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Comparative Assessment of the Total Lipid Profile, Faecal Cholesterol, Very Low Density Lipoprotein Cholesterol (VLDL-C) and Altherogenic Index (A.I.) of the Aqueous Fruit Extract of *Solanum macrocarpum*, α-solanidine and Antihyperlipidaemic Drugs on Triton-Induced Hyperlipdaemic Rats

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ABSTRACT

Studies were undertaken on the effect of 50mg/kg each of the aqueous fruit extract of *Solanum macrocarpum*, α-solanidine, (a steroidal glycoalkaloid found in the Solanaceae), three antihyperlipidaemic drugs namely nicotinic acid, simvastatin and cholestyramine) on forty two (42) rats made hyperlipidaemic by treating them with 400 mg/kg triton-X for 7 days. The rats were divided into 7 groups of 6 rats each. At 24hrs, 48hrs and 72hrs respectively, the rats in each group were humanely sacrificed and blood samples collected for analysis of total lipid profile [total cholesterol, triglyceride, high density lipoprotein-cholesterol (LDL-C) and low density lipoprotein cholesterol (LDL-C)]. Very low density lipoprotein cholesterol (VLDL-C) and atherogenic index (A.I.) were also calculated. Faecal samples were also collected, homogenized and extracted with chloroform/methanol in the ration 2:1 for faecal cholesterol determination. The extract, α-solanidine and the three hypolipidaemic drugs all significantly decreased (P<0.05) LDL-C and triglycerides at 48hrs and 72hrs, whilst HDL-C increased significantly (0.05) throughout the period of study (24hrs, 48hrs and 72hrs). There was no change in total cholesterol (P>0.05) for all the five substances tested throughout the period of study, whilst VLDL-C and A.I. decreased significantly (P<0.05) at 24hrs, 48hrs and 72hrs. These results imply that under the condition of this study, the aqueous fruit extract of *S. macrocarpum* compared favourably with α-solanidine and the three hypolipidaemic drugs in reducing the risk of development of heart diseases.

INTRODUCTION

In the traditional North East Arid zone of Nigeria, the unripe fruit of *S. macrocarpum* (Synonyms: *S. macrocarpum* L. and *S. daysphyllum* Schumach and Thonn) called "Gorongo" in Kanuri, (Solanaceae) is know for its laxative, antihypertensive and hypolipidaemic effects. The fruit and flowers are also used in cleaning the teeth (Bokhari and Ahmed, 1980; Grubben and Denton, 2004). Experimental support for the ethnopharmacological use of this plant in folk medicine has been reported (Sodipo *et al.,* 2008a, b; 2009a). Recently, we have documented hepatoprotective effects of aqueous fruit extract of *S. macrocarpum* in diet-induced hypercholesterolaemic rats (Sodipo *et al.,* 2009b), acute and chronic triton-induced hyperlipidaemic rats respectively (Sodipo *et al.,* 2011c; 2012a). However, the mechanism of hypolipidaemia has not been extensively studied. Sodipo *et al.* (2009c; 2011a; 2012a) observed a favourable lipid profile in diet-induced hypercholesterolaemic, acute and chronic triton-induced hyperlipidaemic rats administered with the aqueous fruit extract, the exact mechanism of cholesterol lowering and hypolipidaemia was not known.

The current drugs that lower hyperlipidaema have renal and hepatotoxicities and are usually expensive (Sodipo *et al.,* 2011c). In an attempt to find alternative in plants which are less expensive and probably less toxic than the existing antihyperlipdaemic drugs, the present study compared the ability of the aqueous fruit extract of *S. macrocarpum* to lower hyperlipidaemia with that of α-solanidine (a glycoalkaloid said to lower hyperlipidaemia in the Solanaceae), [ANONa, 2007] and three hypolipidaemic drugs (nicotinic acid, simvastatin and cholestyramine) in triton-induced hyperlipidaemic rats.

MATERIALS AND METHODS

Plant collection and identification

The plant material (*Solanum macrocapum* Linn.) used in this study was obtained from Alau in Konduga Local Government, Borno State, Nigeria, between October and November, 2007. The plant was identified and authenticated by Prof. S.S. Sanusi of the Department of Biological Sciences, University of Maiduguri, Nigeria. Specimen voucher No. 548 was deposited at the Research Laboratory of the Department of Chemistry.

Extraction

The fruit of *S. macrocarpum* with the calyx removed was air dried and pulverized by using pestle and mortar. The 2.2kg of the ground fruit was subjected to exhaustive Soxhlet-extraction in distilled water at 100°C to give the extract yield 15.3% $^{w}/_{w}$ (Mittal *et al.,* 1981; Fernado *et al.,* 1991; Lin *et al.,* 1999). The resultant solution was concentrated *in vacuo* and it was stored in specimen bottle and kept in a desicator at room temperature until when required.

Animals and Treatment

Forty two (42) male albino rats of Wistar strain weighing 160-200g were used in this study. The animals were obtained from the Animal House Unit of the Department of Veterinary Physiology and Pharmacology, University of Maiduguri. The animals were housed under standard laboratory condition in plastic cages. They were fed with commercial grower's mash feed (ECWA, Feeds, Jos, Nigeria) and water was provided *ad libitum*. All the animals were handled according to the International Guiding Principles for Biomedical Research Involving Animals (CIOMS, 1985) as certified by the Animal Ethics Committee of the Faculty of Veterinary Medicine, University of Maiduguri (Approved on October 15th, 2008 at its 12th Ethical Committee Meeting).

A total of forty two (42) male albino rats weighing between 160 and 200g were used for the work. They were randomly distributed into seven groups of 6 rats per group.

Group one: Rats in this group served as the negative control. They were fed with normal feed diet and given water *ad libitum*

Group two: Rats in this group served as the positive control. They were fed with normal diet and given water *ad libitum.* They were also administered 400mg/kg triton-X orally (p.o) for 1 week to make them hyperlipidaemic.

Group three: Rats in this group were fed with normal feed diet and given water *ad libitum*; administered 400mg/kg triton-X p.o. for 1 week and then given 50mg/kg aqueous fruit extract of *S. macrocarpum* i.p. from a stock concentration of 200mg/ml (2g extract dissolved in 10ml distilled water)

Group four: Rats in this group were fed with normal feed diet and given water *al libitum*, administered 400mg/kg triton-X p.o. for 1 week and then given 50mg/kg α-solanidine i.p. – a steroidal glycoalkaloid that is found in the Solanaceae and is said to lower hyperlipidaemia (by dissolving 50mg of approximately 95% α-solanine while powder, Sigma, USA in 1ml distilled water H_2O to give a stock concentration of 50mg/ml)

Group five: Rats in this group were fed with normal feed diet, given water *ad libitum,* 400mg/kg triton-X p.o. for 1 week and then given 50mg/kg nicotinic acid B.P. orally – hypolipidaemic drug, from a stock concentration of 50mg/ml (by dissolving 50mg white round tablet in 1ml distilled water).

Group six: Rats in this group were fed with normal feed diet, given water *adlibitum*, 400mg/kg triton-X p.o. for 1 week and then given 50mg/kg cholestyramine – a hypolipdaemic drug, (Questran, Bristol-Meyers Squibb) p.o. froma stock concentration of 100mg/ml (dissolving 1g powder in 10ml distilled water)

Group seven: Rats in this group were fed with normal feed diet, given water *ad libitum*, 400mg/kg triton-X p.o. for 1 week and then given 50mg/kg simvastatine – hypolipidaemic drug (Gimvastat-10, Stallion Lab, PVT Ltd, India, and NAFDAC Reg. No. A4-0010 with sole agent as Pharmabase Nig. Ltd) p.o. from a stock concentration of 10mg/ml (by dissolving 20mg light yellow film-coated tablets in 1ml distilled water).

After administration of the extract, α-solanidine and the three hypolipidaeic drugs given to the rats in groups three-seven respectively, every 24hrs for 3 consecutive days, 2 rats from each group (Groups one-seven) were humanely sacrificed and blood samples were collected for total lipid profile VLDL-C and A.I. analysis. (Adapted from Williamson *et al.,* 1996).

All the rats in the 7 groups were weighed at day zero (i.e. before administration of triton-X) and 1 week after before they were sacrificed.

Determination of Total Lipid Profile

Two rats from each of the groups were humanely sacrificed after 24hrs, 48hrs and 72hrs respectively of the effect of the extract on chronic hyperlipidaemic rats by cutting their throat with a sterile blade. Blood was collected into a clean, sterile, labelled centrifuge tubes without an anticoagulant and centrifuged at a rate of 12,000 revolutions per minute (rpm) for 10 minutes. The clear, yellow serum was then separated from settled cellular elements and subjected to determination of total lipid profile.

The total lipid profile estimated from the serum was total cholesterol triglycerides, high density lipoprotein-cholesterol (HDL-C) and low density iipoprotein-cholesterol (LDL-C). Total cholesterol was assayed by Tindar's reaction (Evans and Stein, 1986; NIH, 1990) using commercial kits from Fortress Diagnostics Ltd; Antrim. Serum triglycerides level was determined as described by Fossati and Prencipe (1982), Cole *et al*., (1997) using commercial kit (Human cholesterol using Liquicolour Test Kit, Germany) [Grove, 1970]. The serum LDC-L level was calculated by Friedwald's formular (Friedwald *et al*., 1972; Hardman and Limbird, 2001; Sood, 2006). The calculation for serum LDL-C is given by:

Serum LDL-C = Total cholesterol – Trigylcerides ÷ 2.2 — HDL — C.

Determination of Faecal Cholesterol

Faeces from two rats in each of the groups were collected after 24hrs, 48hrs and 72hrs respectively that the extract had acted on the hyperlipidaemic rats into clean, cellophane bags and deep frozen. They were homogenized and extracted with chloroform/methanol in the ratio 2:1 (Folch *et al*., 1957) for analysis of faecal cholesterol. The faecal cholesterol determination was like that of the serum total cholesterol (Tindar's reaction) [Evans and Stein, 1986; NIH, 1990] using commercial kits from Fortress Diagnostic Ltd; Antrim.

Calculation of Very Low Density Lipoprotein Cholesterol (VLDL-C) (mmol/L)

VLDL-C was calculated using the formula (Henry, 1991; Igweh et al., 2005; Satheesh and Paris, 2008):

$$\text{VLDL-C (rnmol/L)} = \frac{\text{Triglycerides}}{2.2}$$

Calculation of Atherogenic Index (A.I)

Although index was calculated with the formula given below (Williamson *et al*., 1996) a:

$$\text{A. I.} = \frac{\text{VLDL-C + LDL-C}}{\text{HDL-C}}$$

Where:

VLDL-C is very lower density lipoprotein cholesterol

LDL-C is low density lipoprotein cholesterol
HDL-C is high density lipoprotein cholesterol.

Statistical Analysis

Data were expressed as the mean ± S.D. The results obtained were subjected to Analysis of Variance (ANOVA) and Student t-test using Graph Pad Software (1998).

RESULTS

Change in Mean Body Weight of Male Albino Rats Wistar strain) after being Administered Orally with Triton-X for 7 Days

The effect of triton-X on mean body weight of albino rats fed orally with triton-X is shown in Table 1. There was increase in body weight of the rats in groups one, two and five ($p < 0.05$) when compared to day zero (i.e. when no triton-X was administered).

Table 1: Change in body weight of male albino rats after being administered orally with triton-X (400 mg/kg) for 7 days

Group	Body Weight (g) Days of Treatment	
	0	7
	Mean ± S.D.	
One*	148.00 ± 9.38^a	170.80 ± 10.59^b
Two	117.80 ± 26.68^a	128.00 ± 23.93^a
Three	148.80 ± 5.26^a	166.00 ± 4.58^b
Four	117.80 ± 26.6^a	128.00 ± 23.93^a
Five	165.40 ± 41.71^a	173.00 ± 42.57^b
Six	164.80 ± 38.75^a	181.80 ± 40.02^a
Seven	86.60 ± 16.10^a	100.40 ± 18.56^a

Within rows, means with different superscripts are statistically significant ($p < 0.05$) when compared to zero (0) using student t-test

0 day = before triton-X administration

n = 6 rats per group-

Group One* = Rats fed with normal diet and had free access to water, but were not administered triton-X

Effect of the Aqueous Fruit Extract of *Solanum macrocarpum*, α-Solanidine, Nicotinic Acid, Cholestyramine and Simvastatin on Total Lipid Profile of Hyperlipidaemic Rats Administered Triton-X Orally for 7 Days

The effect of the aqueous fruit extract of *S. macrocarpum*, α-solanidine and the three hypolipidaemic drugs on total lipid profile of hyperlipidaemic rats are shown in Table 2:

Table 2: Effect of the aqueous fruit extract of *S. macrocarpum*, α-solanidine, nicotinic acid, cholestyramine and simvastantin on total lipid profile of hyperlipidaemic rats administered triton-X orally for 7 days

Hours after extract/drug administration	Dosage mg/kg	Extract/ Drug	Total cholesterol (mm/L)	Total cholesterol (mmol/L)	erides ol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)
			Mean ± S.D.				
	50	-ve control	2.75±0.07^a	1.30±0.14^a		1.95±0.07^a	1.30±0.14^a
	50	+ve control	3.50±0.28^a	1.50±0.14^b		0.80±0.07^b	1.80±0.14^a
	50	Aqueous extract	2.95±0.07^a	1.00±0.00^b		1.15±0.07^b	1.30±0.14^a
24	50	α-solanidine	2.80±0.28^a	1.10±0.00^b		1.30±0.14^b	1.00±0.14^a
	50	Nicotinic acid	2.75±0.07^a	0.85±0.07^b		1.15±0.07^b	1.25±0.07^a
	50	Cholestyramine	3.00±0.00^a	1.00±0.00^b		1.45±0.07^b	1.05±0.07^a
	50	Simvastatin	2.80±0.00^a	1.10±0.14^b		1.30±0.14^b	1.00±0.14^a
	50	-ve control	2.70±0.14^a	1.10±0.14^a		1.85±0.07^a	1.20±0.14^a
	50	+ve control	4.10±0.14^a	2.00±0.28^b		0.90±0.21^b	1.90±0.07^b
	50	Aqueous extract	2.85±0.21^a	1.15±0.07^b		1.05±0.21^b	1.60±0.00^b
48	50	α-solanidine	2.50±0.14^a	0.95±0.07^b		1.15±0.07^b	0.90±0.00^b
	50	Nicotinic acid	2.70±0.00^a	0.95±0.07^b		1.10±0.14^b	1.15±0.07^b
	50	Cholestyramine	2.80±0.14^a	1.15±0.07^b		1.15±0.21^b	1.15±0.07^b
	50	Simvastatin	2.60±0.57^a	1.70±0.28^b		1.20±0.71^b	0.90±0.28^b
	50	-ve control	2.65±0.07^a	1.10±0.14^a		1.95±0.07^a	1.25±0.07^a
	50	+ve control	3.50±0.07^a	1.95±0.07^a		0.80±0.14^b	1.95±0.00^b
	50	Aqueous extract	2.65±0.07^a	1.15±0.07^a		1.05±0.07^b	1.05±0.07^b
72	50	α-solanidine	2.55±0.07^a	1.10±0.14^a		1.15±0.07^b	0.85±0.07^b
	50	Nicotinic acid	2.95±0.07^a	0.85±0.07^a		1.20±0.14^b	1.05±0.07^b
	50	Cholestyramine	2.90±0.00^a	1.10±0.14^a		1.25±0.07^b	1.10±0.00^b
	50	Simvastatin	3.00±0.00^a	1.15±0.07^a		1.25±0.07^b	1.25±0.07^b

ve control = Rats fed with normal feed diet and had free access to water
+ve control = Rats fed with normal feed diet and triton-X
Within columns, means with different means are statistically significant ($p < 0.05$)

There was no change in the total cholesterol ($p > 0.05$), triglycerides and LDL-C decreased significantly ($p < 0.05$) at 24 and 48 hrs and 48 and 72 hrs respectively, whilst HDL-C increased significantly ($p < 0.05$) throughout the study. The triglycerides and LDL-C were all lower than that of the positive control, but they were not as high as those of the negative control throughout the period of study. The lowest value of triglycerides at 24 hrs was recorded for nicotinic acid, 0.85 ± 0.07 mmol/L, at 48, it was both α-solanidine and nicotinic acid had the lowest triglyceride level, 0.95 + 0.07mmol/L. The lowest level of LDL-C was recorded at 24 hrs with α-solanidine and simvastatin 100 ± 0.14 mmol/L, whilst at 48 hrs, α-solanidine and nicotinic acid that had the lowest triglyceride level, 0.95 ± 0.07 mmo/L. The lowest level of LDL-C was recorded at 24 hrs with α-solanidine and simvastatin, at 48hrs, with simvastatin and α-solanidine, 0.90 ± 0.28mmol/Land 0.90 ± 0.00 mmol/L respectively. At 72hrs, however, there was no change in the LDL-C ($p > 0.05$). At 24, 48 and 72hrs, the values of HDL-C were significantly higher ($p<0.05$) than those of the positive control, but they were not as high as those of the negative control. The highest value of HDL-C at 24hrs was recorded with cholestyramine, 1.45±0.07mm/L followed by those of α-solanidine and simvastatin, 1.30±0.14mm/L, nictotinic acid and the aqueous extract recorded 1.15±0.07mm/L. At 48hrs, simvastatin recorded a HDL-C value of 1.20±0.71mm/L; α-solanidine and cholestyramine had the same value, 1.15±0.07mm/L and 1.15±0.21mm/L respectively; and the aqueous extract had a HDL-C value of 1.05±0.21mm/L. At 72 hrs, the HDL-C values of the aqueous extract, and α-solanidine remained at the same value as that recorded at 48 hrs i.e. 1.15 ±0.07mm/L and 1.15±0.07mm/L respectively; whilst the value for nicotinicacid, cholestyramine and simvastatin rose slightly i.e. 1.20±0.14mm/L,1.25±0.07mm/L and 1.25±0.07mm/L respectively.

Effect of the Aqueous Fruit Extract of Solarn.wz macrocarpum, aSolanidine, Nicotinic Acid, Cholestyramine and Simvastatin on VLDL-C and Atherogenic Index (A.I.) of Hyperlipidaemic Rats Administered Triton-X Orally for 7 Days

The effects of the aqueous extract of *S. macrocarpum*, α-solanidine, nicotinic acid, cholestyramine and simvastatin on VLDL-C and atherogenic index (A.I.) are shown in Table 3.

Table 3: Effect of the aqueous fruit extracts of *S. macrocarpum*, α-solanidine,nicotinic acid, cholestyramine and simvastatin on VLDL-C and atherogenicindex (A.I.) of hyperlipidaemic rats administered triton-X orally for 7 days

Hours after extract/drug administration	Dosage mg/kg	Extract/ Drug	VLDL-C (mmol/L)	Atherogenic index (A.I.)
			Mean ± S.D.	
24	50	-ve control	0.40±0.14[a]	1.02±0.12[a]
	50	+ve control	0.85±0.07[b]	2.69±0.48[b]
	50	Aqueous extract	0.50±0.00[b]	1.64±0.20[b]
	50	α-solanidine	0.55±0.00[b]	1.30±0.00[b]
	50	Nicotinic acid	0.53±0.04[b]	1.51±0.03[b]
	50	Cholestyramine	0.50±0.00[b]	1.23±0.09[b]
	50	Simvastatin	0.55±0.07[b]	1.33±0.13[b]
48	50	-ve control	0.30±0.21[a]	1.10±0.26[a]
	50	+ve control	0.80±0.07[b]	2.69±0.48[b]
	50	Aqueous extract	0.48±0.04[b]	1.14±0.35[b]
	50	α-solanidine	0.48±0.04[b]	1.26±0.01[b]
	50	Nicotinic acid	0.48±0.00[b]	1.24±0.23[b]
	50	Cholestyramine	0.50±0.18[b]	1.20±0.42[b]
	50	Simvastatin	0.55±0.00[b]	1.30±0.21[b]
72	50	-ve control	0.40±0.14[a]	1.01±0.16[a]
	50	+ve control	0.85±0.14[b]	2.69±0.48[b]
	50	Aqueous extract	0.40±0.00[b]	1.30±0.14[b]
	50	α-solanidine	0.48±0.04[b]	1.33±0.14[b]
	50	Nicotinic acid	0.48±0.04[b]	1.51±0.05[b]
	50	Cholestyramine	0.50±0.07[b]	1.35±0.15[b]
	50	Simvastatin	0.50±0.14[b]	1.55±0.18[b]

-ve control = Rats fed with normal feed diet and had free access to water
+ve control = Rats fed with normal feed diet and triton-X
Within columns, means with different superscripts are statistically significant ($p<0.05$)

The changes were significant ($p < 0.05$) throughout the study. The VLDL-C for the negative control (rats neither given triton nor extract) was the lowest at 24, 48 and 72 his, 0.40 ± 0.14 mmol/L, 0.30 ± 0.07 mmol/L and 0.40 ± 0.07 mmol/L respectively. The VLDL-C values at 24hrs,were almost of the same value for the extract, α-solanidine, nicotinic acid, cholestyramine and simvastatin 0.50 ± 0.00 mmol/L, 0.55 ± 0.00 mmol/L, 0.53 + 0.04 mmol/L, 0.50 ± 0.00 mmol/L and 0.55 ± 0.07 mmol/L respectively. The VLDL-C values for the positive control (rats administered
triton but not given the aqueous extract) were all significantly higher ($p < 0.05$) than those of the extract, α-solanidine and the three hypolipidaemic drugs throughout the period of study - 0.85 ± 0.07 mmol/L at 24 hrs, 0.80 ± 0.07 mmol/L at 48 hrs and 0.85 ± 0.14 mmol/L at 72 hrs. There was a sharp significant decrease ($p < 0.05$) in the VLDL-C for the extract, α-solanidine and nicotinic acid at 48 hrs - 0.48 ± 0.04mmol/L. The atherogenic index (A.I.) for the negative control was significantly lower ($p <0.05$) than those of the positive control throughout the study period. The A.I. for the extract, α-solanidine and the three hypolipidaemic drugs were all significantly lower ($p <0.05$) than those of the positive control. At 24 hrs, the A.I. values are as follows: aqueous extract, 1.64 ± 0.20, α-solanidine, 1.30 ± 0.00, nicotinic acid, 1.51 ± 0.03, cholestyramine, 1.23 ± 0.09 and simvastatin, 1.33 ± 0.13. At 48 hrs, the A.I. significantly reduced ($p< 0.05$) to the following α- aqueous extract, 1.14 ± 0.35, α-

solanidine, 1.26 ± 0.01, nicotinic acid, 1.24 ± 0.23, cholestyramine, 1.20 ± 0.42 and simvastatin, 1.30 ± 0.21. At 72 hrs, the A.I. significantly went up ($p < 0.05$) for all the substances tested - aqueous extract 1.30 ± 0.14, α-solanidine, 1.33 ± 0.14, nicotinic acid, 1.51 ± 0.05, cholestyramine, 1.35 ± 0.15 and simvastatin, 1.55 ± 0.18.

Effect of the Aqueous Fruit Extract of *Solamum macrocarpum*, α-solanidine, Nicotinic Acid, Cholestyrainine and Simvastatin on Faecal Cholesterol Of Hyperlipidaemic Rats Administered Triton-X Orally for 7 Days

The effect of the aqueous fruit extract of *Solanum macrocarpum* on faecal cholesterol of hyperlipidaemic rats are shown in Table 4. There was no change in the faecal cholesterol throughout the study ($p > 0.05$).

Table 4: Effect of the aqueous fruit extract of *S. macrocarpum*, α-solanidine, nicotinic acid, cholestyramine and simvastatin on faecal cholesterol of hyperlipidaemic rats administered triton-X orally for 7 days

Hours after extract/drug administration	Dosage mg/kg	Extract/ Drug	Faecal cholesterol (mmol/L) Mean ± S.D.
24	50	-ve control	0.40±0.00[a]
	50	+ve control	0.20±0.28[a]
	50	Aqueous extract	0.30±0.07[a]
	50	α-solanidine	0.25±0.07[a]
	50	Nicotinic acid	0.35±0.07[a]
	50	Cholestyramine	0.35±0.07[a]
	50	Simvastatin	0.25±0.07[a]
48	50	-ve control	0.40±0.20[a]
	50	+ve control	0.25±0.00[a]
	50	Aqueous extract	0.35±0.07[a]
	50	α-solanidine	0.35±0.07[a]
	50	Nicotinic acid	0.30±0.14[a]
	50	Cholestyramine	0.35±0.07[a]
	50	Simvastatin	0.25±0.07[a]
72	50	-ve control	0.40±0.00[a]
	50	+ve control	0.20±0.07[a]
	50	Aqueous extract	0.30±0.14[a]
	50	α-solanidine	0.30±0.14[a]
	50	Nicotinic acid	0.35±0.14[a]
	50	Cholestyramine	0.35±0.07[a]
	50	Simvastatin	0.25±0.07[a]

-ve control = Rats fed with normal feed diet and had free access to water
+ve control = Rats fed with normal feed diet and triton-X
Among groups, means with the same superscripts are not statistically significant ($p>0.05$).

DISCUSSION

The increase in mean body weight of rats after Triton-X administration for 7 days (Table 1 was statistically significant ($p <0.05$) in Groups one, two and five when compared to day zero (i.e. before Triton-X administration). This probably implies that Triton-X at the dosage employed, 400 mg/kg or for the length of time given, induced hyperlipidaemia, even though differences in the rats' metabolism may account for the differences in the statistics exhibited in their significance.

The result from the administration of 50 mg/kg each of the aqueous fruit extract of *S. macrocarpum*, α solanidine, nicotinic acid, cholestyramine and simvastatin on triton-X induced hyperlipidaemic rats revealed a significant reduction in the level of triglycerides at 24 hrs and 48 hrs, LDL-C at 48 hrs and 72 hrs and an elevation in HDL-C throughout the study (Table 3) when compared to the positive control (rats administered only Triton-X). There was no change in cholesterol level ($p > 0.05$). Clinical studies in humans have shown that lowering levels of serum cholesterol (especially LDL-C) with diet or drugs decreases the incidence of coronary heart disease (Gotto *et al*., 1990). In the present study, the LDL-C levels decreased. The implication of this is that the use of the aqueous fruit extract of *S. macrocarpum*, α-solanidine and the three hypolipidaemic drugs (nicotinic acid, cholestyramine and

simvastatin will ameliorate the occurrence of heart disease by lowering cholesterol level. It has been shown that solasodine ($C_{27}H_{42}0_2N$), a nitrogen analogue of diosgenin (a steroidal glycoalkaloid like solanidine found in the *Solanaceae*), reduced serum cholesterol and LDL-cholesterol by 73.3% ad 73.5% respectively and prevented atherogenesis whilst the HDL ratio was raised significantly. Solasodine treatment prevented the accumulation of cholesterol in the liver and aorta and regressed plaque size in the thoracic and abdominal aorta. Faecal excretion of cholesterol was significantly increased suggesting that modulation of absorption was affected (ANONc, 2008; Sodipo *et al.,* 2012a). Nicotinic acid has been shown to lower serum cholesterol and triglycerides in triton-induced-hyperlipidaemic rats and the mechanism had been attributed to either inhibition of lipid biosynthesis or stimulation of lipid catabolism (Schurr *et al*., 1972). Results with standard hypolipidaemic agents are reproducible and conform well to performance levels of the screen predicted from statistical analysis (Schurr *et al*., 1972). Simvastatin is a lipid-lowering agent synthesized from a fermentation product of *Aspergillus terreus*. It raises HDL-C and therefore lowers the ratio of LDL-C to HDL-C and that of total cholesterol to HDL-C (ANONb, 2007). The active form of simvastatin is a specific inhibitor of HMG-CoA reductase, the enzyme that catalyses the conversion of HMG-CoA to mevalonate (Hardman and Limbird, 2001). It is well established that rats injected with Triton WR-1339 show an increase in hepatic cholesterol synthesis (Kuroda *et al*., 1977); hence drugs with an inhibitory action on HMG-CoA reductase are effective in lowering hyperlipidaemia (Endo *et al*., 1979). Thus, the extract like simvastatin, might exhibit hypolipidaemic effect due to suppression of endogenous cholesterol biosynthesis in the liver. Because the conversion of HMG-CoA to mevalonate is an early step in the biosynthetic pathway of cholesterol, therapy with simvastatin would not be expected to cause an accumulation of potentially toxic sterols. In addition, HMG-CoA is also metabolized readily back to acetyl-CoA, which participates in many biosynthetic processes in the body (ANONb, 2007). In a study of 12 healthy volunteers, the pharmacokinetics of single (80 mg) and multiple doses of simvastatin showed that no accumulation of medicine occurred after multiple dosing and the maximum plasma concentration of inhibitors occurred 1.3 to 2.4 hrs post dose (ANONb 2007). Nicotinic acid lowers plasma triglyceride and cholesterol concentration. It acts as an antilipolytic agent in adipose tissue, reducing the supply of non-esterified free fatty acids and hence the availability of substrate for hepatic triglyceride synthesis (Hardman and Limbird, 2001). The extract from phytochemistry contains saponins (Sodipo *et al.,* 2008a, 2012b). Saponins according to MacDonald *et al*., (2005) are cholesterol-lowering agents. They do this by causing a depletion of body cholesterol by preventing its reabsorption, thus increasing its excretion in much the same way as other cholesterol-lowering drugs such as cholestyramine (a bile acid sequestrant). Saponins have been found to be useful in cholesterol lowering, so the cholesterol cannot be reabsorbed into the system, and is therefore excreted from the body (MacDonald *et al*., 2005), Cholestyramine (an anion exchange resin or a bile acid sequestrant), being negatively charged, binds positively charged acids. Because of the large size, resins are not absorbed and the bound bile acids are excreted in the stool Hardrnan and Limbird, 2001). The results of the study show then that the aqueous fruit extract of *S. macrocarpum*, just like α-solanidine, nicotinic acid, cholestyramine and simvastatin lowered hyperlipidaemia.

The hyperlipidaernia induced by Triton-X in rats was reduced by 50 mg/kg each of the aqueous fruit extract of *S. macrocarpum*, α-solanidine, nicotinic acid, cholestyramine and simvastatin as shown in the significant reduction ($p < 0.05$) in VLDL-C and atherogenic index (A.I.) throughout the study (Table 3). The values for the positive control i.e. hyperlipidaemic rats administered only Triton-X, were high; these are atherogenic and undesirable. These values reduced in groups of rats treated with the extract, α-solanidine and the three hypolipidaernic drugs. This shows the extract (in which the plant contains falvonoids which lower hyperlipidaemia [Sodipo *et al.,* 2012c]), just like the other four substances has the potential to reduce the risk of development of heart diseases since low VLDL-C and low A.I. have been shown to be beneficial and indicative of a lower risk of coronary heart diseases (Williamson *et al*., 1996; Chander *et al*., 2005; Sodipo *et al.,* 2012a).

The faecal cholesterol in the hyperlipidaemic rats treated with 50 mkg each of the extract, α-solanidine, nicotinic acid, cholestyrarnine and simvastatin did not change ($p > 0.05$) when compared to the untreated hyperlipidaemic rats (positive control) [Table 4]. The faecal cholesterol in hyperlipidaemic rats administered simvastatin did not change ($p > 0.05$) throughout the period of study. Drugs with an inhibitory action on HMG-CoA reductase like simvastatin may exhibit their hypolipidaemic effect due to suppression of endogenous cholesterol biosynthesis in the liver because it is well established that rats injected with Triton WR-1339 showed an increase in hepatic cholesterol synthesis (Kuroda *et al*., 1977; Sodipo *et al.,* 2011a, 2012a). Thus it is not surprising that the faecal cholesterol of simvastatin remained constant i.e. unaffected throughout the period of study.

CONCLUSION

The present study shows that the aqueous fruit extract of *Solanum macrocarpum* compares favourably with α-solanidine, nicotinic acid, simvastatin and cholestyramine in reducing lipids in acute-triton induced hyperlipidaemic rats probably by reducing absorption of lipids and increasing faecal cholesterol excretion, thus reducing hyperlipidaemia, thus buttressing the claim in traditional medicine that the fruit lowers hyperlipidaemia. Also, the extract, just like the other four substances has

the potential to reduce the risk of development of heart diseases, since low VLDL-C and low A.I. have been shown to be beneficial and indicative of a lower risk of coronary heart diseases.

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