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Original Article

Normoglycaemic, Normolipidaemic and Antioxidant Effects of Ethanolic Extract of *Acacia ataxacantha* Root in Streptozotocin - induced Diabetic Rats

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Abstract

The antidiabetic, normolipidaemic, antioxidant and safety evaluations of ethanolic extract of *Acacia ataxacantha* roots (EEAAR) were investigated in streptozotocin - induced diabetic rats, to verify its use in traditional African medicine and as alternative to synthetic normoglycaemic agents in diabetic treatments. Thirty albino rats (*Rattus novergicus*) were randomized into six groups - control, diabetic control, EEAAR-treated at 125 mg/kg, 250 mg/kg, 500 mg/kg body weights (b.wts.) and metformin groups, respectively. Phytochemical screening showed the presence of alkaloids, polyphenols, flavonoid, saponins, tannins and terpenoid. Blood glucose was significantly reduced ($p < 0.05$) especially after 7 days of oral administration of EEAAR at 125 mg/kg b.wt with values (110.01 ± 9.64 mg/dl) similar to that of the control (106.33 ± 4.13 mg/dl). There was an increase ($p < 0.05$) in the ALT and AST activities of the liver and serum of rats in all the groups except in those that received 125 mg/kg b.wt. Serum total cholesterol, low density lipoprotein cholesterol and triglyceride were decreased ($p < 0.05$) upon administration of the extract and metformin. There was no difference ($p > 0.05$) in malondialdehyde concentration of rats administered with 125 mg/kg b.wt. of extract and metformin. Superoxide dismutase activity was elevated ($p < 0.05$) in all groups and compared favourably with the control in each of the tissues. This study revealed the antidiabetic and hypolipidaemic effects of EEAAR, which may be due to the antioxidant properties of some of the phytochemical constituents. However, the extract may not be safe at large and repeated doses.

Keywords: *Acacia ataxacantha*, flame thorn, metformin, normoglyceamic, normolipideamic

Abbreviations: ALT - alanine aminotransferase, AST - aspartate aminotransferase, b.wt. - body weight, EEAAR - ethanolic extract of *Acacia ataxacantha* roots, MDA - malondialdehyde

Introduction

Diabetes is a group of metabolic diseases characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action or both (American Diabetes Association, 2012). Hyperglycaemia and hyperlipidaemia are two important characters of diabetes mellitus. Diabetic patients experience various vascular complications, such as atherosclerosis, diabetic nephropathy and neuropathy, retinopathy, angiopathy and several others (Sheetz, 2002; Maritim *et al*., 2003). Excessive oxidative stress has been implicated in the pathology and complications of diabetes mellitus (Wolff, 1967). International Diabetic Federation (IDF) reported in 2011 that many regions of Asia and Africa show a high prevalence of the disease, while the incidence is increasing in East and North Africa where six of the ten countries had the highest prevalence of diabetes in the world.

Hyperglycaemia can be handled initially with oral synthetic agents and insulin therapy, but these synthetic agents produce some serious side effects and are relatively expensive for developing countries (Kumar *et al*., 2011a). The toxicity of oral antidiabetic agents differs widely in clinical manifestations, severity and treatment (Kumar *et al*., 2011b). In addition, certain oral hypoglycaemic agents are not effective in lowering the blood sugar in chronic diabetic patients. The global information on ethnobotanicals includes about 800 medicinal plants used for controlling diabetic mellitus and associated diseases conditions (Jerald *et al*., 2009). Dietary management includes the use of traditional medicines that are mainly derived from plants (Gayathri and Kannabiran, 2008). Even now,

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approximately 80% of the third world population is almost entirely dependent on traditional medicines. Numerous traditional medicinal plants such as *Hemidesmus indicus* (Gayathri and Kannabiran, 2008), *Vernonia anthelmintica* (Fatima *et al*., 2010), *Pterocarpus marsupus* (Maruthupandian and Mohan, 2011), *Eugenia floccosa* (Kala *et al*., 2012a), *Eugenia singamattina* (Kala *et al*., 2012b), *Psidium guajava* (Shakeera *et al*., 2013) etc. have been reported to have normoglycemic properties.

Acacia ataxacantha (family: Fabaceae, otherwise called Flame thorn) is an African tree species with conspicuous red pods and numerous hooked prickles. It is widespread in sub-Saharan Africa from Senegal in the West to Sudan in the East, Namibia, Botswana, Zimbabwe, and in the Transvaal and KwaZulu-Natal and some Northern parts of Nigeria. Its normal habit is that of a multi-stemmed, untidy, large shrub with a tendency for the shoots to scramble using their recurved prickles and often develops into a single-stemmed tree of 5-10 m in height and 300 mm trunk diameter. Flowers occur as clusters of off-white or cream-coloured terminal spikes which are fragrant and bloom during spring and summer (Lynette and Barbara, 1981). There are however, no reports on the normoglycemic, normolipidaemic and antioxidant activities of *A. ataxacantha* roots. This study thus, investigated the normoglycemic, normolipidaemic and antioxidant activities of *A. ataxacantha root* ethanolic extract in streptozotocin - induced diabetic rats.

Materials and Methods

Collection of Acacia ataxacantha

The roots of *Acacia ataxacantha* were collected in September, 2012, from a farmland in Uruan, Kano State, Nigeria. The plant was identified and authenticated at the Herbarium of the Department of Plant Biology, University of Ilorin, Ilorin, Nigeria, where voucher number 892 was deposited for future references.

Experimental animal

Thirty male albino rats (*Rattus norvegicus*) with an average weight of 158 ± 2.19 g were obtained from the Animal Holding Unit of the Department of Biochemistry, Faculty of Life Sciences, University of Ilorin, Ilorin, Nigeria. The animals were housed in clean cages, placed in well-ventilated house conditions (temperature 28-31 °C; photoperiod 12 h light and 12 h dark; humidity 55-60%) at the Department of Biochemistry, Faculty of Life Sciences, University of Ilorin. They were given standard food pellets and allowed drinking water *ad libitum*. All animals were carefully monitored and maintained in accordance with ethical recommendations and directives of EU Directives 2010/63/ EU for animal experiments.

Preparation of ethanolic extract of A. ataxacantha root

The ethanolic extract of *A. ataxacantha* root (EEAAR) was prepared by soxhletion. The powdered plant material (250 g) was repeatedly extracted in a 1,000 ml round bottomed flask with 500 ml ethanol (95%). The reflux time for each solvent was 40 cycles for complete extraction. The extracts were cooled at room temperature, filtered and evaporated to dryness under reduced pressure in a rotary evaporator and kept under refrigeration at –4 °C till further use. The extract was prepared daily for each administration over the seven-day experimental period, 1.25 mg/ml, 2.50 mg/ml and 5mg/ml doses were prepared to deliver daily 125 mg/kg, 250 mg/kg and 500 mg/kg body weight concentrations respectively to rats.

Induction of experimental diabetes

Diabetes was induced by intra-peritoneal injection of 65 mg/kg body weight of streptozotocin (STZ), Batch No. U925 obtained from Sigma St. Louis, M.O. USA. Prior to diabetes induction, the animals were fasted for 12 hours. Confirmation of diabetes was done 48 hours after induction using One Touch glucometer (Lifescan Inc 1995 Milpas, California, USA). Blood sample for the fasting blood sugar (FBS) determination was obtained from tail puncture of the rats, and animals with FBS ≥ 200 mg/dl were considered diabetic, thus included in the study as diabetic animals and blood sugar level was checked every 2 days.

Animal grouping and treatments

Thirty albino rats (*Rattus norvegicus*) were used for the experiment. The environment was kept cleaned and disinfected. The rats were acclimatized for one week and were given standard rodent diet and water *ad libitum*. The weights of the rats were taken after fasting them for 12 hrs prior to the commencement of the experiment. The rats were randomly distributed into six treatment groups of five rats each.

Group A: Rats administered only distilled water (normal control)

Group B: Rats in this group were diabetic and untreated (diabetic control)

Group C: Rats administered EEAAR at a dose of 125mg/kg body weight

Group D: Rats administered EEAAR at a dose of 250mg/kg body weight

Group E: Rats administered EEAAR at a dose of 500mg/kg body weight

Group F: Rats administered reference antidiabetic drug (metformin at 10mg/kg body weight)

Preparation of serum and tissue homogenates

The procedure described by Yakubu *et al.* (2005) was employed. Briefly, under ether anaesthesia, the veins after being slightly displaced (to prevent blood contamination by interstitial fluid) were cut with a sterile scalpel blade and 5 ml of the blood was collected into clean dry centrifuge tubes. The blood was then left undisturbed to clot for 10 minutes at room temperature. The tubes were thereafter centrifuged for 15 minutes using Uniscope Laboratory centrifuge (Model SM800B, Surgifriend Medicals, Essex, England). The sera were aspirated with Pasteur pipettes into dry sample bottles and used within 12 hours of preparation for the biochemical assays. The liver, kidney and pancreas were also carefully removed, and placed in ice-cold 0.25 M sucrose solution to maintain the integrity of the tissues. The organs were blotted with tissue paper, weighed and homogenized in ice-cold 0.25 M sucrose solution using homogenizer.

Determination of biochemical parameters

The method described by Reitman and Frankel (1957) was used for the assay of ALT and AST activities. Malondialdehyde (MDA) concentration was assayed using the method described by Varshney and Kale (1990) and superoxide dismutase activity was determined by the method of Misra and Fridovich (1972). Serum urea was determined by the method described by Varley (1976) and serum creatinine by the method described by Owen *et al*. (1954). Total cholesterol, triglyceride, high density lipoprotein cholesterol and low density lipoprotein cholesterol were assayed using the method of Zlakis *et al*. (1953), Foster and Dunn (1973), Burstein *et al*. (1970) and Friedewald *et al*. (1972) respectively.

Statistical analysis

All data are expressed as mean of five replicates ± standard deviation (SD). Statistical evaluation of data was performed by SPSS version 16 using one-way analysis of variance (ANOVA), followed by Dunett's posthoc test for multiple comparison. Values were considered statistically significant at $p < 0.05$ (confidence level = 95%).

Results

Secondary metabolite constituents of ethanolic extract of A. ataxacantha root

The secondary metabolite constituents present in EEAAR include alkaloids, polyphenols, flavonoids, saponins, tannins, terpenoids; however, glycoside was not detected (Table 1).

Table 1. Secondary metabolite constituents of *Acacia ataxacantha* root

Secondary metabolite	Extract
Alkaloids	+
Polyphenols	+
Flavonoids	+
Saponins	+
Glycosides	-
Tannins	+
Terpenoids	+

Keys: Presence of constituents (+); Absence of constituents (-)

Table 2. Effect of daily administration of EEAAR for seven days on fasting blood glucose of streptozotocin - induced diabetic rats

Groups	Glucose level (mg/dl)		
	Day 1	Day 3	Day 7
Control	99.00 ± 2.05^a	90.33 ± 5.03^a	106.33 ± 4.13^a
Diabetic control	284.00 ± 10.15^b	302.00 ± 12.14^b	310.00 ± 19.46^b
125 mg/kg b.wt. EEAAR	296.00 ± 9.50^b	222.33 ± 10.60^b	110.01 ± 9.64^a
250 mg/kg b.wt. EEAAR	242.00 ± 21.00^b	241.16 ± 24.23^b	226.00 ± 18.23^b
500 mg/kg b.wt. EEAAR	274.14 ± 26.13^b	434.00 ± 13.52^b	429.00 ± 28.48^b
10 mg/kg b.wt. metformin	120.00 ± 15.00^b	100.00 ± 6.87^a	103.05 ± 5.10^a

Values are mean ± SD for n = 5, column values with different superscripts are significantly different ($p < 0.05$) when compared to the control

Table 3. Effect of administration of EEAAR daily for seven days on kidney function indices of streptozotocin–induced diabetic rats

Parameter (mg/dl)	Groups					
	Control	Diabetic control	125 mg/kg b.wt	250 mg/kg b.wt	500 mg/kg b.wt	10 mg/kg b.wt metformin
Creatinine	3.36 ± 0.32^a	5.62 ± 0.32^b	3.60 ± 0.39^a	5.33 ± 0.27^b	6.30 ± 0.30^b	3.45 ± 0.90^a
Urea	28.60 ± 2.06^a	43.16 ± 2.62^c	28.02 ± 2.30^a	38.36 ± 1.12^c	41.67 ± 1.44^c	30.45 ± 1.73^a

Values are mean ± SD for n = 5, column values with different superscripts are significantly different ($p < 0.05$) when compared to the control

Table 4. Effect of daily administration of EEAAR on ALT activity of streptozotocin–induced diabetic rats

Tissues	Groups					
	Control	Diabetic control	125 mg/kg b.wt	250 mg/kg b.wt	500 mg/kg b.wt	10 mg/kg b.wt metformin
Liver (U/L)	40.17 ± 0.14^a	75.43 ± 6.35^b	38.75 ± 2.73^a	428.00 ± 3.00^d	443.50 ± 2.17^d	35.08 ± 6.19^a
Serum (U/L)	3.32 ± 0.31^a	30.69 ± 0.69^c	3.71 ± 0.10^a	45.26 ± 0.41^d	53.01 ± 0.03^b	3.29 ± 0.51^a

Values are mean ± SD for n = 5, column values with different superscripts are significantly different ($p < 0.05$) when compared to the control

Table 5. Effect of EEAAR on AST activity of streptozotocin–induced diabetic rats

Tissues	Groups					
	Control	Diabetic control	125 mg/kg b.wt	250 mg/kg b.wt	500 mg/kg b.wt	10 mg/kg b.wt metformin
Liver (U/L)	15.06 ± 0.11^a	51.94 ± 0.23^b	380.17 ± 0.47^c	75.68 ± 0.62^d	10.38 ± 0.47^e	55.17 ± 1.01^f
Serum (U/L)	3.68 ± 0.26^a	35.02 ± 0.57^b	66.96 ± 0.25^c	37.42 ± 0.15^d	30.93 ± 0.21^e	3.76 ± 0.49^a

Values are mean ± SD for n = 5, column values with different superscripts are significantly different ($p < 0.05$) when compared to the control

Effect of seven-day daily administration of ethanolic extract of A. ataxacantha root on fasting blood glucose of streptozotocin - induced diabetic rats

There was a significant increase ($p < 0.05$) in the blood glucose level on day 1 in all tested groups when compared with the control (Table 2). There was also an increase ($p < 0.05$) in the blood glucose level on days 3 and 7 in all the groups (≥ 226.00 ± 28.23) except the groups that received 125 mg/kg body weight (b.wt.) of EEAAR and 10 mg/kg b.wt. of metformin respectively, in which there was no significant difference (≤ 110.01 ± 9.64) when compared to the control (106.33 ± 4.13).

The effects of daily administration of EEAAR for seven days on some kidney parameters of streptozotocin - induced diabetic rats were analysed (Table 3). There was an increase ($p < 0.05$) in the serum urea and creatinine in all groups except in those that received 125 mg/kg b.wt. of EEAAR and 10 mg/kg b.wt. of metformin, which gave no significant difference ($p > 0.05$) compared to the control.

Table 6. Effect of administration of EEAAR on lipid profile and atherogenic index of streptozotocin–induced diabetic rats

Groups	Parameters			
	TC (mg/dl)	HDL (mg/dl)	LDL (Mg/dl)	Atherogenic index (LDL/HDL)
Control	91.66 ± 8.54[a]	23.23 ± 2.34[a]	56.73 ± 4.91[a]	2.39 ± 0.11[a]
Diabetic control	151.14 ± 2.79[b]	5.52 ± 0.48[b]	130.66 ± 5.55[b]	24.72 ± 2.94[b]
125 mg/kg b.wt.	94.03 ± 0.54[a]	29.75 ± 0.31[c]	25.46 ± 2.16[a]	2.16 ± 0.20[a]
250 mg/kg b.wt.	101.04 ± 2.14[a]	36.62 ± 1.07[d]	25.86 ± 3.02[c]	1.98 ± 0.05[a]
500 mg/kg b.wt.	104.81 ± 4.38[ab]	44.25 ± 2.36[c]	40.62 ± 3.63[c]	3.18 ± 0.30[a]
10 mg/kg b.wt. metformin	106.68 ± 8.92[a]	45.43 ± 0.22[c]	24.28 ± 2.14[b]	3.08 ± 0.10[a]

Values are mean ± SD for n = 5, column values with different superscripts are significantly different ($p < 0.05$) when compared to the control

Table 7. Effect of administration of ethanolic root extract of *Acacia ataxacantha* on MDA concentration of streptozotocin–induced diabetic rats

Tissues	Groups					
	Control	Diabetic control	125 mg/kg b.wt	250 mg/kg b.wt	500 mg/kg b.wt	10 mg/kg b.wt metformin
Liver (U/L)	143.00 ± 2.00[a]	158.10 ± 2.15[b]	144.16 ± 1.78[a]	222.74 ± 2.04[c]	201.11 ± 1.14[c]	144.66 ± 2.36[a]
Serum (U/L)	2.80 ± 0.12[a]	4.41 ± 0.33[b]	3.39 ± 0.23[a]	4.16 ± 0.16[b]	6.79 ± 0.04[a]	3.47 ± 0.27[a]

Values are mean ± SD for n = 5, column values with different superscripts are significantly different ($p < 0.05$) when compared to the control

Table 8. Effect of administration of ethanolic extract of *Acacia ataxacantha* root on liver, serum and pancreatic SOD activities of streptozotocin–induced diabetic rats

Tissues	Groups					
	Control	Diabetic control	125 mg/kg b.wt.	250 mg/kg b.wt	500 mg/kg b.wt	10 mg/kg b.wt metformin
Liver	592.67 ± 1.13[a]	124.63 ± 4.70[b]	741.27 ± 2.51[c]	620.30 ± 2.00[d]	905.10 ± 1.00[e]	601.16 ± 4.04[f]
Pancreas	508.00 ± 1.04[a]	104.11 ± 0.24[b]	535.05 ± 2.41[c]	536.30 ± 1.15[c]	518.13 ± 3.20[d]	527.02 ± 1.71[c]
Serum	190.54 ± 0.45[ac]	160.01 ± 0.68[b]	184.16 ± 1.44[c]	155.10 ± 0.94[b]	209.98 ± 0.95[d]	196.67 ± 12.14[f]

Values are mean ± SD for n = 5, column values with different superscripts are significantly ($p < 0.05$) when compared to the control

Effects of daily administration of ethanolic extract of A. ataxacantha root on the activities of ALT and AST in streptozotocin - induced diabetic rats

The effects of daily administration of ethanolic root extract of *A. ataxacantha* on ALT and AST activities of streptozotocin–induced diabetic rats are presented in Tables 4 and 5 respectively. There was an increase ($p < 0.05$) in the ALT and AST activities of the liver and serum of rats in all the groups except in those that received 125 mg/kg b.wt. of EEAAR and 10 mg/kg b.wt. of metformin, which had no difference ($p > 0.05$) compared to the control.

Effects of daily administration of ethanolic extract of A. ataxacantha root on lipid profile and atherogenic index of streptozotocin - induced diabetic rats

The effect of daily administration of ethanolic extract of *A. ataxacantha* root on lipid profile and atherogenic index of streptozotocin - induced diabetic rats were examined (Table 6). There was no difference ($p > 0.05$) in the serum total cholesterol in all the groups except the diabetic control group, which had an increase ($p < 0.05$) when compared with the control. There was a significant increase ($p < 0.05$) in all groups in the high-density lipoprotein except the group that was diabetic, which had a significant decrease ($p < 0.05$) compared to the control. There was a decrease ($p > 0.05$) in the low density lipoprotein in all the groups except for the diabetic control, which had an increase ($p < 0.05$) compared to the control. There was no difference ($p > 0.05$) in the atherogenic indices in all treated groups compared to the control, but there was a significant increase ($p < 0.05$) in the diabetic control compared to the non-diabetic control.

Effects of daily administration of ethanolic extract of A. ataxacantha root on liver and pancrease MDA concentration in streptozotocin - induced diabetic rat

The effects of daily administration of ethanolic extract of *A. ataxacantha* root daily for seven days on liver and pancrease MDA concentration of streptozotocin–induced diabetic rats are presented in Table 7. There was no significant difference ($p > 0.05$) in the MDA concentration of liver and pancreas of rats administered 125 mg/kg b.wt. of EEAAR and 10 mg/kg b.wt. of metformin (reference drug) compared to the control, but there was a significant increase ($p < 0.05$) in the diabetic control group and among those that received 250 mg/kg and 500 mg/kg b.wts. of EEAAR.

Effects of administration of ethanolic extract of A. ataxacantha root on liver and pancreas superoxide dismutase activities of streptozotocin - induced diabetic rats

The effects of administration of ethanolic root extract of *A. ataxacantha* on hepatic and pancreatic superoxide dismutase of streptozotocin - induced diabetic rats were examined (Table 8). There was a significant increase ($p < 0.05$) in the superoxide dismutase activities of rat liver and pancreas in all the groups except diabetic control group that had a significant decrease ($p < 0.05$) compared to the control.

Discussion

In the present study, *A. ataxacantha* root was selected for normoglycaemic, normolipidaemic and antioxidant activities owing to its traditional uses. Therefore, the study was undertaken to verify its

traditionally claimed uses. Phytochemical analysis of *A. ataxacantha* revealed the presence of alkaloids, polyphenols, flavoniods, saponins, taninns and terpenoids. Flavonoids are known to regenerate the damaged cells in diabetic mice and found to stimulate insulin secretion or possess an insulin-like effect (Rao *et al*., 1997; Eidi *et al*., 2005; Khandelwal, 2007; Ghosh *et al*., 2009). Effects of polyphenols such as flavonoids on pancreatic β-cells leading to their proliferation and stimulation for insulin secretion have been proposed by Mahesh and Menon (2004) as the mechanism by which medicinal plants used in the treatment of diabetes mellitus reduce hyperglycaemia in streptozotocin - induced diabetic rats.

The results revealed that the ethanolic extract of *A. ataxacantha* root reduced blood glucose in STZ-induced hyperglycemic rats to levels comparable to the reference clinical drug metformin after 7 days. This is in agreement with the findings of previous study on the ethanolic extract of *A. ataxacantha* bark (Arise *et al*., 2014). The lower dose 125 mg/kg body weight of *A. ataxacantha* root extract was the most effective dosage, reducing the blood glucose almost to the normoglycemic level by day 7 of administration. However, higher doses of 250 and 500 mg/kg body weight of EEAAR did not show any hypoglycaemic activity; this may be due to high toxicity of the extract at high doses, resulting in overwhelming reduction in the biological active component involved in hypoglycaemia. The mechanism of the antidiabetic properties of *A. ataxacantha* root extract might be through the promotion of glucose uptake or inhibition of hepatic gluconeogenesis. Direct effect in the absence of insulin indicate that the extract has either insulin-like effect on the skeletal muscle or direct stimulatory effect on the enzymes involved in the pathways of glucose uptake in the presence of insulin receptor in the muscle or increase in the number of insulin receptors (Liu *et al*., 2008).

Elevated levels of serum urea and creatinine were observed, which may be due to renal damage caused by abnormal glucose regulation or elevated glucose and glycosylated protein tissues levels (Lal *et al*., 2009). Significant increase in serum urea and creatinine levels were observed in diabetic rats compared to control rats, which indicated impaired renal function in diabetic rats. The treatment with 125 mg/kg body weight of EEAAR decreased the above mentioned parameters significantly ($p < 0.05$) compared to diabetic control rats.

Serum AST and ALT activities were used as markers of tissue damage. Diabetes mellitus induction by administration of STZ produces an experimental damage due to its toxic metabolites (Zhang and Swaan, 1999). AST and ALT are enzymes found mainly in the cell of the liver, heart, skeletal muscle, kidney and pancreas, and to a lesser amount, in red blood cells. Their serum concentrations are proportional to the amount of cellular leakage or damage and are released into serum in larger quantities when any one of these tissue is compromised. The reduction of AST and ALT activities at the dose of 125 mk/kg body weight of EEAAR and 10 mg/kg body weight of metformin is an indication of repair of tissue damage induced by diabetic complications. This is in agreement with Shahidi *et al.* (1992) who reported that serum transminases returned to normal activities with the healing of tissue parenchyma and regeneration of hepatocyted and renal tissues. The EEAAR induced suppression of increased ALT and AST activities.

Significant reduction in the activities of these enzymes in 125 mg/kg body weight of EEAAR treated diabetic rats may be because of revival of insulin secretion into circulation or decreased cellular damage. These reductions may also be the consequence of improvement in the carbohydrate, fat and protein metabolism due to the therapy of EEAAR. This could be due to the presence of flavonoids in the EEAAR, which are reported to be hepatoprotective agents (Sivajothi *et al*., 2008). However, the elevated serum ALT activity at the doses of 250 and 500 mg/kg b.wt. might imply the toxicity of the extract at these higher doses, possibly as a result of damage to the membranes of liver cells and consequent leakage of hepatic cytosolic contents. The observed elevated ALT activity in the liver could indicate that the extract stimulates *de novo* synthesis of the enzyme.

In the present study, STZ-induced diabetes developed into hyperlipidemi,a which is in agreement with previous observations (Fatima *et al*., 2010; Sireesha *et al*., 2011). A variety of alterations in metabolic and regulatory mechanisms due to insulin deficiency or due to insulin resistance are responsible for the observed accumulation of lipids (Rajalingam *et al*., 1993). The EEAAR at all doses significantly reduced the LDL-C and atherogenic index in treated diabetic rats compared to untreated diabetic rats; it also brought the TC near normal levels, with an increase of HDL-C in treated diabetic rats compared to untreated diabetic rats. This may be due to the insulinotropic effects or insulin secretagogue activity of EEAAR. The decrease in atherogenic index is due to an increase in HDL-C levels after treatment. HDL-C is known to play an important role in the transport of cholesterol from peripheral cells to the liver by a pathway termed reverse cholesterol transport, and is considered to be a cardio-protective lipid.

STZ, in addition to inducing diabetes, also induces oxidative stress or relative overload of oxidants e.g. reactive oxygen species (Wright, 1999). Treatment with 125 mg/kg body weight EEAAR brought back lipid peroxidation markers (MDA) to normal levels in the liver and pancreas, which could be as a result of improved glycaemic control and antioxidants status. This study shows that EEAAR has significant glucose reducing property in STZ-induced diabetic rats at the dose of 125 mg/kg body weight. Increased lipid peroxidation in a diabetic state can be due to increased oxidative stress in the cell as a result of depletion of antioxidant scavenger systems. Lipid peroxidation in the diabetic tissues showed a decreased activity of SOD and increase MDA, which play an important role in scavenging the toxic intermediate of incomplete oxidation. Studies in the past have reported that the activity of SOD is low in diabetes mellitus (Feillet-Coudray *et al*., 1999). The result of increased activities of SOD in the present study suggests that EEAAR contains a free radical scavenging activity, which could exert a beneficial effect against pathological alterations caused by the presence of O_2^- and OH^-. This action could involve mechanisms related to scavenging activity of EEAAR.

Conclusions

The ethanolic extract of *Acacia ataxacantha* root possess antioxidant and normoglycaemic properties, inhibiting hepatic glucose formation on STZ-induced diabetic rats, optimally at a dosage of 125 mg/kg body weight. The extract was highly effective in managing complications like hyperlipidaemia associated with diabetes mellitus. However, the extract may not be safe at higher and repeated doses.

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