

Investigation of Toxicological and Hypolipidaemic Effect of Aqueous and Methanol Fruit Extracts of *Xylopiiaethiopia*

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Abstract: This work investigated the effect of aqueous and methanol fruit extracts of *Xylopiiaethiopia* on the serum cholesterol level and some liver marker enzyme activities on wistar albino rats. The animals were randomly selected and divided into seven groups (A-G) of four rats per cage with 3 replicates. Group A served as control, administered commercial feed and water only, while group B-D were administered different concentrations (50 mg/kg, 100 mg/kg and 150 mg/kg) of aqueous extract of *Xylopiiaethiopia* respectively. Rats in groups E-G were treated orally with 50 mg/kg, 100 mg/kg and 150 mg/kg concentration of methanol extract of *X. aethiopia* respectively. The study lasted for 6 weeks with weekly collection of blood samples for the determination of serum levels of the biochemical parameters. Results showed significant ($P < 0.05$) increase in alkaline phosphatase (ALP) activity from week 1-3 and no difference from week 4-6 across different concentrations of extracts when compared to the normal control. Similarly there was no significant ($P > 0.05$) difference in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities from week 1-6 compared to the normal control. Significant ($P < 0.05$) decrease in cholesterol level of rats was observed in Week 1 and Week 3 in both extracts while no significant difference was seen in the other weeks compared to the normal control. The result of this study was similar for both methanol and aqueous extracts and suggests that the extracts may have hypolipidaemic effect and does not confer toxicity even with prolonged use.

Key words: *Xylopiiaethiopia* • Cholesterol • Alkaline phosphatase • Alanine aminotransferase and Aspartate aminotransferase

INTRODUCTION

Plants use by man for the treatment of various diseases has become a common practice and also very popular in many developing countries of the world [1 and 2]. The advent of modern medicine in health care system coupled with industrialization and urbanization in most developed countries has made the use of herbal products to decline from the beginning of 20th century till 1970s. With time there has been a renewal and growing interest in the use of plant -derived biologically active compounds as drugs which has led to the manufacture of more potent medicaments [3]. In tropical areas of Africa, poverty and illiteracy still militate against availability and accessibility of Western medical services, traditional medicine has been beneficial.

Amongst these plants with great therapeutic potential is *Xylopiiaethiopia* which is commonly

referred to as “African guinea pepper” or “Ethiopian pepper”. It is an angiosperm of the Annonaceae family and grows predominantly in humid forest zones of West Africa [4 and 5]. It is found all over the low land rain forest and most fringe forest in the savannah zones of Nigeria. Although it is said to serve as a ‘pepper substitute’ in Europe and India, it is highly valued in other countries for its medicinal and pharmacological properties [6]. The seeds have been reported to contain bitter principles like alkaloids, glycosides, saponins, tannins, sterols, carbohydrate, protein, free fatty acids, mucilage’s

Also, the fruit decoction is used to treat bronchitis, asthma and rheumatism [7]. *X. aethiopia* is used in many herbal preparations to produce Xylopic acid, a substance which has been found to have antimicrobial effects [8]. It has a wide spectrum of biological activities and has played a crucial role in traditional medicines because of their physiological and pharmacological properties [9].

Other works have been reported on *Xylopiiathioipica* also on its biologic activities, such as, antimicrobial [10], antiparasitic [11], insecticidal [12], antifungal [13], antioxidant [14], diuretic and hypotensive [15], antimalarial [16] and membrane stabilization. The objectives of the study were to determine the effect of aqueous and methanolic extracts of *Xylopiiathioipica* on the enzyme levels: serum alanine aminotransferase (ALT) alkaline phosphatase (ALP), aspartate aminotransferase (AST) and cholesterol levels.

Experimental Section

Plants Materials: Dried fruits of *Xylopiiathioipica* were bought from oriorba market, orba, Nsukka, Nigeria. Its botanical identification and authentication was done at the Department of Botany, University of Nigeria, Nsukka, were voucher specimen already exist.

Preparation of *Xylopiiathioipica* Fruit Extract:

The fruits were washed with clean tap water and sun-dried. The sample was made into a powder with a grinding machine. The method of extraction followed that of [17]. A quantity 135g sample of the powdered material and 500ml of 80% analytical methanol was added into a flask and left for 48hr with an occasional shaking to increase the extraction capacity, thereafter the soaked sample was filtered and concentrated to dryness in a rotary evaporator and weighed. Solution of the extract was prepared by dispersing 1g of the dried extract with 10 ml of 2% Tween 80 solutions for oral administration, this formed the methanolic extract while the aqueous extract was obtained by soaking 135g of the powdered plant material in 500ml of distilled water in a flask for two days with an occasional shaking to increase the extraction capacity, then later filtered with a filter paper.

Procurement, Management and Morphometric Indices of Albino rats/Experiment Design Experimental Animals:

Eighty- four male albino rats of the wistar strain of known weight were purchased from the breeding and genetics unit of Department of Zoology University of Nigeria, Nsukka the animals were kept in well ventilated stainless steel cages, they were handled with care and housed in the experimental house Department of Zoology for one week acclimatization, they were fed commercial rat feed (vital growers mash) and clean tap water ad libitum throughout the period of experiment. The experimental rat were randomly selected and divided into seven groups (A-G) of four rats per cage with 3 replicates.

Group A served as control, administered commercial feed and water only, while group B-D were administered different concentration (50mg/kg, 100mg/kg and 150mg/kg) of aqueous extract of *Xylopiiathioipica* respectively while rats in groups E-G were treated orally with 50mg/kg, 100mg/kg and 150mg/kg concentration of methanolic extract of *X.athioipica* respectively.

Acute Toxicity Test (LD₅₀) of *Xylopiiathioipica* (Aqueous and Methanolic Extracts):

This was determined by Lorke (1993) method, where 50 albino rats were used for this determination, the animals were grouped into ten of five rats per cage. Five groups were given aqueous extract of *Xylopiiathioipica* of different concentration, 5mg/kg, 50mg/kg, 300mg/kg, 2000mg/kg and control group was only administered distilled water while the remaining five groups were given methanolic extract of *Xylopiiathioipica* of different concentration, 5mg/kg, 50mg/kg, 300mg/kg, 2000mg/kg and control (distilled water).

The various doses of extract were administered via oral route by means of Gavage method. The animals were observed for 24hrs after administration. Two died under 2hours and the remaining three died the following day from the group that was administered 2000mg/kg aqueous extract while none died in the other groups. The results were subjected to probit log analysis and (LD₅₀) were determined to be 1,474mg/kg concentration for aqueous extract. One animal died after 30minutes in the group given 300mg/kg of methanolic extract of *Xylopiiathioipica* while four rats died after five minutes in the group administered with 2000mg/kg concentration, but no death of animals were observed in other groups as well as the control group. It was also subjected to probit log analysis and the (LD₅₀) was determined to be 458mg/kg.

Biochemical Analysis: Serum cholesterol was determined according to Fredrickson *et al.*, 1967, Alkaline phosphatase (ALP) was determined according to Klein *et al.*, 1960. Alanine aminotransferase GPT (ALT) and Aspartate aminotransferase (AST) was determined according to Reitman and Frankel, 1957.

Statistical Analysis: Data collected were analyzed for significant differences for mean \pm STD ($P \leq 0.05$) compared to respective controls by one way ANOVA using the statistical package for service solutions (SPSS) version 17 mean of groups were separated using Duncan Multiple Range Test LD₅₀ was determined using probit log analysis.

RESULTS

The ALP and AST values of rats administered methanolic and aqueous extracts produced no significant change when compared with the control and when the extract groups were compared ($P > 0.05$). When the ALT values (43.00 ± 5.00), (43.00 ± 9.00) and (52.00 ± 4.00) of aqueous extract were compared with the control (21.00 ± 3.00), they were significantly increased ($P < 0.05$). Comparing the ALT values of methanolic extract, only rats administered 150 mg/kg of the extract (48.00 ± 4.00) manifested significant change when compared with control (21.00 ± 3.00). The difference between methanolic

and aqueous extract was seen only between 150 mg/kg aqueous group and 100 mg/kg methanolic group, with 150 mg/kg aqueous group being significantly higher than 100 mg/kg methanolic group ($P < 0.05$).

The cholesterol level of rats that received aqueous extract was significantly lower in 100 mg/kg group (2.00 ± 0.20) compared with control (3.45 ± 0.25). The cholesterol levels of rats administered methanolic group did not change significantly from control ($P > 0.05$). Comparing the two extracts (aqueous and methanolic) of *X.aethiopica*, there was no significant difference ($P > 0.05$) between the cholesterol value of 150 mg/kg methanolic and 150 mg/kg aqueous extracts.

Table 1: Changes in biochemical parameters of rats administered different concentration of methanolic and aqueous extracts of *Xylopiiaethiopica* in Week 1.

Control	EXTRACTS ¹						
	Distilled water	Aqueous			Methanolic		
Parameters ²	Distilled water	50 mg/Kg	100 mg/Kg	150 mg/Kg`	50 mg/Kg	100 mg/Kg	150 mg/Kg
ALP (U/L)	80.50±8.50 ^a	8200±2.00 ^a	90.50±1.50 ^a	76.50±2.50 ^a	77.00±9.00 ^a	79.00±5.00 ^a	80.00±2.00 ^a
ALT (U/L)	21.00±3.00 ^a	43.00±5.00 ^{bc}	43.00±9.00 ^{bc}	52.00±4.00 ^c	37.00±7.00 ^{abc}	30.00±2.00 ^{ab}	48.00±4.00 ^{bc}
AST (U/L)	41.00±5.00 ^a	54.00±6.00 ^a	50.00±8.00 ^a	54.00±0.00 ^a	43.00±5.00 ^a	36.00±12.00 ^a	35.00±13.00 ^a
Cholesterol (mmol/L)	3.45±0.25 ^b	2.35±0.35 ^{ab}	2.00±0.20 ^a	2.50±0.10 ^{ab}	2.90±0.20 ^{ab}	3.10±0.60 ^{ab}	3.40±0.50 ^b

¹Mean ± S.E values in a row for a given group of extracts compared to control with different superscripts are significantly different ($P < 0.05$).

²The parameters stand for the following:

ALP- Alkaline phosphatase ALT- Alanine aminotransferase

AST- Aspartate aminotransferase.

Table 2: Changes in biochemical parameters of rats given different concentrations of methanolic and aqueous extracts of *X. aethiopica* in Week 2.

Control	EXTRACTS ¹						
	Distilled water	Aqueous			Methanolic		
Parameters ²	Distilled water	50 mg/Kg	100 mg/Kg	150 mg/Kg`	50 mg/Kg	100 mg/Kg	150 mg/Kg
ALP (U/L)	97.50±1.50 ^a	94.00±1.00 ^a	88.00±11.00 ^a	82.50±7.50 ^a	92.00±0.00 ^a	92.50±4.50 ^a	87.00±6.00 ^a
ALT (U/L)	26.00±2.00 ^a	22.00±2.00 ^a	23.00±3.00 ^a	27.00±1.00 ^a	24.00±0.00 ^a	26.00±0.00 ^a	22.00±4.00 ^a
AST (U/L)	39.71±6.00 ^a	41.00±1.00 ^a	45.00±3.00 ^a	42.00±4.00 ^a	39.00±3.00 ^a	37.00±3.00 ^a	36.00±4.00 ^a
Cholesterol (mmol/L)	3.85±0.07 ^a	4.15±0.45 ^a	3.80±0.10 ^a	4.10±0.20 ^a	3.80±0.10 ^a	4.05±0.15 ^a	4.10±0.20 ^a

¹Mean ± S.E values in a row for a given group of extracts compared to control with different superscripts are significantly different ($P < 0.05$).

Table 3: Changes in biochemical parameters of rats given different concentrations of methanolic and aqueous extracts of *X. aethiopica* in Week 3

Control	EXTRACTS ¹						
	Distilled water	Aqueous			Methanolic		
Parameters ²	Distilled water	50 mg/Kg	100 mg/Kg	150 mg/Kg`	50 mg/Kg	100 mg/Kg	150 mg/Kg
ALP (U/L)	88.50±0.50 ^a	87.00±2.00 ^a	87.00±4.00 ^a	89.00±2.00 ^a	87.00±300 ^a	85.00±1.00 ^a	82.50±2.50 ^a
ALT (U/L)	49.00±1.00 ^{ab}	41.00±1.00 ^{ab}	35.00±5.00 ^a	43.00±1.00 ^{ab}	54.00±2.00 ^b	50.00±4.00 ^b	40.00±8.00 ^{ab}
AST (U/L)	55.00±1.00 ^a	38.00±8.00 ^a	51.00±1.00 ^a	59.00±1.00 ^a	54.00±4.00 ^a	58.00±2.00 ^a	53.00±1.00 ^a
Cholesterol (mmol/L)	4.10±0.10 ^{bc}	3.00±0.30 ^a	3.30±0.020 ^{ab}	2.95±0.15 ^a	3.10±0.20 ^a	3.40±0.30 ^{ab}	4.30.030 ^c

¹Mean ± S.E values in a row for a given group of extracts compared to control with different superscripts are significantly different ($P < 0.05$).

The ALP values of 50 mg/kg and 100 mg/kg aqueous and methanolic extract increased while 150 mg/kg decreased. The ALP of the extract groups did not differ from control and each other significantly ($P > 0.05$) ALT values of aqueous extract increased slightly as the dose increased, although there was no significant difference. The ALT value of 100 mg/kg methanolic extract group was greater than those of the other two groups, no significant change. They also did not differ from the ALT of the control group. The AST values of the methanolic extract groups were lower than those of aqueous extract. No significant difference was observed in the AST values of the different groups. Cholesterol value of rats administered extracts did not differ from control values and the extract group did not also differ from each other.

In the third week of administration of the aqueous and methanolic extracts of *Xylopiiaethiopic*, ALP and AST values of extract groups were not significantly different from those of the control. Comparing the extract groups, no significant change was observed. The ALT value of group administered 100 mg/kg aqueous extract (35.00 ± 5.00) significantly decreased when compared with the ALT value (54.00 ± 2.00) of 50 mg/kg and 100 mg/kg methanolic extract (50.00 ± 4.00). No significant difference was observed in ALT value of other groups (Table 5).

There was significant decreases in the cholesterol values of 100 mg/kg aqueous (3.30 ± 0.02) and 100 mg/kg (3.40 ± 0.30) methanolic extract groups compared to control (4.00 ± 0.10) ($P < 0.05$).

In the fourth week, as shown in the Table above, the ALP of rats given 50 mg/kg methanolic extract showed significant increase ($P < 0.05$) when compared with the control and other groups (Table 6). Comparing both extracts, 50 mg/kg methanolic group (80.00 ± 2.50) increased significantly when compared with all the aqueous extract groups (59.50 ± 4.50 ; 66.50 ± 0.50 and 58.50 ± 3.50).

ALT of the rats in the control group (24.00 ± 2.00) was significantly increased ($P < 0.05$) compared with the ALT of rats administered the lower doses of aqueous extract (50 mg/kg and 100 mg/kg) (15.00 ± 1.00 and 15.00 ± 1.00 respectively). Comparing aqueous extract and methanolic extract, there was no significant difference ($P > 0.05$). AST values of rats administered 50 mg/kg aqueous extract, 50 mg/kg and 100 mg/kg methanolic extracts decreased significantly from 100 mg/kg aqueous extract group and 150 mg/kg methanolic group.

Cholesterol levels of rats administered different concentrations of both extracts did not differ from control values and the extract groups did not also differ statistically ($P > 0.05$) from each other.

Table 4: Changes in biochemical parameters of rats given different concentrations of methanolic and aqueous extracts of *X. aethiopic* in Week 4

		EXTRACTS ¹					
Control		Aqueous			Methanolic		
Parameters ²	Distilled water	50 mg/Kg	100 mg/Kg	150 mg/Kg	50 mg/Kg	100 mg/Kg	150 mg/Kg
ALP (U/L)	61.50±3.50 ^a	59.50±4.50 ^a	66.50±0.50 ^a	58.50±3.50 ^a	80.50±2.50 ^b	62.00±1.00 ^a	66.50±0.50 ^a
ALT (U/L)	24.00±2.00 ^b	15.00±1.00 ^a	15.00±1.00 ^a	19.00±3.00 ^{ab}	22.00±4.00 ^{ab}	23.00±3.00 ^{ab}	19.00±1.00 ^{ab}
AST (U/L)	41.00±700 ^{ab}	36.00±8.00 ^a	60.00±6.00 ^b	47.00±5.00 ^{ab}	33.00±3.00 ^a	35.00±3.00 ^a	57.00±3.00 ^b
Cholesterol (mmol/L)	3.60±0.10 ^a	3.45±0.55 ^a	4.40±0.20 ^a	4.85±0.75 ^a	4.60±0.60 ^a	4.15±0.85 ^a	4.60±0.00 ^a

¹Mean ± S.E values in a row for a given group of extracts compared to control with different superscripts are significantly different ($P < 0.05$).

Table 5: Changes in biochemical parameters of rats given different concentration of Methanolic and Aqueous extracts of *X. aethiopic* in Week 5

		EXTRACTS ¹					
Control		Aqueous			Methanolic		
Parameters ²	Distilled water	50 mg/Kg	100 mg/Kg	150 mg/Kg ³	50 mg/Kg	100 mg/Kg	150 mg/Kg
ALP (U/L)	83.00±1.00 ^a	88.00±0.00 ^b	88.50±0.50 ^b	87.50±1.50 ^b	90.00±1.00 ^b	87.50±0.50 ^b	89.00±0.00 ^b
ALT (U/L)	25.00±1.00 ^a	33.00±1.00 ^a	29.00±3.00 ^a	39.00±7.00 ^a	46.00±16.00 ^a	25.00±1.00 ^a	26.00±2.00 ^a
AST (U/L)	54.00±2.00 ^b	55.00±15.00 ^b	69.00±3.00 ^b	59.00±1.00 ^b	25.00±9.00 ^a	53.00±9.00 ^b	54.00±0.00 ^b
Cholesterol (mmol/L)	5.40±0.00 ^a	4.50±0.20 ^a	4.75±0.05 ^a	4.85±0.05 ^a	5.00±0.20 ^a	5.20±0.20 ^a	5.00±0.60 ^a

¹Mean ± S.E values in a row for a given group of extracts compared to control with different superscripts are significantly different ($P < 0.05$).

Table 6: Changes in haematological and biochemical parameters of rats given different concentrations of methanolic and aqueous extracts of *X. aethiopica* in Week 6

Parameters ²	Distilled water	EXTRACTS ¹					
		Aqueous			Methanolic		
		50 mg/Kg	100 mg/Kg	150 mg/Kg	50 mg/Kg	100 mg/Kg	150 mg/Kg
ALP (U/L)	65.00±5.00 ^a	85.00 ± 5.00 ^b	81.50± 0.50 ^b	80.00 ± 2.00 ^b	88.00 ±0.00 ^b	84.00 ± 1.00 ^b	86.00 ± 6.00 ^b
ALT (U/L)	70.00 ± 2. 00 ^{ab}	46.00 ± 2.00 ^a	64.00±1600 ^{ab}	57.00 ± 5.00 ^{ab}	68.00 ±14.00 ^{ab}	81.00 ± 5.00 ^b	73.00 ± 1.00 ^{ab}
AST (U/L)	21.00 ± 1.00 ^a	22.50 ± 0. 50 ^a	21. 00± 0.00 ^a	20.50 ± 0. 50 ^a	25.50 ± 2.50 ^a	25.50 ± 3.50 ^a	22.00 ± 1.00 ^a
Cholesterol (mmol/L)	4.40 ± 0.20 ^{ab}	415 ± 0.25 ^a	410 ± 0.30. ^a	4.10 ± 0.10 ^a	4.60 ±0.00 ^{ab}	4.15 ±0.05 ^a	4.80 ± 0.00 ^b

In the fifth week, as shown in the Table above, the ALP of rats given the different concentration of both extracts (aqueous and methanolic were significantly increased ($P < 0.05$) when compared with the control group.

Aqueous extract when compared with methanolic extract showed no significant difference in their ALP values. The ALT values of all the groups both Control and the extract groups, were statistically similar ($P > 0.05$).

Statistically, AST levels of rats administered different concentrations of aqueous extract were not different from the control. However, comparing the different concentrations of methanolic extract group with each other, the lower dose, 50 mg/kg (25.00 ± 9.00) decreased significantly ($P < 0.05$) compared with the higher doses - 100 mg/kg and 150 mg/kg (53.00 ± 9.00 and 54.00 ± 0.00) respectively of AST values.

However, cholesterol levels of all the groups did not differ significantly ($P > 0.05$) with the Control, although, the extract groups all decreased compared with Control.

In the sixth week post administration of extract, result of effects is as shown in Table above. The ALP levels of rats in all the extract groups statistically increased ($P < 0.05$) compared with the control. No significant difference was observed when aqueous and methanolic extracts were compared. ALT showed no significant difference ($P > 0.05$) when the different concentrations of groups of aqueous extract of *X. aethiopica* was compared with the Control group, although when aqueous and methanolic extracts were compared 100 mg/kg methanolic extract significantly increased ($P < 0.05$) the ALT of rats (81.00 ± 5.00) compared with 50 mg/kg aqueous extract (46.00 ± 2.00).

AST values of all groups were statistically similar ($P > 0.05$).

Cholesterol levels of rats administered the different concentrations of aqueous extract of *X. aethiopica* showed no significant difference compared with Cholesterol levels of rats given 100 mg/kg methanolic

extract decreased significantly compared with 150 mg/kg methanolic extract groups.

DISCUSSIONS

Liver Enzymes are well known biomarkers for the prediction of liver toxicity [18 and 19] and as such, have been used in scientific reports. Available evidence show that damage to liver cells results in elevations of these enzymes in the serum [20] and the measurement of enzyme activities is of clinical and toxicological significance in determining liver damage by toxicants or in diseased conditions [21].

This study showed that initially from Weeks 1-3, there was no significant increase in ALP values of rats fed with aqueous and methanolic extracts of *Xylopiiaethiopica* until in Week 4 where there was significant increase in ALP value of rats administered 50 mg/kg methanolic extract compared to control. This was followed by significant increases of ALP values of rats in all the experimental groups both aqueous and methanolic extract groups compared to the control in Week 5 and 6 respectively. It is known that an increase in the enzymatic activity of ALT, AST and ALP in the serum directly reflects hepatocellular damage. The result of ALP analysis therefore, suggests that extract of *Xylopiiaethiopica* could have hepatotoxicity when use is prolonged from 4 - 6 weeks. This finding is in contrast with the work of Chrissie, *et al.* (2011), [22], in which extract of *X. aethiopica* caused no significant effect on ALP.

Comparing the effect of both aqueous and methanolic extract of *Xylopiiaethiopica* on the ALP of rats, none of them seem to be better than the other.

ALT showed increases in values initially in Week 1 with all the different concentrations of aqueous extract of *X. aethiopica* compared with the control. Methanolic extract did not produce significant effect except in higher dose (150 mg/kg) which produced significant increase, indicating some form of liver damage. There seem to be no

definite trend in the effect of the extracts on the animals as from Weeks 2-6. The animals seem to adjust to the effects of the extract on the ALT after Week 1. This is in contrast to the work of [22], in which the ethanolic extract caused a significant reduction in ALT of rats over 60 days of experience to *Xylopiiaethiopica*.

AST showed no significant change in values in all the groups compared with control from week one to six. AST is found mainly in liver, kidneys, cardiac muscles and skeletal tissues. Liver and heart release AST and ALT; an elevation in plasma concentration is an indicator of liver and heart damage [23 and 24]. This result is in agreement with the work of Ogbonna *et al.* (2008), [9], in which there was no significant increase in AST in the animals treated with lower doses of *X. aethiopic* compared with the Control.

In this study, when compared with the Control, 100 mg/kg aqueous extract caused a significant decrease in cholesterol of rats in Week 1 and Week 3. Significant decrease in cholesterol levels were observed with (50 mg/kg, 150 mg/kg) aqueous extract and 50 mg/kg methanolic extract. This is in agreement with the work of Nnodim, *et al.* (2011), [24], in which plasma cholesterol and LDL Cholesterol were decreased when compared with the Control. This observed decrease could be associated with the presence of hypolipidemic component of the extract. This showed that the extract has some beneficial effects by reducing cardiovascular risk factors. The levels of serum lipids are usually elevated in cardiovascular diseases; such an elevation represents a risk factor for coronary heart diseases. The mechanism of *X. aethiopica* fruit hypolipidemic effects is not known but could be by reduced cholesterol absorption from the intestinal tract, possibly mediated either by the fibre or the phytochemical content. The decrease in absorption of exogenous cholesterol and increased metabolism of endogenous cholesterol into bile acids in the liver leads to increased expression of LDL receptor on hepatocytes and increased clearance of LDL-C from the plasma [25]. Another possible mechanism through which lipid lowering drugs (bile acid sequestrant) act is by binding to bile acid in intestine, which will impair its reabsorption from the intestine. The depletion of bile acid pool leads to up regulation of cholesterol 7- α -hydroxylase and increased conversion of cholesterol to bile acids. This causes an increased demand for cholesterol by the hepatic cells, resulting in the dual effect of increased transcription and activity of HMG-CoA reductase and increased number of hepatic LDL receptors. These compensatory effects result in increased clearance of LDL-C from the blood, resulting

in decreased serum LDL-C levels. Serum TG levels may increase or remain unchanged [26].

Furthermore, *X. aethiopic* could have acted through the inhibition of rate limiting enzyme, HMG-CoA reductase, in the biosynthesis of cholesterol. HMG-CoA reductase catalyse the conversion of HMG-CoA to mevalonic acids [25]. The reversible and competitive inhibition of HMG-CoA reductase leads to decreased hepatic cholesterol synthesis, up regulation of LDL receptor synthesis and increased LDL-C clearance from the plasma into liver cells [27]. The hypolipidemic effects of the powdered fruit *Xylopiiaethiopic* may have been mediated through one or a combination of the above mechanisms. Comparing the effect of aqueous and methanolic extracts of *Xylopiiaethiopica* on the cholesterol levels, aqueous extract seem to perform better than methanolic extract.

CONCLUSION

Since increase in the enzymatic activity of ALT, AST and ALP in the serum reflects hepatocellular damage, results of ALP analysis which showed significant increases compared to control in weeks 5-6 suggests that *X. aethiopic* could have hepatotoxicity effect when use is prolonged from 4-6 weeks. AST did not show significant change while cholesterol had significant decreasing effect, which could be associated with hypolipidemic component of the extract. The results show that aqueous extract had a boosting effect on the hematological parameters, RBC, WBC and PCV (aqueous and methanolic) while both extracts had similar effect on the biochemical parameters studied-ALT, AST and ALP.

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