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Hypoglycemic, antiperoxidative and antihyperlipidemic effects of saponins from *Solanum anguivi* Lam. fruits in alloxan-induced diabetic rats

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ABSTRACT

The present study evaluates the hypoglycemic, antiperoxidative and antihyperlipidemic activities of saponins from *Solanum anguivi* fruits in alloxan induced diabetes rats. Diabetic rats were treated with saponin (20–100 mg/kg) for 21 days. Results indicated that administration of saponins significantly reduced the elevated levels of glucose, decreased total cholesterol (TC), total triglycerides (TG), low density lipoprotein (LDL) and increased high density lipoprotein (HDL) in the serum towards normalcy when compared to the diabetic control ($p < 0.05$). In addition, saponins exhibited strong inhibition of lipid peroxidation and increased the levels of antioxidant enzymes (superoxide dismutase and catalase) in the serum, liver and pancreas when compared to the diabetic control ($p < 0.05$). Our results suggest that saponins from *S. anguivi* fruit can enhance the hypoglycemic, hypolipidemic and antioxidant properties in alloxan-induced diabetic rats, and may have the potential to be used in the prevention or in the management of diabetes.

1. Introduction

Diabetes mellitus (DM) is a major global health problem and is now recognized as one of the leading causes of death worldwide, where the high prevalence of the disease could be attributed to improved nutritional status (Uebanso et al., 2007; Ogbonnia et al., 2008). DM is defined as a metabolic disorder characterized by an elevation of the blood glucose concentration due to absolute or relative lack of insulin leading to hyperglycemia. DM is associated with abnormal metabolism of carbohydrates, fat and protein (Shah et al., 2008; Sharma et al., 2010; Dinesh et al., 2011). Substantial evidence in the literature indicates that hyperglycemia can cause oxidative stress by various mechanisms. For instance, excessive levels of glucose reaching the mitochondria lead to an overdrive of the electron transport chain, resulting in overproduction of superoxide anions which consequently result in damage of a variety of tissues (Nishikawa et al., 2000; Joshep et al., 2002; Dave and Kalia, 2007). Furthermore, hyperglycemia can stimulate oxidative stress by the autoxidation of glucose in the presence of transition metals as well as the generation of reactive oxygen species (ROS) during the process of glycation (Wolff et al., 1989; Kennedy and Lyons, 1997), and also can induce vascular injury through complex overlapping pathways, formation of advanced glycation end products, activation of protein kinase C and generation of ROS.

Villeneuve and Natarajan (2010) have reported that plasma lipid peroxidation levels increased in diabetic patients due to vascular lesions induced by hyperglycemia. This lipid peroxidation which can lead to the development of diabetes complication (Kalaivanam et al., 2010) is thought to occur as a result of the loss of insulin-producing pancreatic β cells by an environmentally triggered autoimmune reaction.

Hyperlipidemia has been incriminated as a contributory factor of atherosclerosis in patients with diabetes (Pearl et al., 1987; Bierman, 1992; Keaney and Localzo, 1999). Excessive intake of fatty acids leads to an accumulation of triglyceride in many tissues, particularly in the fat tissue, in which lipolysis is increased. In the liver which is the main organ of glucose metabolism, high free fatty acid concentration contributes to the resistant action of insulin by enhancing glucose output from the liver (Goldstein, 2002).

Nowadays, synthetic agents and insulin used effectively for the treatment of diabetes have prominent adverse effects (Inzucchi, 2002), such as hypoglycemia, drug-resistance, dropsy, and weight gain (Tahrani et al., 2010). Due to these factors, diabetic patients and healthcare professionals are increasingly considering complementary and alternative approaches, including the use of medicinal herbs with anti-hyperglycemic activities (Grover et al., 2002). In view of this, substantial efforts have been made in recent years to identify antidiabetic from natural herbs

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since their complex components often provide versatile bioactivity and varied mechanisms of action (Kim et al., 2002), and a large number of plants have been recognized to be effective in the treatment of diabetes mellitus (Li et al., 2004).

Solanum anguivi Lam. is a non-tuberous and widely distributed plant that possesses various medicinal properties. Mostly, the plant prefers to grow in humid temperature and commonly found as weed in gardens. It is a rare ethnomedicinal herb belonging to the family Solanaceae. The plant is used as a therapeutic agent for various diseases. The roots are carminative and expectorant which are useful in coughs, catarrhal, dysuria, colic, nasal ulcers, ingredient of dasamula, asthma, difficult parturition, toothache, cardiac disorder, worm complaints, spinal guard disorder, nervous disorder and fever. The leaves and fruits rubbed up with sugar are used as an external application for itch (Warrier et al., 1996; Yoganarasimhan, 1996). The dried powders of the fruits were used in the medication for high blood pressure. Phytochemical reports on *S. anguivi* indicated that the stem, fruits, roots, flowers and leaves contain glycoalkaloids (anguivine and isoanguivine), steroidal alkaloids (solamargine and solasoline), steroidal glycosides (anguiviosides A–C, anguiviosides 1–4) (Chopra et al., 1994; Ripperger and Himmelreich, 1994; Zhu et al., 2000; Honbu et al., 2000). The domesticated species are consumed as leafy and/or fruit vegetables that are rich in essential minerals and vitamins (Bukenya-Ziraba, 2004), and are recommended as a dietary staple supplements for nursing mothers, the young, the aged, and anemic patients (Jansen, 2004). *S. anguivi* fruit is the most edible source of saponin in the south-western and south-eastern parts of Nigeria because of the traditional belief that it can cure hypertension and diabetes. Saponins have been reported as plant phytochemical having insulin sensitization and antihyperlipidemic effects in diabetic state (Bhavsar et al., 2009; Eu et al., 2010; Lee et al., 2011). Recently we have reported that saponins from *S. anguivi* fruit exhibit an antioxidant activity in an in vivo model by increasing the level of antioxidant enzymes in the heart and kidney in normal rats (Elekofehinti et al., 2012a).

Considering the fact that *S. anguivi* fruit is empirically used in folk medicine in the treatment of diabetes and that no work has ever been carried out to evaluate this traditional claim, this study was undertaken to investigate for the first time the antidiabetic activity of saponins isolated from *S. anguivi* fruit in alloxan-induced diabetic rats.

2. Materials and methods

2.1. Chemicals

Alloxan was purchased from Sigma (Sigma-Aldrich, Germany), while thiobarbituric acid was purchased from Fluka (Buchs, Switzerland). Randox kits were purchased from Randox Laboratories Limited, UK. The other reagents used for the execution of the experiment were of analytical grade.

2.2. Plant materials

The fruits of *S. anguivi* were collected from Adekunle Ajasin University, Akungba Akoko horticultural garden. They were identified and authenticated at the herbarium of Plant Science and Forestry Department, University of Ado Ekiti, Nigeria (voucher specimen number UHAE:286). The fruits were air dried and grounded into a powdery fine texture and stored at room temperature in an airtight polythene bag prior to use.

2.2.1. Extraction and isolation of saponins from S. anguivi fruit

A hundred gram (100 g) ground sample was extracted with 500 ml of petroleum ether (40–60 °C) in a soxhlet extractor for 12 h. The air-dried, defatted sample was extracted with methanol (500 ml) for 12 h. The methanolic extract was partitioned with n-butanol and water (1:1, v/v). After a thorough shaking, the mixture was allowed to stand overnight and the n-butanol layer was separated in the next day. The aqueous layer was washed five times with aliquots of n-butanol until it became colorless. The pooled butanolic layer was evaporated under reduce pressure to give a residue which was dissolved in 100 ml methanol and precipitated by adding a large amount of diethyl ether to obtain a solid crystalline dark brown compound (Adanlawo and Akanji, 2003).

The crude saponin fraction was spotted onto pre-coated silica gel TLC plate (Merck, Kleselgel 60F-254). The plates were developed with n-butanol:acetic acid:water (60:10:30 v/v/v). The spots on the chromatograms which were due to saponins were identified by spraying with Lieberman–Burchard reagent (methanol:sulfuric acid:acetic acid (50:5:5 v/v/v)). Saponin extract was spotted alongside a standard solution (5 g/l) of saponin white as described by Adanlawo and Akanji (2003). Concentrated crude saponin extract was applied to a silica gel column of 60–120 mesh. The impurities were washed with n-hexane through a 2.4 × 50 cm bed of silica gel. The column was eluted with n-butanol:acetic acid:water (1:1:1 v/v/v). The fractions were collected and aliquots applied as a series of spots to a strip of TLC plate, dried, sprayed with Lieberman–Burchard reagent and heated. Positive fractions were pooled together and used for the experiment.

The compounds on the plates were detected with ceric sulfate reagent followed by gradual heating. The fractions showing similar TLC profiles were mixed and these collective fractions were individually subjected to repeated column chromatography to furnish the various saponins.

2.3. Animals

Thirty five albino rats with an average weight of 125 ± 39 g were obtained from Animal Unit Achievers University, Owo, Ondo State, Nigeria. They were divided into seven groups of five animals each and allowed to acclimatize to experimental condition for two weeks. They were housed in clean cages and maintained under standard laboratory conditions (temperature 25 ± 2 °C with dark/light cycle 12/12 h). They were fed ad libitum on rat pellets (Top Feeds, Nigeria) and water. The principles of Laboratory Animal Care (Public Health Services, 1986) were followed throughout the duration of the experiment.

2.4. Experimental procedure

Diabetes was induced through a single intraperitoneal injection of a freshly prepared alloxan (Sigma-Aldrich, Germany) solution in normal saline at a dose of 150 mg/kg body weight. Since the injection of alloxan can provoke fatal hypoglycemia due to a reactive massive release of pancreatic insulin, the rats were also orally given 5–10 ml of a 20% glucose solution after 6 h. The animals were then kept with free access to 5% glucose solution for the next 24 h to prevent severe hypoglycemia. Two weeks later, the rats with moderate diabetes having glycosuria and hyperglycemia (i.e. with blood glucose levels of 200–300 mg/dl) were chosen for the experiments. The rats (n = 35) were divided equally into 7 groups. Group I served as normal control, and were given 2 ml saline by gavage, group II served as diabetic control, groups III–VII were diabetic rats treated with saponin at doses of 20, 40, 60, 80, and 100 mg/kg body weight respectively for 21 days. After 21 days of treatment, the rats were weighed and sacrificed by decapitation and the blood collected into clean dry beakers for serum preparation and the serum was prepared as described by Akanji and Nlumanze (1987) and used for the determination of malondialdehyde (MDA), catalase (CAT) and superoxide dismutase (SOD). Glucose levels were estimated using glucose oxidase peroxidase reactive strips and a glucometer. Fasting blood glucose was estimated every 2 days till day 21. The tissues (liver and pancreas) were removed into 0.25 M ice cold sucrose solution in a ratio of 1:5 w/v.

2.5. Biochemical parameters

Using the supernatant of the centrifuged homogenate of the liver and pancreas tissues, the SOD and CAT levels were determined according to the method described by Sun and Zigman (1978) and Aebi (1984) respectively; whereas, the level of lipid peroxidation was determined as described by Okhawa et al. (1979).

The serum levels of total cholesterol (TC), triglyceride (TG) and high density lipoprotein (HDL) were assayed by Randox commercial kit (United Kingdom).

2.6. Statistical analysis

The data are expressed as mean ± S.E.M. (standard error of mean). The differences among groups were analyzed by the one-way analysis of variance (ANOVA). Inter-group comparisons were done using Duncan's Multiple Range Test (DMRT) with 95% confidence intervals. The SPSS 11.0 (SPSS Inc., Chicago, USA), was used for this analysis. For fasting blood glucose, repeated measures ANOVA followed by Bonferroni's Multiple Comparison Test was used. Statistical different is expressed at $p < 0.05$.

3. Results and discussion

In spite of various uses of *S. anguivi* fruit in folk medicine especially its general use in the treatment of diabetes, there is no information in the literature regarding its anti-diabetic property. Thus, the present study reports for the first time the hypoglycemic and antidiabetic effect of saponins, secondary metabolite from *S. anguivi* fruit which is claimed to have an antidiabetic activity. Our results demonstrated that administration of saponin from *S. anguivi* fruit showed marked hypoglycemic, antiperoxidative and antihyperlipidemic effects in alloxan-induced diabetic rats.

3.1. Effect of saponin on body weight

Alloxan-induced diabetic rats showed a significant decrease in body weight during the 3-week period (post-saponin weight) when compared to the control ($p < 0.05$). In contrast, the body weight of diabetic rats treated with saponin for 21 days significantly increases when compared to the diabetic control (Table 1, $p < 0.05$). The significant reduction in total body weight could be attributed to the loss of fat from adipose tissue and catabolism of amino acids in muscle tissue.

3.2. Effect of saponin on blood glucose

Administration of alloxan led to a significant increase in blood glucose levels which was maintained over a period of 3 weeks (Fig. 1). Administration of saponin (20–100 mg/kg) significantly reduced blood glucose at a concentration-dependent manner when compared to the diabetic control ($p < 0.05$). However, it failed to restore the level to that of the control group at the tested dosages.

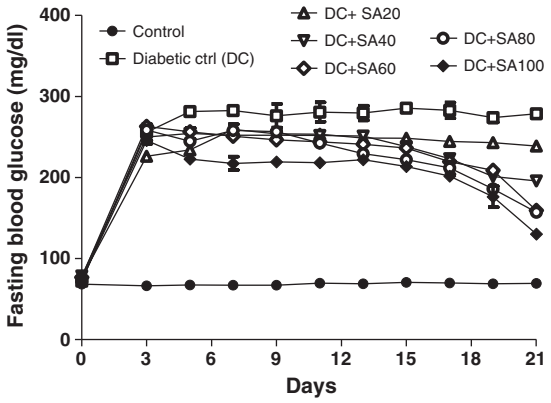

Fig. 1. Effect of oral administration of saponin from *Solanum anguivi* on blood glucose (mg/dl). Fasting blood glucose was measured every 2 days till day 21. Repeated measures ANOVA followed by Bonferroni's Multiple Comparison Test revealed a significant difference between the control and diabetic control at $p < 0.05$. Apart from the group administered 20 mg/kg, every other group was significantly different from the diabetic control at $p < 0.05$.

Alloxan is a toxic glucose analog widely used to induce experimental diabetes in animals. It selectively destroys insulin-producing cells in the pancreas in animals, and has been shown to establish a redox cycle with the formation of superoxide radicals and undergoes dismutation to hydrogen peroxide with the formation of hydroxyl radicals (Szkudelski, 2001; Vanhorebeek et al., 2005, 2009). However, insulin deficiency (type-I diabetes) or decreased insulin action (type-II diabetes) results in a decrease in glucose utilization by insulin requiring tissues like liver and an increase in glucose production through an increased rate of gluconeogenesis; both resulting in hyperglycemia. As a consequence of increased glucose and decreased insulin level in blood plasma, hepatic regulation of lipid metabolism is greatly altered. Thus, the hypoglycemic effect of saponin from *S. anguivi* fruit may be due to the restoration of insulin response or induction of enzymes inhibited by alloxan.

3.3. Effect of saponin on lipid peroxidation

Malondialdehyde (MDA), one of the major products of lipid peroxidation, has been extensively studied and measured as an index of lipid peroxidation and as a marker of oxidative stress (Janero, 1990). In the present study, MDA level was higher in serum, liver and pancreas of diabetic rats when compared to the normal control (Table 3). Saponin administration lowers significantly the MDA concentration in the serum, liver and pancreas with increasing dosage when compared to the diabetic control ($p < 0.05$). Noteworthy is the fact that the alterations in MDA levels were restored to normal levels in the pancreas and lower than that of the control level in the serum and liver (Table 2).

Table 1
Effect of oral administration of saponin from *Solanum anguivi* on body weight.

	Initial weight (g)	Post alloxan weight (g)	Post saponin weight (g)
Control	116.09 ± 5.73	121.37 ± 4.92	125.68 ± 5.81
Diabetic control	116.90 ± 1.99	108.55 ± 3.30	95.55 ± 2.96*
Alloxan + SA (20 mg/kg)	134.48 ± 8.13	124.83 ± 7.08	130.01 ± 7.98**
Alloxan + SA (40 mg/kg)	123.54 ± 3.87	116.32 ± 2.60	122.59 ± 3.64**
Alloxan + SA (60 mg/kg)	133.53 ± 3.67	132.38 ± 4.13	133.35 ± 3.10**
Alloxan + SA (80 mg/kg)	133.19 ± 1.85	131.46 ± 3.21	139.53 ± 3.32**
Alloxan + SA (100 mg/kg)	119.92 ± 1.36	117.04 ± 1.29	125.48 ± 2.35**

Results are expressed as means ± S.E.M. ($n = 5$).
* Significantly different from control ($p < 0.05$).
** Significantly different from diabetic control ($p < 0.05$).

Table 2
Effect of saponin from *Solanum anguivi* on MDA of diabetic rats.

	Serum (nmol/ml)	Liver (nmol/mg protein)	Pancreas (nmol/mg protein)
Control	18.58 ± 1.67	12.11 ± 0.67	23.65 ± 2.15
Diabetic control	21.93 ± 2.03	22.42 ± 3.33*	33.44 ± 1.41*
Alloxan + SA (20 mg/kg)	18.86 ± 1.10	7.41 ± 0.99**	32.77 ± 1.22
Alloxan + SA (40 mg/kg)	10.18 ± 2.01**	5.06 ± 2.42**	32.68 ± 1.46
Alloxan + SA (60 mg/kg)	10.10 ± 0.44**	3.28 ± 0.58**	30.63 ± 1.58
Alloxan + SA (80 mg/kg)	10.10 ± 0.44**	3.09 ± 0.16**	29.64 ± 1.11
Alloxan + SA (100 mg/kg)	8.98 ± 1.53**	2.93 ± 0.81**	23.04 ± 1.42**

Results are expressed as means ± S.E.M. ($n = 5$).
* Significantly different from control ($p < 0.05$).
** Significantly different from diabetic control ($p < 0.05$).

Table 3
Effect of saponin from *Solanum anguivi* on SOD of diabetic rats.

	Serum (nmol/ml)	Liver (nmol/mg protein)	Pancreas (nmol/mg protein)
Control	1.98 ± 0.07	17.99 ± 0.88	5.95 ± 0.14
Diabetic control	1.06 ± 0.19*	10.15 ± 0.44*	2.46 ± 0.93*
Alloxan + SA (20 mg/kg)	2.19 ± 0.97**	20.57 ± 0.57**	3.47 ± 0.69**
Alloxan + SA (40 mg/kg)	2.94 ± 0.56**	26.51 ± 0.48**	5.46 ± 0.73**
Alloxan + SA (60 mg/kg)	3.97 ± 0.44**	39.91 ± 0.68**	7.42 ± 0.79**
Alloxan + SA (80 mg/kg)	5.85 ± 0.73**	49.26 ± 6.55**	10.19 ± 1.05**
Alloxan + SA (100 mg/kg)	6.20 ± 0.41**	48.95 ± 4.96**	10.74 ± 1.17**

Results are expressed as means ± S.E.M. ($n = 5$).
* Significantly different from control ($p < 0.05$),
** Significantly different from diabetic control ($p < 0.05$).

Table 4
Effect of saponin from *Solanum anguivi* on catalase of diabetic rats.

	Serum (nmol/ml)	Liver (nmol/mg protein)	Pancreas (nmol/mg protein)
Control	0.21 ± 0.03	0.28 ± 0.02	0.26 ± 0.08
Diabetic control	0.15 ± 0.04	0.22 ± 0.01	0.05 ± 0.01*
Alloxan + SA (20 mg/kg)	0.67 ± 0.05**	1.16 ± 0.02**	0.13 ± 0.09**
Alloxan + SA (40 mg/kg)	0.81 ± 0.10**	1.21 ± 0.02**	0.17 ± 0.02**
Alloxan + SA (60 mg/kg)	0.91 ± 0.12**	1.56 ± 0.06**	0.28 ± 0.01**
Alloxan + SA (80 mg/kg)	1.07 ± 0.10**	1.61 ± 0.30**	0.32 ± 0.05**
Alloxan + SA (100 mg/kg)	1.11 ± 0.11**	1.69 ± 0.47**	0.38 ± 0.02**

Results are expressed as means ± S.E.M. ($n = 5$).
* Significantly different from control ($p < 0.05$).
** Significantly different from diabetic control ($p < 0.05$).

Under physiological conditions, the level of lipid peroxidation (LPO) in cells is controlled by various cellular defense mechanisms consisting of enzymatic and non-enzymatic scavenger systems. The levels of this defense mechanism are altered in diabetes (Wohaieb and Goldin, 1987; Bagri et al., 2009) and therefore, the ineffective scavenging of free radicals may play a crucial role in determining tissue injury. The increase of MDA formation in the serum, liver and pancreas of alloxan treated animals (diabetic control) could be due to increased levels of oxygen free radicals. In fact, oxygen free radicals exert their cytotoxic effect by peroxidation of membrane phospholipids leading to a change in permeability and a loss of membrane integrity (Esterbauer, 1996). Treatment with saponin from *S. anguivi* fruit for 21 days significantly decreased MDA levels in the serum, liver and pancreas in diabetic rats in comparison to the diabetic control. The reduction of MDA levels can be attributed to its antioxidant activity. In agreement with this, our research group has recently demonstrated that saponin from *S. anguivi* fruit has antiperoxidative properties (Elekofehinti et al., 2012a). Our results are in agreement with those of Rajesh et al. (2008) and Peipei et al. (2011) in which an elevated level of lipid peroxides in the plasma of diabetic rats was observed.

3.4. Effect of saponin on the activity of antioxidant enzymes

Oxidative damage can result when the critical balance between free radical generation and antioxidant defenses is unfavorable. These oxidative damages could be retarded by endogenous defense systems (antioxidant) such as superoxide dismutase (SOD) and catalase (CAT) which work in concert to detoxify free radicals (Edziri et al., 2012).

Diabetes mellitus is associated with increased oxidative stress and decreased antioxidant status (Marica et al., 2005). As showed in Table 3, the activity of SOD was significantly decreased in alloxan-treated rats in the serum, liver and pancreas when compared to the control ($p < 0.05$). Similar to that of SOD, the activity of CAT was also significantly decreased in the pancreas ($p < 0.05$, Table 4), but such effect was not observed in the serum and liver (although there was a decrease in the activity of the enzymes). The decreased levels of CAT and SOD observed in diabetic rat can be explained by the accumulation of superoxide anion and hydrogen peroxide respectively, which would have otherwise been effectively scavenged by these enzymes. According to the results obtained, the levels of SOD and CAT were significantly restored after saponin treatment, suggesting that saponins have effective antioxidative properties and could scavenge excess free radicals ($p < 0.05$, Tables 3 and 4). The increased activities of SOD and CAT suggest a compensatory response to oxidative stress as it reduces the endogenous hydrogen peroxide produced, thus, diminishing the toxic effects due to this radical or other free radicals derived from secondary reactions (Sharma and Garg, 2009). Consequently, saponin may have an efficient protective mechanism in response to ROS which may help to regenerate β-cells and protect pancreatic islets against cytotoxic effects of alloxan.

3.5. Effect of saponin on the lipid profile of diabetic rats

There was a significant increase ($p < 0.05$) in TG, TC, and LDL and a significant decrease in HDL in the serum of the diabetic control when compared to that of the normal control (Table 5). Administration of saponin significantly brought back these parameters in a concentration-dependent manner when compared to the diabetic control ($p < 0.05$). Interestingly, the reversal of the lipid profile by saponin in diabetic-treated rats was even lower than that of normal control, suggesting that saponin by itself seems to have lipid lowering potentials.

The level of serum lipids is usually raised in diabetes due to the increase of blood glucose and such an elevation represents a risk factor for coronary heart disease (Sakatani et al., 2005). The decrease in TG observed in this study, could be due to various factors which may include: i) decrease in fatty acid synthesis, ii) enhanced LDL receptors, iii) activation of Lecithin-cholesterol acyl transferase (LCAT) and lipases, and also iv) inhibition of acetyl-CoA carboxylase. The observed reduction in TC level in diabetic rats could be due to a decrease in cholesterol absorption from the intestine, through binding to bile acids, and an increase in fecal bile acid excretion. Another mechanism which may be involved in lowering of total cholesterol might be related to the suppression of cholesterol biosynthesis by a decrease in the

Table 5
Effect of saponin from *Solanum anguivi* on lipid profile of diabetic rats.

	TG (mg/dl)	TC (mg/dl)	HDL (mg/dl)	LDL (mg/dl)
Control	45.77 ± 3.29	55.91 ± 3.37	6.96 ± 0.85	39.79 ± 4.40
Diabetic control	71.43 ± 7.18*	71.25 ± 5.08*	3.57 ± 0.44*	53.39 ± 5.06*
Alloxan + SA (20 mg/kg)	53.22 ± 2.03**	52.04 ± 3.21**	4.27 ± 0.44	37.12 ± 2.28**
Alloxan + SA (40 mg/kg)	41.77 ± 10.32**	31.08 ± 2.7**	4.47 ± 0.83	20.87 ± 1.62**
Alloxan + SA (60 mg/kg)	27.18 ± 8.32**	21.49 ± 1.55**	4.89 ± 0.43	11.17 ± 1.36**
Alloxan + SA (80 mg/kg)	25.93 ± 9.26**	19.56 ± 1.7**	6.81 ± 0.65**	7.57 ± 1.73**
Alloxan + SA (100 mg/kg)	24.40 ± 6.47**	15.22 ± 1.22**	9.49 ± 0.5**	5.84 ± 0.9**

* Represents significantly different from control.
** Represents significantly different from diabetic control ($p < 0.05$).

3-hydroxy-3-methyl-glutaryl-CoA reductase HMG-CoA reductase activity which is the rate-limiting enzyme in the cholesterol biosynthetic pathway (Elekofehinti et al., 2012b). These results confirm that saponins have antilipidemic, hypoglycemic and antiperoxidative properties in diabetic states. Also saponin from *S. anguivi* fruit can be useful in the treatment of diabetes since it has a hypolipidemic effect.

Many new classes of hypolipidemic agents have been widely used for the improvement of hyperlipidemia associated with atherosclerosis during the last decades (Dujovne and Harris, 1989). In this regard, saponin from *S. anguivi* fruit might be beneficial to diabetic patients with atherosclerosis, since an elevated HDL level is associated with a reduced risk of the development of atherosclerosis in diabetes mellitus (Vasan et al., 2003; Cho et al., 2005).

4. Conclusion

Overall, the present study demonstrated for the first time the anti-diabetic effect of saponin from *S. anguivi* fruit which was observed by attenuating the hyperglycemia-mediated oxidative stress, and hyperlipidemia, a contributory factor of arteriosclerosis. Furthermore, saponin was effective enough to alleviate alloxan-induced diabetes by decreasing the level of lipid peroxidation and increasing the antioxidant defense system in the serum, liver and pancreas. Our results suggest that the beneficial effect of saponins is at least in part, mediated by its antioxidant, antidyslipidemic and hypoglycemic activities and seems to justify the traditional use of dietary *S. anguivi* fruit saponin in folk medicine. Further studies are now in progress to identify the type and structure of saponins from *S. anguivi* fruit in order to elucidate the exact mechanism by which saponin elicits its modulatory effect.

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