

Full Length Research Paper

Effects of aqueous root extract of *TRECULIA AFRICANA* on blood glucose, lipid profile and body weight changes of streptozotocin-induced diabetic and normal rats

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In this study, the effects of aqueous root extract of *TRECULIA AFRICANA* on blood glucose, triglycerides, total cholesterol, LDL-cholesterol, HDL-cholesterol and body weights of both STZ-induced diabetic and normal rats were investigated. Oral administration of aqueous root extract of *TRECULIA AFRICANA* at a dose of 200 mg/kg body weight per day, for a period of 14 days, caused a significant ($p < 0.05$) reduction in the blood levels of glucose, triglycerides, total cholesterol and LDL-cholesterol of both diabetic and normal rats. This dose also caused a significant ($p < 0.05$) increase in the HDL-cholesterol concentrations and body weights of both diabetic and normal rats. These effects portend the effectiveness of the plant in the management of diabetic conditions and hyperlipidemic states.

Key words: Streptozotocin (STZ), medicinal herbs, *Treculia africana*, lipid profile, hyperlipidemia, diabetes mellitus.

INTRODUCTION

Diabetes mellitus is a chronic disease characterized by derangement in carbohydrate, fat and protein metabolism, which manifest as ketoacidosis, hyperglycemia e.t.c. (Harris, 1997). In most instances, diabetes results from diminished secretion of insulin by beta cells of the islets of Langerhans. In diabetes, every tissue continues to play the catabolic role it was designed to play during starvation, in spite of delivery of adequate or even excess fuel with severe wasting of body tissues and ultimately death unless insulin is administered (Harris and Crabb, 1997). Insulin affects many sites of mammalian lipid metabolism. It stimulates synthesis of fatty acids in the liver, adipose tissue and in the intestine.

The insulin has also been reported to increase the synthesis of cholesterol (Harris and Crabb, 1997). The activity of lipoprotein lipase is also increased (Suryawashi et al., 2006). Diabetes can be induced by pharmacologic or surgical means (Frederick and Richard, 1993). Type I diabetes may be pharmacologically induced via a number of agents that selectively destroy pancreatic cells. Streptozotocin and alloxan are the most commonly used drugs. In contrast to total pancreatectomy, administration of these chemical agents leaves the remainder of pancreatic function intact (Frederick and Richard, 1993). Streptozotocin action in β cells is accompanied by characteristic alterations in blood insulin and glucose concentrations (West et al., 1996). It impairs glucose oxidation (Bedoya et al., 1996), and decreases insulin biosynthesis and secretion (Bolaffi et al., 1987; Nukatsuka et al., 1990). Impaired carbohydrate utilization in the diabetic also leads to accelerated lipolysis, which

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results in elevated plasma triacylglycerol (TAG) levels (hyperlipidaemia) (Granner et al., 1996; Horton et al., 1996). Consequently, the large amounts of fatty acids available to the liver in diabetic patients lead to excess acetylcoenzyme A (acetylCoA), which is converted to ketone bodies with consequent damage to the liver (Momo et al., 2006).

Since antiquity, diabetes has been treated with plant medicines. Recent scientific investigation has confirmed the efficacy of many of these preparations, some of which are remarkably effective. Only those herbs that appear effective are relatively non toxic and have substantial documentations of efficacy. More than 400 traditional plants treatment for diabetes mellitus have been recorded, but only small numbers of these have received scientific and medical evaluation to assess their efficacy (Bailey and Day, 1989; Satyavati et al., 1987). *Treculia africana* Decne which belongs to the family Moraceae and commonly known as African breadfruit, is a plant food native to tropical West and parts of East Africa (Ogbonnia et al., 2008). In Ghana, the root decoction is used as an anthelmintic and febrifuge. Ethnomedically, it is used as a verbrifuge, vermifuge, galactogogue and laxative (Ogbonnia et al., 2008). The caustic sap of male *Africana* breadfruit is applied on carious teeth; a bark decoction is used for cough and whooping cough, and ground bark with oil and other plant parts for swellings. Survey among tradomedical practitioners revealed that African breadfruit is an important component of some ancient anti-diabetic recipe used in Western and Middle Belt of Nigeria. *Treculia africana*, a valued food plant growing abundantly in Nigeria, may have beneficial effects in type-1 diabetes mellitus and may serve as a source of bioactive molecules for future generation of anti-diabetic drugs (Oyelola et al., 2007). Despite the various use of this plant especially in the management of diabetes, research studies are however limited on its effect on glucose and lipid profile, as well as body weight changes of experimental animals. Thus, the aim of this research is to elucidate the effects of the aqueous root extract of *Treculia africana* on serum glucose, triglycerides, total cholesterol, HDL-cholesterol, LDL-cholesterol and body weight in streptozotocin-induced diabetic wistar albino rats, with a view to ascertaining its antidiabetic effects.

MATERIALS AND METHODS

Experimental animals

Twenty Wistar albino rats, weighing between 110 to 180 g were obtained from the national institute of medical research (NAIMR), Lagos State, Nigeria, and used for the study. They were housed in standard cages in a room with a 12 h light/dark cycle and 50 to 60% relative humidity, at a temperature of about 30°C. The animals were allowed free access to feed (guinea grower's mash) and tap water, and were treated according to the International guidelines for the care and use of laboratory animals. They were allowed to

acclimatize to the new environment for a period of two weeks, after which they were randomized into four groups of five animals each as follows:

Group A: Normal control rats

Group B: STZ-Induced diabetic control rats

Group C: STZ-Induced diabetic rats treated with *Treculia africana* root extract

Group D: Normal rats treated with *Treculia africana* root extract.

Experimental induction of diabetes

Diabetes was induced by 65 mg/kg body weight of streptozotocin (STZ) Sigma® administered intraperitoneally (i.p) in physiologic saline, with pH adjusted to 4.5 using 0.05 M citrate buffer (Palanichamy et al., 1998). After one week of STZ administration and 12 h of fasting, blood glucose was determined and values that were at least twice the basal values were taken to be diabetic.

Plant extract

Treculia africana roots were obtained from medicinal plant dealers at Oyingbo market in Lagos. Taxonomic identification of the plant was established in the Department of Pharmacognosy, University of Benin. The roots were washed, dried, chopped into bits, and pulverized. The powdered root was weighed and boiled in distilled water for three days, using 10 ml of water per 1g of the powder. It was boiled for 6 h the first day, 3 h the second day, and 2 h the third day. The mixture was then allowed to cool and subsequently filtered using sintered funnel (which is equivalent to four folds of bandage or sheet of cheese cloth). The extract (filtrate) was then concentrated using rotary evaporator and weighed.

Administration of extract

Prior to the administration of extract, the plasma levels of glucose, triglycerides, total cholesterol, HDL-cholesterol and LDL-cholesterol, as well as their body weight were determined. 200 mg/kg body weight of the extract was administered to the test groups (that is groups C and D), while the control groups (that is groups A and B) received equivalent amount of distilled water orally each day for a period of 14 days.

Sample collection and data analysis

Blood samples were collected, via the tails of the rats, before inducement (baseline/day 0), one week after inducement (day 7), one week after treatment (day 14) and two weeks after treatment (day 21), and analyzed for glucose (collected in lithium heparin bottles), triglycerides, total cholesterol, HDL-cholesterol and LDL-cholesterol, using the spectrophotometric method (with their respective reagent kits from Randox Laboratory Limited, U.K). Their respective body weights were also obtained. Data are mean \pm SEM of five independent determinations, using one way analysis of variance.

RESULTS

As observed in this study, Table 1 shows the effect of *Treculia africana* root extract on blood glucose of the experimental animals. The blood glucose was shown to

Table 1. Effect of aqueous root extract of *Treulia africana* on blood glucose concentration (mg/dl).

Group	Day			
	0	7	14	21
A	90.5 ± 3.1	93.3 ± 2.3	96.2 ± 4.5	95.3 ± 4.8
B	81.14 ± 1.2	178.9 ± 16.4	182.3 ± 12.5	169.1 ± 10.3 [†]
C	73.31 ± 5.2	194.5 ± 3.7 ^{**}	156.2 ± 6.3	138.3 ± 1.5 ^{**†}
D	86.6 ± 2.5	91.5 ± 3.1 [*]	80.4 ± 4.2	68.3 ± 1.8 [*]

Blood glucose concentrations are expressed as mean ± SEM, n = 5, *p < 0.05 (day 21 compared to day 7), **p < 0.05 (day 21 compared to day 7), [†]p < 0.05 (group C compared to group B). Group A: Normal control rats; Group B: STZ-Induced diabetic control rats; Group C: STZ-Induced diabetic rats treated with *Treulia africana* root extract; Group D: Normal rats treated with *Treulia africana* root extract.

Table 2. Effect of aqueous root extract of *Treulia africana* on serum triglyceride concentration (mg/dl).

Group	Day			
	0	7	14	21
A	88.7 ± 5.8	92.5 ± 7.3	90.8 ± 10.1	93.7 ± 6.6
B	65.9 ± 14.4	142.3 ± 9.5	151.6 ± 10.1	146.2 ± 8.6 [†]
C	93.1 ± 10.9	140.4 ± 6.5 ^{**}	126.2 ± 8.9	110.0 ± 10.8 ^{**†}
D	91.2 ± 8.6	93.5 ± 3.8 [*]	86.5 ± 6.4	78.6 ± 5.8 [*]

Serum triglyceride concentrations are expressed as mean ± SEM, n = 5, *p < 0.05 (day 21 compared to day 7), **p < 0.05 (day 21 compared to day 7), [†]p < 0.05 (group C compared to group B). Group A: Normal control rats; Group B: STZ-Induced diabetic control rats; Group C: STZ-Induced diabetic rats treated with *Treulia africana* root extract; Group D: Normal rats treated with *Treulia africana* root extract.

increase significantly (p < 0.05) at day 7 after STZ administration to the test groups. After treatment with the aqueous extract of *Treulia africana* root, the blood glucose was shown to decrease significantly (**p < 0.05) in the treated group. That of the untreated group (group B) remained elevated. At day 21, there was a significant difference ([†]p < 0.05) between the glucose level of the treated and the untreated group, with that of the treated far lower than that of the untreated (diabetic control group or group B). Group D, that was given only the extract, showed a significant (*p < 0.05) reduction in the blood glucose level at day 21. The reductions in groups C and D as observed can be traced to the effect of the plant extract.

Table 2 which shows the effect of the plant extract on serum triglyceride concentrations, indicates that there was a significant (p < 0.05) increase in the levels of triglycerides one week after STZ administration. Treatment with the extract caused a steady significant (**p < 0.05) decrease in the triglyceride concentration in group C (induced and treated) at day 21. Though the reduction which was steady from day 7, was also noticed in group D (given extract alone), with that at day 21 significantly (*p < 0.05) lower than that at day 7. The triglyceride concentration in group B (induced and untreated) showed a steady increase, significant ([†]p < 0.05) at day 21 when compared to the treated group (group C). This however points to the fact that the

reduction was most probably due to the effect of the extract.

Table 3 which showed the effect of the extract on serum total cholesterol indicates that 7 days after the administration of STZ, the serum total cholesterol levels increased significantly (p < 0.05). The increase persisted in group B (induced and untreated), and remained significantly ([†]p < 0.05) higher than the cholesterol level in group C (induced and treated), at day 21. The steady increase observed in group B was however reversed in group C, where the administration of the extract caused a steady decrease in the cholesterol level. Thus, it was significantly (**p < 0.05) lower at day 21 compared to the value at day 7 (after STZ administration). Group D (given extract only) also showed a steady reduction in cholesterol level, which was significant (*p < 0.05) at day 21 as compared to that at day 7. These go to show that the reduction observed in group C was occasioned by the effect of the plant extract.

Table 4 shows the effects of aqueous root extract of *Treulia africana* on the serum HDL-cholesterol concentration of the experimental animals. STZ administration caused a slight reduction in the concentration of HDL in both test groups (groups B and C). However, treatment with the extract caused a steady and significant (**p < 0.05) increase in the HDL concentrations in group C, and also a steady and significant (*p < 0.05) increase in the HDL concentration in group D the STZ-induced

Table 3. Effect of aqueous root extract of *Treculia africana* on serum total cholesterol concentration (mg/dl).

Group	Day			
	0	7	14	21
A	195.3 ± 9.8	199.6 ± 10.1	193.8 ± 6.4	196.7 ± 10.2
B	201.4 ± 11.2	238.8 ± 8.9	248.5 ± 10.6	245.6 ± 9.8 [†]
C	198.6 ± 8.6	231.3 ± 6.6**	215.8 ± 10.1	201.4 ± 9.2*** [†]
D	192.8 ± 10.5	190.3 ± 8.5*	181.5 ± 6.3	165.3 ± 5.2*

Serum total cholesterol concentrations are expressed as mean ± SEM, n = 5, *p < 0.05 (day 21 compared to day 7), **p < 0.05 (day 21 compared to day 7), [†]p < 0.05 (group C compared to group B). Group A: Normal control rats; Group B: STZ-Induced diabetic control rats; Group C: STZ-Induced diabetic rats treated with *Treculia africana* root extract; Group D: Normal rats treated with *Treculia africana* root extract.

Table 4. Effect of aqueous root extract of *Treculia africana* on serum HDL-cholesterol concentration (mg/dl).

Group	Day			
	0	7	14	21
A	145.6 ± 10.5	143.5 ± 8.8	148.3 ± 6.9	145.6 ± 5.8
B	139.3 ± 7.5	132.8 ± 8.1	127.2 ± 6.2	120.5 ± 10.6 [†]
C	144.6 ± 8.3	139.1 ± 10.2**	149.5 ± 7.8	161.6 ± 8.9*** [†]
D	150.8 ± 8.5	152.3 ± 5.7*	165.1 ± 3.9	176.2 ± 10.1*

Serum HDL-cholesterol concentrations are expressed as mean ± SEM, n = 5, *p < 0.05 (day 21 compared to day 7), **p < 0.05 (day 21 compared to day 7), [†]p < 0.05 (group C compared to group B). Group A: Normal control rats; Group B: STZ-Induced diabetic control rats; Group C: STZ-Induced diabetic rats treated with *Treculia africana* root extract; Group D: Normal rats treated with *Treculia africana* root extract.

Table 5. Effect of aqueous root extract of *Treculia africana* on serum LDL-cholesterol concentration (mg/dl).

Group	Day			
	0	7	14	21
A	97.4 ± 4.2	101.5 ± 6.3	103.3 ± 7.4	100.5 ± 3.8
B	129.3 ± 10.3	148.5 ± 5.6	153.8 ± 6.8	142.6 ± 6.3 [†]
C	109.4 ± 5.3	156.2 ± 4.8**	131.3 ± 8.4	105.0 ± 6.3*** [†]
D	115.6 ± 3.8	118.3 ± 5.3*	106.3 ± 7.2	92.8 ± 3.9*

Serum LDL-cholesterol concentrations are expressed as mean ± SEM, n = 5, *p < 0.05 (day 21 compared to day 7), **p < 0.05 (day 21 compared to day 7), [†]p < 0.05 (group C compared to group B). Group A: Normal control rats; Group B: STZ-Induced diabetic control rats; Group C: STZ-Induced diabetic rats treated with *Treculia africana* root extract; Group D: Normal rats treated with *Treculia africana* root extract.

untreated group (group B) showed a rather steady and significant (p < 0.05) decrease in HDL concentration. At day 21, the HDL concentration was significantly ([†]p < 0.05) lower in group B as compared to that in group C. The increase in HDL in both groups given the extracts (groups C and D) serves as a pointer to the potential of the plant at increasing the HDL-cholesterol levels of the test animals.

The effects of the plant extract on LDL-cholesterol concentration is as shown in Table 5. Here, the LDL-cholesterol level was seen to increase significantly (p < 0.05) after STZ administration. Treatment with the plant

extract however, caused a steady and significant (**p < 0.05) decrease in the LDL concentration in group C, and also a steady and significant (*p < 0.05) decrease in group D. The induced and untreated group (group B) showed a slight increase in LDL level at day 14 and a significant (p < 0.05) decrease at day 21. Comparatively, the LDL level at day 21 was shown to be significantly lower in group C than it is in group B. The decrease in the treated groups (groups C and D), which is more significant ([†]p < 0.05) than the slight decrease in group B, at day 21, shows that the reduction in LDL levels in these groups is most probably due to the treatment with the

Table 6. Effect of aqueous root extract of *Treculia africana* on body weight (g).

Group	Day			
	0	7	14	21
A	153.4 ± 10.5	156.2 ± 11.2	159.5 ± 9.8	165.5 ± 10.7
B	165.0 ± 15.0	155.5 ± 14.5	141.5 ± 15.5	145.5 ± 13.5 [†]
C	146.7 ± 20.3	137.7 ± 19.7 ^{**}	144.7 ± 20.0	155.7 ± 20.3 ^{***†}
D	151.6 ± 11.2	158.0 ± 10.5 [*]	163.3 ± 13.3	171.8 ± 10.0 [*]

Body weight changes are expressed as mean ± SEM, n = 5, *p < 0.05 (day 21 compared to day 7), **p < 0.05 (day 21 compared to day 7), [†]p < 0.05 (group C compared to group B). Group A: Normal control rats; Group B: STZ-Induced diabetic control rats; Group C: STZ-Induced diabetic rats treated with *Treculia africana* root extract; Group D: Normal rats treated with *Treculia africana* root extract.

extract.

The weight changes as observed in Table 6 indicate that there was a significant (p < 0.05) decrease in body weight of the test groups (groups B and C) after STZ administration. This reduction persisted in group B at day 14, which eventually increased slightly at day 21. However, reverse was the case in group C, where treatment with the extract caused a steady and significant (**p < 0.05) increase in body weight. The steady and significant (*p < 0.05) increase was also observed in group D (given extract only). At day 21, the body weight in group C was shown to be significantly ([†]p < 0.05) higher than that in group B. The increases observed in groups D and C as a contrast to the decrease observed in B suggest that the treatment with the plant extract actually led to increase in body weight of the test animals.

DISCUSSION

Accelerated coronary and peripheral vascular atherosclerosis is one of the most common and serious chronic complications of long term diabetes mellitus. Along with other risk factors, such as hypertension, smoking, obesity. Increasing importance has been given to secondary hyperlipidemias in the causation of accelerated atherosclerosis (Dunn, 1988). Hyperlipidaemia as a metabolic abnormality is frequently associated with diabetes mellitus. Hyperlipidaemia is the commonest complication of diabetes mellitus and it predisposes them to premature atherosclerosis and macrovascular complications. Common lipid abnormalities in diabetes are raised triglycerides, LDL-cholesterol, total cholesterol and low HDL-cholesterol. Therefore good glycaemic control can prevent development of and progression of lipid abnormalities among patients with diabetes mellitus.

In diabetes mellitus, insulin is either not secreted in high amounts or does not efficiently stimulate its target cells. It has been suggested that the increase in triglyceride may be due to insulin deficiency which results faulty glucose utilization, causes hyperglycemia and mobilization of fatty acids from adipose tissues

(Suryawashi et al., 2006). In diabetes, blood glucose is not utilized by tissues resulting in hyperglycemia. The fatty acids from adipose tissues are mobilized for energy purpose and excess fatty acids are accumulated in the liver, which are converted to triglyceride (Shih et al., 1997). Our results indicate that administration of the aqueous root extract of *Treculia africana* at a dose of 200 mg/kg body weight caused a reduction in the blood glucose concentrations of both diabetic and normal rats. The hypoglycemic effect of the plant extract may therefore be useful in diabetic condition which is associated with hyperglycemia. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels. Thus, the plant may be protective against these conditions. The increase in triglyceride which is also associated with diabetes, as occasioned by STZ-inducement, may be controlled or managed by this medicinal plant as our findings indicated. Treatment with the plant extract was shown to reduce the blood level of triglyceride of the diabetic rats, as well as that of the normal rats. This lowering effect of the plant was also observed in the values of the blood total cholesterol of the test animals. Treatment with the aqueous root extract caused a reduction in the blood total cholesterol of the diabetic animals as well as that of the normal animals. This may portend the protective effect of the plant, as high cholesterol concentrations are associated with an increased incidence of coronary artery disease whose end result is myocardial infarction. Thus, the aqueous root extract of *Treculia africana* possess hypotri-glyceridemic and hypocholesterolemic properties which are useful in the management of diabetes. This study also showed that treatment with the plant caused an increase in the HDL-cholesterol level in normal and diabetic rats. Many studies have strongly suggested an inverse correlation of HDL-cholesterol level with the development of ischaemic heart disease (Goldbourt and Medalie, 1979; Muller et al., 1977). Most of the studies have revealed the inverse relationship of HDL-cholesterol with atherosclerosis to be independent of other lipid abnormalities. The effect of the plant at increasing the

HDL-cholesterol in both the diabetic and normal rats may result in consequent reduction in the risk of developing ischaemic heart disease or atherosclerosis. The study of Suryawashi et al. (2006) indicates that insulin increases the number of LDL receptor, so chronic insulin deficiency might be associated with a diminished level of LDL receptor. This causes the increase in LDL particles and results in the increase in LDL-cholesterol value in diabetes mellitus. This increase is however evident in our study, as treatment with STZ cause an increase in the LDL-cholesterol level of the test animals. But, treatment with the aqueous root extract of *Treculia africana* caused reduction in the LDL-cholesterol of the test animals. The effect of the plant at reducing the LDL-cholesterol level of the diabetic animals as well as that of the normal animals may suggest the ability of the plant to increase the number of LDL receptors, with consequent reduction in LDL particles which result in decrease LDL-cholesterol. In untreated diabetes, there is an increase in the rates of fat oxidation and ketone body formation, which therefore results to lose of weight (Lehninger et al., 2005). This was evident in the diabetic rats, as STZ treatment caused a reduction in the body weight. Treatment with the plant extract however caused an increase in the body weight of the diabetic animals. The increase in body weight was also observed in the normal animals. This may suggest the ability of the plant to effect proper tissue/cell utilization of glucose, therefore sparing the fat and reducing the rate of ketone body formation. The sparing effect on fat or reduction in fat oxidation will therefore lead to accumulation of fat and consequent increase in body weight.

The mechanism of action of some of the medicinal plants has been investigated (Kako et al., 1996). Two modes of actions are open to the plants;

- (1) Stimulation of insulin synthesis and secretion from the beta cells of pancreas of normal animals
- (2) Insulinomimetic effects such as increase cellular utilization of glucose.

The studied plants exert their actions by one or both of these mechanisms. The sulphonylureas that are used in the clinical management of diabetes patients (Oakley et al., 1978) also exert their hypoglycemic effects in normal experimental animals by stimulating the release of insulin from the beta cells into the circulation (Goth, 1978). In addition, the active principles of some medicinal plants, for example *Cuminum nigrum*, produce hypoglycemia in normal rabbits by stimulation of insulin release and by mimicking the action of the hormone (Akhtar, 1985). It is possible that the decreases in the blood glucose concentrations, by this plant (*Treculia africana*), possibly by these mechanisms, are similar to those reported for the medicinal plant *Cuminum nigrum*. The lowering of glucose, triglyceride, cholesterol and LDL-cholesterol, and the increasing of HDL-cholesterol by roots of *Treculia africana* indicates that local medicinal herbs may be

effective in the treatment of diabetes mellitus, hypertriglyceridemic and hyperlipidemic state. The declaration of the usefulness of this plant in the management of this diseases demand an investigation of their effect in a real diabetic condition, hypertriglyceridemic and hyperlipidemic state.

Conclusion

It is evident from this study that the local medicinal plant, *Treculia africana* (aqueous root extract) had a lowering effect on blood glucose, triglycerides, cholesterol and LDL-cholesterol of both diabetic and normal rats. It also showed an increasing effect on the blood HDL-cholesterol and body weight of both diabetic and normal rats. These effects indicate that this local medicinal plant may be effective in the management of diabetes mellitus, hypertriglyceridemic and hyperlipidemic state.

REFERENCES

- Akhtar MS (1985). Pharmacological Screening of Indigenous Medicinal Plant for Antidiabetic Activity. Final Research Report. Punjab Agricultural Research Coordination Board, University of Agriculture Faisalabad. pp. 55-88.
- Bailey CJ, Day C (1989). Traditional Plants Medicines as Treatments for diabetes. *Diabetes Care*, 12(8): 553-564.
- Bedoya FJ, Solano F, Lucas M (1996). N-monomethyl-arginine and Nicotinamide Prevent Streptozotocin-induced Double Strand DNA Break Formation in Pancreatic Rat Islets. *Experientia*, 52: 344-347.
- Bolaffi JL, Nagamatsu S, Harris J, Grodsky GM (1987). Protection by Thymidine, an Inhibitor of Polyadenosine Diphosphate Ribosylation, of Streptozotocin Inhibition of Insulin Secretion. *Endocrinology*, 120: 2117-2122.
- Dunn FL (1988). Treatment of Lipid Disorders in Diabetes Mellitus. *Med. Clin. North. Amr.*, 72: 1379-1398.
- Frederick ES, Richard JT (1993). Ethical Issues Involved in the Development of Animal Models for Type I Diabetes. *ILAR J.*, 35 (1).
- Goldbourt U, Medalie JH (1979). High Density Lipoprotein Cholesterol and Incidence of Coronary Heart Disease- The Isreali Heart Disease Study. *Am. J. Epidemiol.*, 109: 296-308.
- Goth A (1978). *Medical Pharmacology*. The C.V. Mosby Company, St. Louis, Missouri. p. 766
- Granner DK, Mayes PA, Rodwell VW (1996). *Harper's Biochemistry*, ed 24, Connecticut, U.S.A. Appleton and Lange. Pp 586-587.
- Harris RA (1997). *Carbohydrate Metabolism I: Major Pathways and Their Control*. In: *Textbook of Biochemistry*. 4th ed. Willey-Liss, Inc. New York, U.S.A. p. 287.
- Harris RA, Crabb DW (1997). *Metabolic Interrelationships*. In: Devlin, T. M. *Textbook of Biochemistry*. 4 ed. Willey-Liss, Inc. New York, USA.
- Horton HR, Moran LA, Ochs RS, Rawn JD, Scringeur KG (1996). *Principles of Biochemistry*, ed. 2, NJ. U.S.A. Prentice Hall Inc. pp. 474-475.
- Kako M, Miura T, Nishiyama Y, Ichimaru M, Moriyasu M, Kato A (1996). Hypoglycemic Effect of the Rhizomes of Polygala Senega in Normal and Diabetic Mice and its Main Component, the Triterpenoid Glycoside Senegrin-II. *Planta Med.*, 62: 440-443.
- Lehninger N, Nelson DL, Cox MM (2005). *Fatty Acid Catabolism*. In: *Principles of Biochemistry*, 4th ed. Freeman (Palgrave Macmillian) Publishers U.S.A. pp. 631-647.
- Momo ENC, Julius EO, Dagobert T, Etienne D (2006). Antidiabetic and Hypolipidemic Effects of *Laportea ovalifolia* (Utriceae) in Alloxan Induced Diabetic Rats. *Afr. J. Tradit. Complement. Altern. Med.*, 3(1): 36-43.

- Muller DPR, Lloyd JK, Bird AC (1977). Long term Management of Abetalipoproteinemia: Possible Role for Vitamin E. Arch. Dis. Child., 52: 209-214.
- Nukatsuka M, Yoshimura Y, Nishida M, Kawada J (1990). Importance of the Concentration of ATP IN Rat Pancreatic Beta Cells in the Mechanism of Streptozotocin Induced Cytotoxicity. J. Endocrinol., 127: 161-165.
- Oakley G, Pyke DA, Taylor KW (1978). Diabetes and its Management. Blackwell Scientific Publications, Oxford. p. 132
- Ogbonnia SO, Odimegwu JI, Enwuru VN (2008). Evaluation of Hypoglycemic and Hypolipidemic Effects of Aqueous Ethanolic Extract of *Treculia africana* Decne and Bryophyllum Pinnatum Lam and Their Mixture on Streptozotocin(STZ)-induced Diabetic Rats. Afr. J. Biotechnol., 7(15): 2535-2539.
- Oyelola OO, Moody JO, Odeniyi MA, Fakeye IO (2007). Hypoglycemic Effects of *Treculia africana* Decne Root Bark in Normal and Alloxan-induced Diabetic Rats. Afri. J. Tradit. Complement. Altern. Med., 4(4): 387-391.
- Palanichamy S, Nagarajan S, Devasagayam M (1998). Effect of Cassia Alata Leaf Extract on Hyperglycemic Rats. J. Ethnopharmacol., 22 (1): 81-90.
- Satyavatsi GV, Gupta A, Tandon N (1987). Medicinal Plants of India. Vol. II New Delhi. India Coun. Med. Res., 2: 407.
- Shih KC, Kwak CF, Hwa CM (1997). Acipinox Attenuates Hypertriglyceridemia in Dyslipidemic Non-insulin Dependent Diabetes Mellitus Patients Without Perturbation of Insulin Sensitivity and Glycemic Control. Diabetic Res. Clin. Pract., 36: 113-119.
- Suryawashi NP, Bluitey AK, Nagdeote AN, Jadhav AA, Manoorkar GS (2006). Study of Lipid Peroxide and Lipid Profile in Diabetes Mellitus. India J. Clin. Biochem., 21(1): 126-130.
- West E, Simon OR, Morrison EY (1996). Streptozotocin Alters Pancreatic Beta-Cell Responsiveness to Glucose Within 6hrs of Injection into Rats. West India Med. J., 45: 60-62.