P-Value	NS	NS	NS	NS	
MCH	Day 1	19.42±0.47	13.9±2.86	21.96±2.66	21.68±2.28	P>0.05
	Day 7	19±0.41	17.98±0.13	17.96±0.36	17.04±1.55	P>0.05

	Day 14	18.08±0.38	17.82±0.36	17.4±0.82	18.56±0.38	P>0.05
	P-Value	NS	NS	NS	NS	
MCHC	Day 1	35.04$^{\#\#}$±0.46	27.78±6.57	38.76$^{\#\#\#}$±1.51	39.32$^{\#\#}$±4.19	P>0.05
	Day 7	31.76$^{\#}$±0.6	29.72±0.32	29.86$^{\#}$±0.64	26.88$^{\#}$ ±2.58	P>0.05
	Day 14	35.46$^{\#\#}$±0.47	35.08±0.27	33.32$^{\#\#}$±0.77	34.6$^{\#}$ ±0.96	P>0.05
	P-Value	****P<0.01**	NS	****P<0.01**	***P<0.05**	
MCV	Day 1	56.74$^{\#\#}$±0.66	53.3±7.33	44.98$^{\#}$±6.46	55.21$^{\#}$ ±0.88	P>0.05
	Day 7	59.86$^{\#\#}$±1.24	60.52±0.73	60.74$^{\#\#}$±2.02	63.58$^{\#\#}$±0.85	P>0.05
	Day 14	52.24$^{\#}$±1.75	50.72±0.8	52.16$^{\#}$±1.99	53.82$^{\#}$ ±1.93	P>0.05
	P-Value	****P<0.01**	NS	***P<0.05**	****P<0.01**	
MO%	Day 1	8.52±2.54	8.04±2.46	9.62±2.75	10.38±2.86	P>0.05
	Day 7	5.76±2.75	4.76±0.67	12.72±3.37	7.98±3.25	P>0.05
	Day 14	9.6±5.08	9.24±5.43	5.7±4.19	6.86±4.16	P>0.05
	P-Value	NS	NS	NS	NS	
MPV	Day 1	5.6$^{b\#}$±0.09	5.68^{a}±0.26	5.22$^{b\#}$±0.09	5.88^{a}±0.12	**P<0.01
	Day 7	6.26$^{\#\#}$±0.1	6.1±0.15	6.48$^{\#\#}$±0.18	6.1±0.21	P>0.05
	Day 14	5.9$^{\#}$±0.13	6.28±0.11	6.06$^{\#\#}$±0.17	6.14±0.12	P>0.05
	P-Value	****P<0.01**	NS	****P<0.01**	NS	

PCT	Day 1	0.27±0.02	0.32±0.08	0.15±0.03	10.21±9.95	P>0.05
	Day 7	0.22±0.06	0.39±0.02	0.33±0.07	0.34±0.06	P>0.05
	Day 14	0.35±0.02	0.3±0.04	0.26±0.05	0.26±0.05	P>0.05
	P-Value	NS	NS	NS	NS	
PDW	Day 1	36.76±0.98	38.78±1.88	39.86±4.04	37.14±1.32	P>0.05
	Day 7	41.84±3.92	34.88±0.33	39.82±2.85	38.56±1.61	P>0.05
	Day 14	35.42±2.06	41.22±2.73	38.8±3.08	39.34±1.98	P>0.05
	P-Value	NS	NS	NS	NS	
PLT ($x10^3$)	Day 1	479±42.56	541±106.2	284±68.84	437±69.82	P>0.05
	Day 7	353±93.49	520±130.3	513±117	569±101.1	P>0.05
	Day 14	478±85.7	476±70.63	431±76.62	420±71.34	P>0.05
	P-Value	NS	NS	NS	****P<0.01**	

RBC	Day 1	6.8±0.56	7.26±0.36	10.58±2.24	6.46±0.54	6.25±0.99	P>0.05
	Day 7	7.62±0.61	8.43±0.19	8.32±0.38	7.7±0.35	9.03±1.15	P>0.05
	Day 14	7.97±0.22	9.54±1.71	8.02±0.45	6.66±0.89	7.13±0.7	P>0.05
	P-Value	NS	NS	NS	NS	NS	
RDW	Day 1	17.28±0.17	16.98±0.2	23.14±5.5	17.14±0.29	17.3±0.29	P>0.05

	Day 7	17.46^{b}±0.35	17.2^{b}±0.29	17.94^{b}±0.47	18.68^{b}±0.73	19.76^{a}±0.96	*P<0.05
	Day 14	18.58±0.64	21.6±4.23	17.64±0.34	18.02±0.35	17.74±0.66	P>0.05
	P-Value	NS	NS	NS	NS	NS	
WBC	Day 1	9.2^{a}±2.77	7.54^{a}±1.36	5.88^{a}±1.1	7.06^{a}±1.49	0.93$^{\#\# b}$±0.3	*P<0.05
	Day 7	8.92±3.08	8.16±2.91	9.68±1.08	11.9±2.75	6.06$^{\#}$ ±1.05	P>0.05
	Day 14	8.82±0.37	10.14±2.45	37.08±28.03	8.82±2.12	7.76$^{\#}$ ±1.88	P>0.05
	P-Value	NS	NS	NS	NS	****P<0.01**	

WBC**(x10^{3}/ul**)-white blood cell, HGB(**g/dl**)-haemaglobin, RBC**(x10^{6}/ul**)- red blood cells count, MCV(fl)- mean corpuscular volume, MCH(pg)-mean corpuscular haemoglobin, MCHC(**g/dl**)- mean corpuscular haemoglobin concentration, RDW(%)- red density width, GR(%)- granulocytes count, HCT(%)-hematocrit, PLT**(x10^{3}/ul**)-platelets, LY(%)- lymphocytes, MPV(fl)-mean platelet volume, MO(%)- monocytes, PCT(%)-platelet crit, PDW(%)-platelet density width

DW-Distilled water; All values are expressed as Means±SEM of five animals in each group

*Note: P>0.05- Not Significant, *P<0.05-Significan **P<0.01-Significant*

The different number of $^{\#}$(in columns) shows a significant difference across the sampled means across the days.

Different superscript letters (in rows) show that the mean is significant from others;

NS –No Significant difference in days across the columns.

Effect of *A. barbadensis* on Lipid parameters

High-density lipoprotein cholesterol (HDL-C).

The extract at the administered doses had no significant effect (P>0.05) on HDL-C, as shown in Table 2 on days 1, 7 and 14. The extract at 100 mg/kg had the highest effect on HDL, with 221.92±58.1 mg/dl concentrations on day 14.

Table 2. Effect of ethanol extract of *A. barbadensis* on high-density lipoprotein cholesterol (HDL-C) concentrations (mg/dl) of male rats.

Groups	Day 1	Day 7	Day 14	
Control(DW)	52.18$^{\#}$±14.53	118.45$^{\#}$±30.63	133.72$^{\#\#}$±9.55	*P<0.05
100mg/kg	54.21$^{\#}$±23.96	126.41$^{\#}$±33.7	221.92$^{\#\#}$±58.1	*P<0.05
200mg/kg	54.21$^{\#}$±23.96	94.1$^{\#}$±38.51	211.15$^{\#\#}$±18.94	**P<0.01
400mg/kg	26.02$^{\#}$±16.1	160.94$^{\#\#}$±4.72	128.75$^{\#\#}$±18.33	**P<0.01
P-value	P>0.05	P>0.05	P>0.05	

DW-Distilled water; All values are expressed as Means±SEM of five animals in each group
*Note:**P<0.01-Highly significant, *P<0.05-Significant, P>0.05-Not Significant*
Same $^{\#}$(in rows) shows no significant difference across the sampled means across the days. NS – No Significant difference in days across the rows

Low-density lipoprotein cholesterol (LDL-C)

Table 3 revealed the effect of the extract on LDL-C. The administered doses of the extract to the male rats had no significant effect (P>0.05) on LDL-C, on days 1 and 14 (Table 3). The highest concentration of LDL-C observed at the 200 mg/kg dose level was 150.05±15.19 mg/dl.

Table 3. Effect of ethanol extract of *A. barbadensis* on low-density lipoprotein cholesterol (LDL-C) concentrations (mg/dl) of male rats.

Groups	Day 1	Day 7	Day 14	P-Value
Control(DW)	109.62±15.99	105.15^{a}±7.3	65.48±18.55	NS
100mg/kg	113.21±32.86	29.39^{b}±12.11	99.43±57.16	NS
200mg/kg	54.83±22.85	78.55^{a}±23.66	150.05±15.19	NS
400mg/kg	47.69$^{\#}$±15.59	119.3$^{a\#\#}$±11.64	84.64$^{\#}$±18.56	*P<0.05
P-value	P>0.05	**P<0.05	P>0.05	

DW-Distilled water; All values are expressed as Means±SEM of five animals in each group
*Note:**P<0.01-Highly significant, *P<0.05-Significant, P>0.05-Not Significant*
Different superscript letters (in columns) show that the mean is significant from others.
Same $^{\#}$(in rows) shows no significant difference across the sampled means across the days. NS – No Significant difference in days across the rows

Triglyceride (TRIG)

The effect of the extract on TRIG concentrations of all same dose groups at different days was non- significant. The administered doses of the extract to the male rats had no significant effect (P>0.05) on TRIG on days 1 and 14 (Table 4).

Table 4. Effect of ethanol extract of *A. barbadensis* on triglyceride concentrations (mg/dl) of male rats.

Groups	Day 1	Day 7	Day 14	P-Value
Control(DW)	122.99±36.17	66.86^{b}±24.23	136.42±33.14	NS
100mg/kg	116.62±32.03	253.22^{a}±40.91	215.09±36.97	NS
200mg/kg	77.69±23.53	99.09^{b}±20.14	121.38±36.9	NS
400mg/kg	132.05±36.64	121.65^{b}±47.77	131.04±39.96	NS
P-value	P>0.05	**P<0.01	P>0.05	

DW-Distilled water; All values are expressed as Means±SEM of five animals in each group
*Note:**P<0.01-Highly significant, *P<0.05-Significant, P>0.05-Not Significant*
Different superscript letters (in columns) show that the mean is significant from others.

NS –No Significant difference in days across the rows

Total cholesterol concentrations

A significant decrease in total cholesterol concentrations as the doses increased on days 1, 7 and 14 were observed (Table 5). On day 1, there was no significant difference in the effect of all the tested doses on cholesterol but were significantly different (P<0.01) from the control (distilled water).

Table 5. Effect of ethanol extract of *A. barbadensis* on total cholesterol concentrations (mg/dl) of male rats.

Groups	Day 1	Day 7	Day 14	P-Value
DW	$184^{a\#\#}$±19.03	$62.26^{\#b}$±4.4	$71.96^{b\#}$±14.38	**P<0.01
100mg/kg	113.89^{b}±42.53	186.04^{a}±12.15	145.39^{a}±26.47	NS
200mg/kg	99.83^{b}±28.35	84.78^{b}±16.62	63.52^{b}±12.82	NS
400mg/kg	64.28^{b}±18.5	67.02^{b}±5.83	46.73^{b}±12.13	NS
P-value	**P<0.01	**P<0.01	**P<0.01	

DW-Distilled water; All values are expressed as Means±SEM of five animals in each group
*Note:**P<0.01-Highly significant, *P<0.05-Significant, P>0.05-Not Significant*
Different superscript letters (in columns) show that the mean is significant from others.
Same #(in rows) shows no significant difference across the sampled means across the days. NS – No Significant difference in days across the rows

DISCUSSION

The haematological and lipid profiles of male Wistar rats were evaluated following the assessment of functional biochemical indices or "markers." Reports show that a significant change in any organ function's biochemical indices will impair the normal function of the organ (Afolayan and Yakubu, 2009). Therefore, haematological and lipid parameters are essentially

necessary tools in clinical diagnosis and toxicological studies like serum enzyme levels (Ashafa et al. 2009).

Haematological parameters have been used to unravel the magnitude of the harmful effect of foreign substances such as plant extracts on an animal's blood constituents. Also, haematological parameters had been used to explain blood-relating functions of chemical compounds, including extracts of plants (Yakubu et al. 2007). The non-significant ($p>0.05$) effect following the oral administration of the extract on RBC and indices relating to it (HGB, PCT, MCV, MCH, and MCHC) (Table 1) indicates that there was no destruction of matured RBC's and erythropoiesis was not changed. Furthermore, the blood's oxygen-carrying capacity was unhindered because of the non-significant effect of the extract on RBC and HGB (de Gruchy, 1976). The blood diagnostic parameters (MCV, MCH and MCHC) of anaemia (Coles, 1986), as displayed in Table 1, were not affected, suggesting an unremarkable effect on the average size of RBC (microcytes) and haemoglobin as well as the weight per RBC. These findings imply that the extract cannot induce anaemia within 14 days of administration. The WBC and all indices relating to it (GR, LY, HCT and MO) were not altered. It implies that the ability of the animal to eliminate infection was not affected. It also suggests that there was an unremarkable stimulation of the immune system. The platelets -blood cells involved in coagulation (Williams and Levine, 1982) were not significantly ($p>0.05$) altered. It indicates that the extract did not adversely affect the platelets' size, number, and function. The extract had no significant localized systemic toxicity, affecting the WBC's normal functioning and related indices. These findings were dissimilar to previous reports by Adebayo et al. (2005) on the ethanolic extract of *Bougainvillea spectabilis;* Yakubu et al. (2007), and Yakubu and Afolayan (2009) on the aqueous extracts of *Fadogia argrestis* stem and *Bulbine natalensis* stem.

445 The concentrations of major lipids such as cholesterol, high–density lipoprotein cholesterol
446 (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglycerides, when altered, can give
447 vital information on the metabolism of lipids. These alterations can also give useful information
448 on the predisposition of the heart to atherosclerosis and other associated cardiovascular diseases
449 (Yakubu et al. 2008). The administration of the extract significantly ($p<0.01$) decreased
450 cholesterol on day 1 but significantly ($p<0.01$) increased it on days 7 and 14 at 100 mg/kg when
451 compared to control (Table 5). This may be due to impairment in cholesterol biosynthesis on day
452 1 and non-impairment in cholesterol biosynthesis on days 7 and 14. This increase in cholesterol
453 can be due to an increase in acetyl CoA concentration as a key substrate in the biosynthesis of
454 cholesterol (Range et al. 1995). However, Treasure et al. (1995) reported that high blood
455 cholesterol concentration is one of the vital risk factors for cardiovascular disease, suggesting
456 that such an increase may not be beneficial to the animals as it may enhance atherosclerosis and
457 hypertension (Enas, 1999). The non-significant ($p>0.05$) effect of the extract on HDL - C (Table
458 2) is an implication that the anti-atherogenic property of HDL-C was not affected. LDL-Cs form
459 plaque that clots the arteries resulting in atherosclerosis. LDL-Cs are primary carriers of
460 cholesterol that build up in the arteries' walls supplying blood to the heart and brain (Ashafa et
461 al. 2009). The non-significant ($p>0.05$) effect of the extract on the lipid parameter-LDL-C (Table
462 3) shows that the extract may not predispose the heart to atherosclerosis. Again, the non-
463 significant ($p>0.05$) effect of the extract on triglyceride (Table 4) implies that lipolysis was not
464 enhanced, which indicates a non-depletion in the storage of fatty acids. It can be inferred that the
465 ethanol extract of *A. barbadensis* may not predispose the male animals to atherosclerosis and
466 other associated coronary heart diseases despite isolated significant alterations in LDL- C,

triacylglycerol and cholesterol on day 7 at 100 mg/kg. This increase was alleviated by the non-significant increase in HDL – C ('good cholesterol').

CONCLUSIONS

The toxicological study shows that the extract was comparatively safe for consumption at the administered doses. There was no significant harmful consequence on the haematological parameters of the male rats. In contrast, there were isolated alterations in the evaluated lipid parameters. Additionally, no significant localized systemic toxicity was noticed. Still, caution is needed when using the extract of *A. barbadensis* root for oral remedies following its potential selective ability to alter specific lipid parameters in male rats. Further studies on the effect of chronic administration of the root of *A. barbadensi*s are recommended.

ACKNOWLEDGEMENTS

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