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Hypolipidemic and Toxicological Potential of Aqueous Extract of *Rauvolfia vomitoria* Afzel Root in Wistar Rats

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The aim of this study was to investigate the hypolipidemic potential of aqueous extract of *Rauvolfia vomitoria* root and assess its toxicological effect in selected tissues of rats. Aqueous extract of *Rauvolfia vomitoria* root was administered to wistar rats daily at 24 h interval at a dosage of 200 mg kg^{-1} b.wt. following which the rats were sacrificed after receiving 1, 3, 5, 10, 20 and 30 daily oral doses. Administration of the extract produced significant reduction ($p<0.05$) in the concentration of the Low-density Lipoprotein Cholesterol (LDL-C), triglyceride and atherogenic indices while a dose-dependent significant increase ($p<0.05$) occurred in the High-density Lipoprotein Cholesterol (HDL-C) concentration. Significant changes were also observed ($p<0.05$) in the activities of alkaline phosphatase (ALP) and acid phosphatase (ACP) in all the tissues studied except small intestine. There were significant fluctuations ($p<0.05$) in the activities of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in the tissues except in the kidney. The results suggest that aqueous extract of *Rauvolfia vomitoria* root possesses hypolipidemic potential but caused alterations in the concentration of the enzymes studied and so may not be completely safe at the dose used in this study.

Key words: *Rauvolfia vomitoria*, acid phosphatase, toxicity, hypolipidemic, cholesterol

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INTRODUCTION

Atherosclerosis is a complex inflammatory process characterised by the accumulation of lipid, macrophages and smooth muscle cells in the plaques of the arteries (Kumar and Clarke, 2002). It is otherwise referred to as coronary atherosclerosis or Coronary Artery Disease (CAD). It is well known that Coronary Artery Disease (CAD) is the leading cause of death in both men and women in developed countries (Onyeneke *et al.*, 2007). Dyslipidemia is the major and most pronounced risk factor of CAD. It is characterised by low concentration of HDL-C, high triglyceride and elevated LDL-C (Wilson *et al.*, 1991; Austin *et al.*, 1998). LDL-C, HDL-C and triglyceride are all independent and significant predictors of cardiovascular risk. High blood cholesterol is one of the greatest risk factors contributing to the prevalence and severity of coronary heart disease (Wilson *et al.*, 1998).

Several chemotherapeutic agents had been employed in the treatment of dyslipidemia. This includes 3-hydroxy-3-methylglutaryl CoA (HMG-CoA) reductase inhibitors like atorvastatin and simvastatin. Others are the bile acid sequestrant such as colestipol, cholestyramine and nicotinic acid. Gemfibrozil and clofibrate are also used for lowering high triglyceride levels (AHA, 1997). Due to the high cost involved in obtaining these drugs and the widespread side-effect associated with their usage, several plants had been screened for their hypolipemic potential. These plants include *Verbesina encelioides* (Sindhu *et al.*, 2011), *Cajanus cajan* leaves (Akinloye and Solanke, 2011) and *Rauvolfia vomitoria* (Akpanabiatu *et al.*, 2009).

Rauvolfia vomitoria is a tree with white or greenish flowers. It is commonly called African snake root, Swizzle stick or Poison devil's pepper. It is known locally in Nigeria as 'Asofeyeje' (Yoruba), 'Wadda' (Hausa) and 'Ntu oku' (Igbo) (Amole *et al.*, 2009). This plant originated majorly from Africa and is distributed in the dry regions of the continent such as West Africa. It is found in Lagos, Abeokuta, Ibadan and in the Eastern part of the country (Eteng *et al.*, 2009). It contains many chemicals among which are reserpine, rescinamine, ajmaline, alstonine, rauvomitine, serpentinine and yohimbine (Trease and Evans, 2009). It has been reported that the infusion made from its root can be used in the treatment of nervous disorder, insomnia, mental illness and snake-bite (Gbile and Soladoye, 2002; Amole *et al.*, 2009).

Due to the widespread use of this plant in alternative medicine without the scientific proof of efficacy and safety, the present study is aimed at evaluating the effect of administration of this plant on the lipid profile and activity of some enzymes in selected tissues of rats, so as to ascertain its safety or otherwise.

MATERIALS AND METHODS

Materials: Thirty-five albino rats of an inbred Novergicus strain (*Rattus novergicus*) with average weight of 220 g were obtained from the Animal Holding Unit of the Department of Biochemistry, University of Ilorin, Ilorin, Nigeria. The assay kits for the determination of the total cholesterol, LDL-C, HDL-C, triglyceride, acid and alkaline phosphatase were procured from Quimica Clinica Applicada, S.A., Spain while the aminotransferase assay kits were supplied by Randox Laboratories Ltd., United Kingdom. Other reagents used were of analytical grade and were prepared in all glass-distilled water.

Plant material and extract preparation: Samples of *Rauvolfia vomitoria* root was obtained from the herbal section of the New Market, Ilorin. The plant was authenticated at the Department of Botany of the University of Lagos, Akoka, Nigeria where voucher specimen (LUH 5099) was deposited. Samples of the root of the plant were sun-dried for 7 days, ground into powder and stored in a sealed plastic container until required. Twenty gram of the powder was extracted in 100 mL of distilled water. This was stirred with magnetic stirrer for 1 h and allowed to settle for 24 h (Yakubu *et al.*, 2002). It was then filtered, concentrated using rotary evaporator (Cole Parmer SB 1100, Shangai, China) and lyophilized using Virtis Bench Top (SP Scientific Series, USA) freeze dryer.

Phytochemical screening: The phytochemical screening was done on the sample using methods as described by Sofowara (1993).

Experimental design: The rats were kept in well-ventilated house conditions (temperature: 28-31°C; photoperiod: 12 h natural light and 12 h dark; humidity: 50-55%) with free access to normal rat chow (Bendel Feeds and Flour Mills, Ltd., Ewu, Nigeria) and tap water. They were housed in plastic cages of dimension 165×102.5×95 cm with cleaning done twice daily. The acclimatization was done for two weeks before the start of the experiment. The animal grouping consisted of two groups of animals as follows:

Group A: Five rats that were orally administered with 1 mL of distilled water (control)

Group B: Thirty rats that were orally administered with 200 mg kg^{-1} b.wt. of aqueous extract of *Rauvolfia vomitoria* root

Animals in group A and B were administered with their appropriate dosages on daily basis for 30 days. Five rats each from group B were sacrificed 24 h after days 1, 3, 5, 10, 20 and 30, respectively.

Tissue sample collection and preparation: Rats were anaesthetized in slight chloroform and blood samples collected into clean, dry centrifuge tubes by cardiac puncture. The animals were quickly dissected and the organs (liver, kidney, small intestine and stomach) removed. The kidney was decapsulated while the small intestine and stomach were cleared of metabolic waste. The liver was also cleansed of superficial connective tissues. They were thereafter blotted with clean tissue paper, weighed and homogenized in ice-cold 0.25 M sucrose solution [1:5 w/v] using Teflon homogenizer. The homogenates were kept frozen overnight to ensure maximum release of the enzymes (Malomo, 2000).

Lipid profile determination: Total cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol levels were measured spectrophotometrically using the methods described by Fredrickson *et al.* (1967), Trinder (1969), Albers *et al.* (1978) and Bergmenyer (1985), respectively while the atherogenic indices were simply calculated.

Enzyme activities determination: Alkaline phosphatase (EC 3.1.3.1) and acid phosphatase (EC 3.1.3.2) activities were assayed using the method described by Wright *et al.* (1972). The procedure as described by Reitman and Frankel (1957) was employed for the assay of aspartate aminotransferase (AST) (EC 2.6.1.1) and alanine aminotransferase (ALT) (EC 2.6.1.2). Protein content was determined using Biuret reagent as described by Plummer (1978). All measurements were done using Spectronic 21 digital spectrophotometer (Bausch and Lomb, N.Y.).

Statistical analysis: Data were presented as mean of 5 Replicates±standard Error of Mean (SEM). Data were subjected to One-Way Analysis of Variance (ANOVA) followed by test of significance. The level of statistical significance was taken at 5% confidence level.

RESULTS

The phytochemical screening of the *Rauvolfia vomitoria* root (Table 1) showed that out of all the phytochemicals tested for, the sample only contain saponins, flavonoids, alkaloids and phenolics.

The effect of administration of aqueous extract of *Rauvolfia vomitoria* root on the serum lipid profile is shown in Table 2. The administration of the extract to the experimental rats resulted in significant increase (p<0.05) in the total cholesterol on the 1st, 3rd and 5th day only. HDL-C concentration increased significantly (p<0.05) in all the animals while LDL-C concentration decreased significantly (p<0.05) in all the groups tested. Administration of the extract to the animals produced a significant reduction (p<0.05) in the level of triglyceride only in the latter part of the experiment. The result of atherogenic indices calculated from the serum lipid profile is presented in Table 3. There exists a significant reduction (p<0.05) in all the atherogenic indices estimated when compared to the control group.

The effect of administration of 200 mg kg^{-1} b.wt. of aqueous extract of *Rauvolfia vomitoria* root on the activities of alkaline phosphatase (ALP), acid phosphatase (ACP), aspartate aminotransferase (AST)

Table 1: Phytochemical composition of the aqueous extract of *Rauvolfia vomitoria* root

Phytochemicals tested	Inference
Alkaloids	+
Anthraquinones	-
Flavonoids	+
Glycosides	-
Phenolics	+
Philobatannins	-
Saponins	+
Steroids	-
Tannins	-

+: Present, -: Not detected

Table 2: Effect of administration of aqueous extract of *Rauvolfia vomitoria* root on serum lipid profile

Group	mg dL^{-1}			
	Total cholesterol	HDL-cholesterol	LDL-cholesterol	Triglyceride
Control	3.02±0.54[a]	1.75±0.46[a]	2.21±0.52[a]	1.60±0.56[a]
Day 1	3.70±0.10[b]	2.25±0.26[b]	2.03±0.10[a]	1.43±0.09[a]
Day 3	3.47±0.06[b]	2.58±0.13[b]	1.92±0.18[a]	1.43±0.12[a]
Day 5	3.17±0.25[b]	2.62±0.17[b]	1.56±0.13[b]	0.86±0.24[b]
Day 10	3.10±0.09[a]	2.95±0.21[b]	1.46±0.07[b]	1.23±0.18[a]
Day 20	3.07±0.12[a]	3.25±0.26[b]	0.68±0.07[b]	1.05±0.09[b]
Day 30	3.00±0.25[a]	3.39±0.19[b]	0.29±0.09[b]	0.92±0.18[b]

Values are means of 5 replicates±SEM. Values with different alphabetical superscript along columns are significantly different at p<0.05

Table 3: Atherogenic indices calculated from the values obtained from serum lipid profile

Group	TC/HDL	LDL/HDL	TG/HDL	Log (TG/HDL)
Control	1.84±0.24[a]	1.94±0.21[a]	0.78±0.15[a]	0.96±0.006[a]
Day 1	1.16±0.13[b]	0.63±0.03[b]	0.44±0.02[b]	0.36±0.013[b]
Day 3	1.09±0.15[b]	0.76±0.05[b]	0.42±0.05[b]	0.38±0.010[b]
Day 5	1.15±0.09[b]	0.60±0.10[b]	0.32±0.02[b]	0.50±0.025[b]
Day 10	1.51±0.20[a]	0.44±0.05[b]	0.68±0.05[a]	0.57±0.029[b]
Day 20	1.02±0.07[b]	0.21±0.04[c]	0.26±0.01[b]	0.60±0.045[a]
Day 30	1.19±0.11[b]	0.11±0.07[c]	0.35±0.02[b]	0.46±0.025[b]

Values are means of 5 replicates±SEM. Values with different alphabetical superscript along column are significantly different at p<0.05. TC: Total cholesterol, LDL-C: Low density lipoprotein cholesterol, HDL-C: High density lipoprotein cholesterol, TG: Triglyceride

Table 4: Effect of administration of aqueous extract of *Rauvolfia vomitoria* root on the activities of some enzymes in the liver

| Group | nM/min/mg protein | | | |
	ALP	ACP	AST	ALT
Control	34.29±4.49[a]	83.18±10.78[a]	14.62±4.07[a]	17.18±4.20[a]
Day 1	21.04±4.09[b]	107.11±5.650[b]	13.29±1.63[a]	19.15±3.02[a]
Day 3	10.87±1.78[b]	141.17±5.53[b]	12.86±2.40[b]	14.69±1.98[b]
Day 5	16.07±1.05[b]	124.85±7.41[b]	14.38±0.68[a]	11.25±2.59[b]
Day 10	19.80±2.98[b]	87.07±6.92[a]	8.14±1.07[b]	5.60±0.50[b]
Day 20	10.72±1.38[b]	94.17±4.93[b]	9.15±1.83[b]	7.43±0.57[b]
Day 30	11.30±3.34[b]	66.85±4.01[c]	2.43±0.98[b]	1.25±0.73[b]

Values are means of 5 replicates±SEM. Values with different alphabetical superscript along column are significantly different at p<0.05. ALP: Alkaline phosphatase, ACP: Acid phosphatase, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

Table 5: Effect of administration of aqueous extract of *Rauvolfia vomitoria* root on the activities of some enzymes in the kidney

| Group | nM/min/mg protein | | | |
	ALP	ACP	AST	ALT
Control	275.21±9.580[a]	172.36±5.350[a]	15.68±3.91[a]	7.40±2.26[a]
Day 1	218.44±8.260[b]	195.48±10.28[b]	13.67±2.67[a]	9.68±4.63[a]
Day 3	181.19±9.130[b]	204.34±9.250[b]	14.82±1.87[a]	7.65±2.37[a]
Day 5	153.78±11.58[b]	122.77±6.050[b]	16.60±1.90[a]	4.08±0.23[b]
Day 10	136.72±9.590[b]	138.64±8.400[b]	14.53±1.31[a]	8.75±2.76[a]
Day 20	118.36±10.01[b]	117.79±5.330[b]	14.67±3.03[a]	3.54±0.39[b]
Day 30	92.14±7.080[b]	106.16±6.370[b]	14.18±1.17[a]	1.57±0.23[b]

Values are means of 5 replicates±SEM. Values with different alphabetical superscript along column are significantly different at p<0.05. ALP: Alkaline phosphatase, ACP: Acid phosphatase, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

Table 6: Effect of administration of aqueous extract of *Rauvolfia vomitoria* root on the activities of some enzymes in the stomach

| Group | nM/min/mg protein | | | |
	ALP	ACP	AST	ALT
Control	79.97±9.20[a]	27.75±4.23[a]	15.03±3.68[a]	11.13±2.67[a]
Day 1	67.34±6.08[b]	35.60±5.83[b]	8.90±3.88[b]	7.70±1.44[b]
Day 3	61.75±7.26[b]	38.01±6.16[b]	6.21±1.90[b]	10.90±2.03[a]
Day 5	53.42±5.89[b]	45.40±5.96[b]	5.18±0.56[b]	16.81±3.41[b]
Day 10	46.16±11.72[b]	54.44±7.97[b]	4.04±1.20[b]	4.50±0.46[b]
Day 20	52.74±4.26[b]	21.19±2.95[b]	4.20±0.74[b]	3.74±1.60[b]
Day 30	35.54±5.39[b]	14.45±2.74[b]	3.15±0.81[b]	4.08±1.21[b]

Values are means of 5 replicates±SEM. Values with different alphabetical superscript along column are significantly different at p<0.05. ALP: Alkaline phosphatase, ACP: Acid phosphatase, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

Table 7: Effect of administration of aqueous extract of *Rauvolfia vomitoria* root on the activities of some enzymes in the Small intestine

| Group | nM/min/mg protein | | | |
	ALP	ACP	AST	ALT
Control	33.88±5.040[a]	33.75±6.67[a]	13.28±4.37[a]	18.69±4.48[a]
Day 1	61.39±10.26[b]	27.87±4.02[b]	9.35±2.68[b]	22.82±2.42[b]
Day 3	59.70±6.640[b]	26.06±4.24[b]	15.30±3.70[a]	9.16±0.62[b]
Day 5	42.85±7.410[b]	31.92±6.68[a]	10.95±2.86[b]	3.34±1.87[b]
Day 10	31.52±8.210[a]	24.96±3.63[b]	9.79±2.08[b]	12.56±1.68[b]
Day 20	29.74±3.390[b]	24.33±4.25[b]	5.59±1.69[b]	14.41±2.01[b]
Day 30	10.61±3.520[b]	22.47±3.64[b]	5.48±2.17[b]	10.78±3.06[b]

Values are means of 5 replicates±SEM. Values with different alphabetical superscript along column are significantly different at p<0.05. ALP: Alkaline phosphatase, ACP: Acid phosphatase, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

and alanine aminotransferase (ALT) in the liver, kidney, stomach and small intestine are presented in Table 4-7, respectively. All the enzymes assayed for in the liver (Table 4) were influenced by the extract administration. The activities of the ALP and AST reduced significantly (p<0.05) in all the groups tested while the activities of the ACP increased significantly (p<0.05) on the 1st, 3rd, 5th and 20th day and reduced significantly (p<0.05) on the last day. As for the ALT activity, the initial increase witnessed on the 1st day was not significant (p>0.05) and later reduced significantly (p<0.05) in all the other groups of animals.

ALP and ACP activities in the kidney were significantly reduced (p<0.05) in all the groups of animals tested except at the early part of the experiment (days 1 and 3) where the ACP activities increased significantly (p<0.05) (Table 5). The activity of the AST was not affected as there was no significant difference (p>0.05) in all the groups while ALT activity had a significant reduction only on the 10th, 20th and 30th day. The stomach witnessed significant decrease (p<0.05) in the activities of the ALP, AST and ALT while ACP activity increased significantly (p<0.05) in all the groups studied except on latter part of the experiment (days 20 and 30) (Table 6).

Table 7 showed that all the enzymes assayed for in the small intestine were affected. The activities of both the ALP and ALT initially increased significantly (p<0.05) on the 1st day of the experiment and later reduced significantly (p<0.05) on the other days. As for ACP and AST, their activities decreased significantly (p<0.05) throughout the period of the experiment.

DISCUSSION

The levels of various lipids in the serum of animals have been shown to serve as indices of hypertension, atherosclerosis and coronary heart disease (Ruidavets *et al.*, 2000; Maghrani *et al.*, 2004). The initial significant increase in the total cholesterol following the first three doses of extract administration may be attributed to increase in the concentration of acetylcoA resulting from a corresponding increase in the oxidation of fatty acids. This is because acetylcoA is a key substrate in the biosynthesis of cholesterol (Gorinstein *et al.*, 1998). However, the intermittent reduction to the control level may be an attempt by the blood cells to return to normal rate of cholesterol metabolism, which was finally achieved by the end of the experiment.

Studies have shown that HDL-cholesterol is good cholesterol (Kumar *et al.*, 2005). This is because it helps the body to get rid of unwanted cholesterol. It also acts in several other protective ways-as an antioxidant deterring

the harmful oxidation of LDL-cholesterol, as an anti-inflammatory agent and as an anti-clotting agent which help keep blood clots from blocking the arteries (Kumar *et al.*, 2005). The result presented showed that there was significant increase in the level of HDL-cholesterol throughout the period of the experiment. This implies that there is a continuous transport of excess cholesterol to the liver for excretion into the bile, thereby reducing the risk of hypertension and atherosclerosis (Patil *et al.*, 2004).

Significant reduction in the LDL-cholesterol levels after the first day till the end of the study suggests that the trend is dependent on the dose of the extract. When LDL-cholesterol is oxidized, it becomes glued to the lining of arteries that feed the heart, brain and other tissues in the body, thereby setting the stage for hypertension and heart diseases (Kumar *et al.*, 2005). However, reduction in the level of LDL-cholesterol, as shown in this study will likely prevent the oxidation of LDL-cholesterol. The presence of some chemical compounds in the plant such as saponins and flavonoids might also assist in this function (Aletor, 1993). It has been shown that saponin helps to lower level of cholesterol by binding with excess cholesterol, thereby preventing its reabsorption leading to increased excretion of the cholesterol from the body (Aletor, 1993). Certain flavonoids have been shown to protect the LDL-cholesterol from oxidation. They include catechin, antocyanidin and coumaric acid. In fact, flavonoid has been suggested to be inversely related to coronary heart disease (Ruidavets *et al.*, 2000; Buhler, 2003).

Triglyceride functions as one of the energy reservoirs in animal, though not components of membranes (Voet *et al.*, 1999). The significant decrease in the level of triglyceride on the 5th, 20th and 30th day complements the reduction in LDL-cholesterol. This is because hypertriglyceridaemia is a risk factor for hypertension and atherosclerosis (Kumar and Clarke, 2002). This significant reduction in TG levels may be attributed to an increasing lipid peroxidation activity (LPL), which will lead to an increase in the degradation of TG which is usually produced in the liver and aids in lipolytic removal of TG-rich lipoproteins from the circulation (Megalli *et al.*, 2006).

Several atherogenic indices such as (TC/HDL-C, TG/HDL-C and LDL-C/HDL-C) have also been used to predict CHD risk. The TC/HDL-C, TG/HDL-C and LDL-C/HDL-C molar ratios have good predictive value for future cardiovascular events (Grover *et al.*, 1999). However, another molar ratio, log TG/HDL-C, is also a significant independent predictor of the disease (Gaziano *et al.*, 1997). All the indices calculated showed

marked decrease in all the test groups when compared to the control. This is an indication that the administration of the plant extract to the animals reduces the risk of atherosclerosis and cardiovascular diseases.

The measurement of the activities of 'marker' or diagnostic enzymes in tissues plays a significant and well-known role in diagnosis, disease investigation and in the assessment of plant extract for safety or toxicity risk (Yakubu *et al.*, 2005). This is so because activities of enzymes sum up the catalytic influence of various factors like activators or inhibitors, during such pathological conditions (Malomo, 2000). Tissue enzyme assay can also indicate tissue cellular damage long before structural damage can be picked up by conventional techniques (Akanji *et al.*, 2004). Such measurement can also give an insight to the site of cellular and tissue damage as a result of assault by plant extract (Adebayo *et al.*, 2003).

Alkaline phosphatase is a membrane bound enzyme often employed to assess the integrity of plasma membrane and endoplasmic reticulum (Yakubu, 2006). There was persistent reduction in its activities throughout the experiment in the tissues studied. This loss in enzyme activities may be an indication of possible alteration in the binding and permeability properties of the various membrane systems of the tissues studied (Yakubu and Akanji, 2002). It may also be due to loss of membrane components (including alkaline phosphatase) into the intracellular environment on inhibition of enzyme activity by the extract, leading to decreased synthesis of enzyme molecules (Yakubu *et al.*, 2002; Adebayo *et al.*, 2003). The initial significant increase in these enzyme activities on the 1st, 3rd and 5th day in the small intestine may be due to increased synthesis of plasma membrane proteins during repairs of the damage caused by the extract (Akanji and Ngaha, 1989).

Acid phosphatase is a 'marker' enzyme for the lysosomal membrane (De Duve *et al.*, 1962). The status of this enzyme in tissues following administration of chemical compound will give an indication of the state of lysosome in the tissue (Yakubu *et al.*, 2001). In all the tissues except small intestine, an initial sharp increase in enzyme activity was observed after the first administration. This could be an attempt by the tissues to respond to the effect of the extract. It is possible that the extract may bind to the enzymes, thereby directly activating the enzyme (Malomo, 2000). The significant loss that occur subsequently in the acid phosphatase activity in these tissues may be attributed to either loss of membrane components, due to destruction of lysosomal membrane into intracellular fluid (Akanji and Yakubu, 2000) or inhibition of enzyme activity *in situ* by the chemical compound (Akanji *et al.*, 1993). The activity of

this enzyme in the small intestine reduced significantly throughout the period except on the 5th day. This may be an attempt by the tissue to recover from the assault and this was a consequence of *de novo* synthesis of the enzyme molecule (Yakubu *et al.*, 2002).

Aspartate aminotransferase along with alanine aminotransferase is normally localized within the cells of the liver, heart, kidney, muscles and other organs (Yakubu *et al.*, 2005). They are present majorly in the cytoplasm, though some are present in the mitochondria (Tietz, 1987). Both enzymes occupy a central position in amino acid metabolism as they help in retaining amino groups (to form a new amino acid) during the degradation of amino-acid. They are involved in the regulation of intracellular amino acid pool. They also help in providing necessary intermediates for gluconeogenesis (Yakubu *et al.*, 2005). The lack of significant change in the AST activity of the kidney points to the fact that the administration of the extract does not have an effect on the level of this enzyme. This may likely due to the fact that the organelles where they are located in the tissue are not adversely affected (Akanji *et al.*, 1993). Reduction in the enzyme activity in other tissues studied may be ascribed to leakage of the cytosolic enzyme following membrane labilization (Akanji and Yakubu, 2000). The decrease was dose-dependent initially in the stomach until the 20th day where further administration produced an increase in the enzyme activity. This also occurs in the small intestine, it is an attempt by the cells to counteract the action of the chemical (extract) on them (Akanji, 1986). However, it is interesting to note that the significant decrease in enzyme activity in the liver was continuous and dose-dependent except on the 5th day to the end of the experiment. This may imply serious adverse effect on the hepatocytes.

The general increase in the activity of alanine amintransferase after the first administration in all the tissues except the stomach can be attributed to *de novo* synthesis of the enzyme molecules or an adaptation by the tissues to the assault from the plant extract, leading to activity higher than control (Yakubu *et al.*, 2001). The subsequent significant decrease in the alanine aminotransferase activities in all the tissues studied may be attributed to reduced rate of synthesis of this enzyme. It may also be that the extract has caused leakage of the enzyme into the blood via altered membrane permeability (Malomo, 2000). Cellular damage arising from plant extract administration can result in the leakage of marker enzymes to the extracellular fluid (Akanji and Onyekwelu, 1986). Though, there were some elevations in the activity of this enzyme in the small intestine and stomach but were not sustained in the course of the study. These elevations

may be due to an attempt by the cell to recover from the effect of the extract (Akanji and Onyekwelu, 1986) or increased synthesis of the enzyme.

CONCLUSION

This study has demonstrated that rats administered aqueous extract of *Rauvolfia vomitoria* root significantly showed evidence of hypolipidaemia in a dose related manner via the combined effects of all the active ingredients mainly the flavonoids, saponins, phenolics and alkaloids among others present in the plant. The administration of the aqueous extract of *Rauvolfia vomitoria* root to rats has resulted in alteration of all the enzymes assayed for in the tissues. These alterations may adversely affect the integrity of the tissues investigated. Therefore, it can be concluded that oral administration of the aqueous extract of *Rauvolfia vomitoria* root exhibited hypolipidemic potentials but may not be safe for treatment at the dosage studied.

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