Natural Product Sciences
13(1) : 17-22 (2007)

Evaluation of Antidiabetic and Antihyperlipidemic Activity of *Luffa tuberosa* (Roxb.) Fruits in Streptozotocin Induced Diabetic Rats

Veerendra C. Yeligar[1,2], K. Murugesh[2], Deepak Kumar Dash[2], Siva Shankar Nayak[2], B. C. Maiti[3], and Tapan K. Maity[2]*

[1]*K.L.E.Society's College of Pharmacy, Rajajinagar, Bangalore, Karnataka-10, India*
[2]*Division of Medicinal Chemistry, Dept. of Pharmaceutical Technology, Jadavpur University, Kolkata-700032, India*
[3]*Indian Institute of Chemical Biology, 4, Raja S. C. Mullick road, Kolkata-700032, India.*

Abstract – Fresh unripe whole fruits of *Luffa tuberosa* (Roxb.) or *Momordica tuberosa* (Roxb) Cogn. (Cucurbitaceae) were evaluated for the antidiabetic and hyperlipidemic potential in streptozotocin (STZ) induced diabetic rats. Diabetes was induced by administration of intra-peritoneal injection of streptozotocin at a dose of 55 mg/kg body weight. After the induction of diabetes aqueous extract of *L.tuberosa* (AELT) was administered orally at doses of 250 and 500 mg/kg. body weight/day for a period of 14 days. The Fasting blood glucose (FBG) levels, serum insulin levels, changes in body weight, food and liquid intake were measured. In diabetic rats, the AELT exhibited significant reduction in blood glucose levels. Biochemical assay of plasma total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDLc), low-density lipoprotein cholesterol (LDLc), glycogen content and glucose-6-phosphatase activity in liver were assessed. Antihyperlipidemia in diabetic rats after the extract supplementation was confirmed by significant reduction in the levels of above mentioned hyperlipidemic indicators. This study focus on the efficacy of *L.tuberosa* fruits for the management of experimental STZ induced diabetic rats and provides the scientific basis of ancient herbal therapy and use of these fruits as vegetable.
Keywords – *Luffa tuberosa* (Roxb.), streptozotocin, antihyperglycemic activity, antihyperlipidemic activity

Introduction

Hyperglycemia and hyperlipidemia are two important characters of Diabetes mellitus, an endocrine disorder based disease. In modern medicine, no satisfactory effective therapy is still available to cure diabetes mellitus (Ghosh *et al.*, 2001). Though the pharmaceutical drugs like sulfonylureas and biguanides are used for the treatment of diabetes, but these are either too expensive or have undesirable side effects or contraindications (Berger *et al.*, 1985; Rang and Dale, 1991). Diabetes is the leading cause of noncongenital blindness among adults aged 20 to 70 years, the leading cause of kidney failure, it doubles the risk of heart disease, gangrene of the extremities and there is a clinical recognition of cataract as a diabetic complication (Job *et al.*, 1975; Piters *et al.*, 1975). The most common conventional treatment for diabetes is insulin, which has prominent side effects. Neither insulin nor other modern pharmaceuticals have been shown to modify the course of diabetic complications (Grover *et al.*, 2002)

The field of herbal medicine research has been gaining significant importance in the last few decades and the demand to use natural product in the treatment of diabetes is increasing worldwide. The available literature shows that there are more than 400 plant species showing antidiabetic activity (Rai *et al.*, 1995; Mukharjee *et al.*, 1981). Although some of these plants have great reputation in Ayurveda, the indigenous Indian system of medicine, many remain to be scientifically established (Marles *et al.*, 1995).

Luffa tuberosa (*Roxb*) or *Momordica tuberosa* (Roxb) Cogn family (Cucurbitaceae) is perennial monocious trailing plant, with large turnip shaped tuberous root stock and synonymously called *Momordica cymbalaria* Hook. F (Fenzl). The other members of the same genus *M. charantia* Linn. and *M. foetida* Schum and Thonn are well known for their hypoglycemic activity (Leatherdale *et al.*, 1981; Akhter *et al.*, 1981). *L. tuberosa* found in the south Indian states of Karnataka, Andra pradesh, Madhya

*Author for correspondence
Fax: +91-332-8371078; E-mail: yveerendra@yahoo.co.in

pradesh, Maharastra and Tamil Nadu as a weed. This species has been transferred to the genus Luffa from Momordica by (Chakravarty, 1959). Fruits of *L. tuberosa* are routinely used as a vegetable, and also for the treatment of diabetes mellitus by the local people (Kameshwara Rao *et al.*, 1999). A study shows that the *L. tuberosa* fruits contains higher amount of nutritional values than bitter gourd (*Momordica charantia*) (Parvathi *et al.*, 2002).

The present aim of this work is to explore the scientific basis of the utility of *L. tuberosa* fruit extract for ameliorating hyperglycemia and hyperlipidemia in streptozotocin induced diabetic rats.

Experimental

Chemicals – Streptozotocin (STZ) is obtained from the Sigma Chemical Company, St. Louis, MO, (USA). All other chemicals and reagents used were of analytical grade.

Plant material – Green, Unripe fresh whole Fruits of *Luffa tuberosa* (Roxb.) were collected from Gadag district of North Karnataka, India and surrounding areas in the month of November and identified by taxonomist of Central National Herbarium (CAL), Botanical Survey of India (B.S.I.), Botanical Garden, Sibpur, Howrah. (No. CNH/1-1 (52)/2004-Tech II/706). Dated 17-06-2004. A voucher specimen of the whole plant is deposited in the herbarium of the department for future references.

Preparation of aqueous extract – The fresh unripe fruits of *L. tuberosa* were dried in an incubator for 2 d at 40 °C, crushed in an electrical grinder and then powdered. 500 g was suspended in redistilled water in a ratio of 1 : 5 and extracted (4 h, 2 times). A deep orange aqueous extract was obtained. The combined fractions are then filtered using Whatman filter paper and the filtrate is dried at reduced pressure at a temperature of 40 °C and lyophilized. It is stored at temperature of (0-8) °C until used. When needed, the residual extract was suspended in distilled water and used in the study. Phytochemical screening of extract has shown the presence of glycosides, alkaloids, phenols tannins, carbohydrates and amino acids.

Animals – Male Wister albino rats weighing between 180-230 g were obtained from the animal house, Indian Institute of Chemical Biology (IICB), Kolkata, India. The animals were grouped and housed in polyacrylic cages (38 × 23 × 10 cm) and maintained under standard laboratory conditions at a temperature 24 ± 2 °C. with 12 h dark and light cycle. They were allowed free access to standard pellet diet (Hindustan Lever, Kolkata, India) and water *ad-libitum*. The rats were acclimatized to laboratory condition for 7 days before commencement of experiment. All procedures described were reviewed and approved by the University Animals Ethical Committee.

Acute oral toxicity studies – Male Albino mice of 10 animals per group and weighing between 20 and 25 gm were administered graded doses (100-5000 mg/kg body weight, p.o) of the aqueous extract of *Luffa tuberosa* (AELT). After administration of AELT the mice were observed for toxic effects during 24 h of treatment. The toxicological effects were observed in terms of mortality expressed, as LD_{50}. The number of animals dying during a period was noted (Ghosh *et al.*, 1984). The LD_{50} of the extract was calculated by the method of Litchfield and Wilcoxon (Litchfield and Wilcoxon, 1959).

Induction of experimental diabetes – After one week of acclimatization, the rats were subjected for a 16 h fast. Diabetes was induced with a single i.p. injection of Streptozotocin (STZ) at a dose of 55 mg/ml/kg body weight. The STZ was freshly dissolved in citrate buffer (0.01 M, pH 4.5) (Bolkent *et al.*, 2000). Hyperglycemia was confirmed by the elevated glucose levels determined by measuring fasting blood glucose (FBG) at 72 h and on day 7 after injection and the diabetic rats exhibiting blood glucose levels in the range of 275 to 300 –mg/dl were selected for the study.

Experimental design – In the experiment, a total of 40 rats (8 normal; 32 STZ induced diabetic rats) were used. The rats were divided into five groups of eight animals each. Group I: (Normal Control), received normal saline solution 1 ml/kg. Group II: STZ diabetic control, Group III: STZ + AELT 250 mg/kg; Group IV: STZ + AELT 500 mg/kg and Group V: STZ + Glibenclamide 0.25 mg/kg for 14 days.

The extracts and the standard drugs were administered for 14 days from the day of induction. FBG was estimated on overnight fasted rats on day 1, and on an interval of 5 days, food and fluid intake amount and changes in body weights were also measured. After 14 days of treatment all the rats were sacrificed by decapitated after fasting for 16 h and blood was collected from dorsal aorta and used for the estimation of blood glucose. Serum was separated by centrifugation at 3000 × **g** for 5 min kept at –20 °C for the determination of insulin, biochemical assay of total cholesterol (TC), (one step method of Wybenga and Pileggi for total cholesterol) and triglycerides (TG) (Enzymatic method, GPO/Trinder, End point Colorimetry for triglycerides, Span diagnostics) Blood glucose levels were determined using glucometer (One Touch Ultra blood glucose monitoring system from Lifescan, Johnson and

Johnson Company, Milpitas, CA). liver and skeletal muscle glycogen were estimated (Nicolas, 1956) and for serum insulin assay following ELISA technique.

Liver and skeletal muscle of rats were dissected out and stored at –20 °C until used for biochemical estimations of liver and muscle glycogen, and liver glucose-6-phosphatase activity. Prior to sacrifice, the body weight of all the animals were recorded.

Biochemical assay of glucose-6-phosphatase activity – The liver glucose-6-phosphatase activity was measured according to Swanson. (Swanson MA. 1955) Tissue was homogenized in ice-cold phosphate buffer saline (0.1 M, pH 7.4) at the tissue concentration of 50 mg/ml. In a calibrated centrifuge tube, 0.1 ml of 0.1 M glucose-6-phosphate solution and 0.3 ml of maleic acid buffer (0.05 M, pH 6.5) were taken and brought to 37 °C in water bath for 15 min. The reaction was stopped with 1 ml of 10% TCA followed by chilling in ice and centrifuged at 3000 × *g* for 10 min. The optical density was measured at 340 nm. The enzyme activity was expressed as mg of inorganic phosphate liberated per g of tissue.

Serum lipoprotein cholesterol – Serum LDLc and VLDLc were measured according to the method of Friendwald *et al.* (1972) and other lipoprotein cholesterol Such as HDLc was measured by the method of Burstein *et al.* (1970).

Statistical analysis – Data were expressed as Mean ± SEM for 8 rats in each group. The biochemical parameters were analyzed statistically using one-way ANOVA, followed by Dunnett's multiple comparison test. The minimum level of significance was fixed at $P < 0.05$.

Results and Discussion

Oral administration of AELT at doses of 250 and 500 mg/kg body weight and glibenclamide (0.25 mg/kg) were able to reverse hyperglycemic and hyperlipidemic effect in streptozotocin-induced diabetic rats as indicated by various biochemical parameters. There was a significant elevation of FBG levels in Streptozotocin-treated rats with respect to control group ($P < 0.001$). Administration of AELT significantly reduced FBG levels in STZ induced diabetic rats (Group III to V) and brought the FBG values near to the control level. The results were shown in Table 2 and were found statistically significant.

The body weight, food and liquid intake were measured and summarized in Table 1. The initial body weight were almost similar in normal and diabetic groups, whereas the final body weights were significantly ($P < 0.001$) decreased in diabetic control (Group II) when compared with Normal control (Group I). At the same time, AELT treated diabetic rats (Group III and IV) showed no significant difference in body weight compared to that of Normal control (Group I). In case of diabetic rats treated with AELT, after attaining a normal glycemic control the body weight of the animals increased significantly, may be due to improvement in insulin secretion and glycemic control (Augusti *et al.*, 1994; Anitha Devi *et al.*, 2003). Food and fluid intake amount were significantly ($P < 0.001$) higher in diabetic group than the normal (Table 1). Treatment of

Table 2. Effect of aqueous extract of *L. tuberosa* after 14 d treatment on blood glucose level in STZ- induced male albino rats

group	treatment	fasting blood glucose level (mg/dl) days of AELT supplement 0	14
I	Normal saline	83.4 ± 7.14	87.08 ± 8.3
II	STZ	310.5 ± 7.84^a	291.85 ± 10.8^a
III	STZ + AELT	306.5 ± 11.2^b	186.45 ± 11.3^b
IV	STZ + AELT	304.6 ± 7.8^b	125.8 ± 9.66^b
V	STZ + glibenclamide	309.2 ± 4.9^b	102.80 ± 4.06^b

Each values represents mean ± S.E.M. (n = 8). ANOVA followed by Dunnett multiple comparison Test: Mean with superscripts Statistically significant, diabetic rats compared to normal and treated rats compared to diabetic control. ^{a}P < 0.001, ^{b}P < 0.01, ^{c}P < 0.05, $^\#$NS, non significant.

Table 1. Effect of AELT on body weight, food and liquid intake in male albino rats

group		body weight (g) initial	final	food intake (g/rat/Day)	liquid intake (ml/rat/day)
I	normal saline	191.0 ± 0.8	200.15 ± 1.2.	11.31 ± 0.13	16.19 ± 0.14
II	STZ	197.8 ± 2.1	174.1 ± 2.0^a	15.77 ± 0.31^a	30.05 ± 0.74^a
III	STZ + AELT	190.9 ± 2.5	203.2 ± 2.5^b	14.74 ± 0.45$^\#$	24.78 ± 0.34^b
IV	STZ + AELT	200.7 ± 2.7	211.2 ± 3.1^b	13.15 ± 0.26^b	22.20 ± 0.37^b
V	STZ + glibenclamide	196.35 ± 2.06	211.3 ± 1.46^b	12.54 ± 0.45^b	23.71 ± 0.64^b

Each values represents mean ± S.E.M, (n = 8). ANOVA followed by Dunnett multiple comparison Test: Mean with superscripts Statistically significant, diabetic rats compared to normal and treated rats compared to diabetic control. ^{a}P < 0.001, ^{b}P < 0.01, ^{c}P < 0.05, $^\#$NS, non significant.

Table 3. Effect of AELT after 14 d treatment on glycogen content and liver glucose-6-phosphatase activity in STZ-induced diabetic male albino rats

group	treatment	glycogen content (μg of glucose/mg of tissue)		glucose-6-phosphatase activity (mg of Pi/g of hepatic tissue)
		liver	skeletal muscle	liver
I	Normal saline	21.3 ± 1.7	21.1 ± 1.3	19.8 ± 1.3
II	STZ	12.4 ± 0.45^a	11.6 ± 0.7^a	30.08 ± 1.2^a
III	STZ + AELT	15.3 ± 1.3^b	14.5 ± 0.74^b	23.5 ± 1.4^b
IV	STZ + AELT	18.4 ± 1.8^b	17.16 ± 1.12^b	18.0 ± 1.4^b
V	STZ + glibenclamide	20.5 ± 2.1^b	20.2 ± 1.8^b	19.2 ± 2.5^b

Each values represents mean ± S.E.M, (n = 8). ANOVA followed by Dunnett multiple comparison Test: Mean with superscripts Statistically significant, diabetic rats compared to normal and treated rats compared to diabetic control. ^{a}P < 0.001, ^{b}P < 0.01, ^{c}P < 0.05, $^\#$NS, non significant.

AELT and glibenclamide brought food and liquid intake nearer to the normal levels.

The serum insulin levels in diabetic group were decreased significantly compared to the normal control group of rats (P < 0.001). In diabetic rats the treatment of AELT has significantly increased the reduced insulin level. The effect of treatment of AELT on serum insulin level in the normal and diabetic rats are represented in Fig. 4.

Glycogen levels were significantly decreased in diabetic rats in comparison to the control (P < 0.001) where as the 14-d treatment of AELT significantly increased the liver glycogen levels in respect to the diabetic groups. The effect is comparable to standard glibenclamide. Induction of diabetes has shown a significant increase in Glucose-6-Phosphatase activity in comparison to control. Supplementation of AELT to the diabetic animals resulted in significant reduction of these parameters and brought back these levels to normal values (Table 3).

The mechanism of antidiabetic effect of AELT can be predicted to the stimulation of residual pancreatic mechanism, probably by increasing peripheral utilization of glucose as per the finding of Erah PO (1996). Or by significantly increasing the level of insulin thereby producing insulinogenic activity as postulated by Karunanayake *et al.* (1984). The treatment with AELT enhanced the rate of glycogenesis in hepatic and skeletal muscle glycogen content indicating the enhancement of rate of glycogenesis. Similar results were reported in alloxan induced diabetic rats (Kameshwar Rao *et al.*, 2003).

The effect of AELT on plasma total cholesterol (TC) and triglycerides (TG) levels were shown in Fig. 1, Plasma total cholesterol and triglyceride levels were significantly elevated in diabetic groups in comparison to control (P < 0.001). Supplementation of AELT and glibenclamide significantly reduced these parameters and the levels of

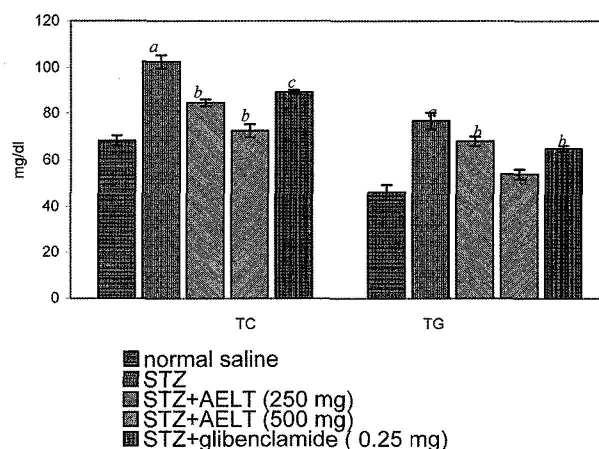

Fig. 1. Effect of AELT on serum total cholesterol and triglycerides levels in rats.

Each values represents mean ± S.E.M, (n = 8). ANOVA followed by Dunnett multiple comparison Test: Mean with superscripts Statistically significant, diabetic rats compared to normal and treated rats compared to diabetic control. ^{a}P < 0.001, ^{b}P < 0.01, ^{c}P < 0.05, $^\#$NS, non significant.

these parameters were resettled near the control levels.

Other hyperlipidemic parameters like serum LDL and VLDL concentrations were elevated in diabetic groups and compared to control (Fig. 2). Treatment with AELT decreased the levels of these parameters significantly in respect to the corresponding diabetic groups and were reset to the control level. In case of diabetic groups the HDL level was decreased in respect to the control (P < 0.001). The supplementation of AELT for 14 days lead to the increased levels of lipoproteins in serum values close to the control levels. The TC/HDL and LDL/HDL ratio of concentrations were significantly elevated in diabetic groups in respect to the control (P < 0.001) but the treatment with AELT resulted in significant diminution of these ratios resettled towards the control levels the results are in comparison to glibenclamide (Fig. 3).

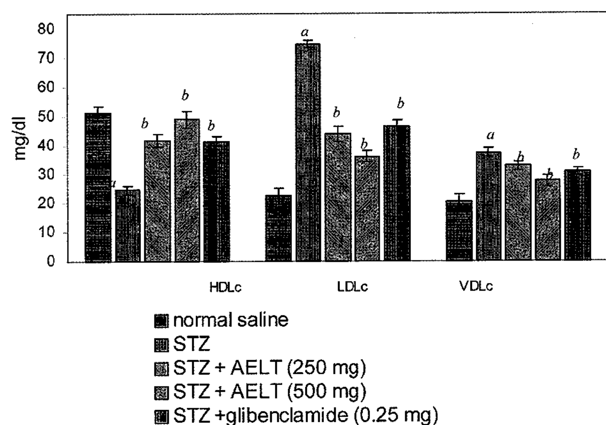

Fig. 2. Effect of AELT on serum HDLc, LDLc and VLDLc levels in rats.

Each values represents mean ± S.E.M, (n = 8). ANOVA followed by Dunnett multiple comparison Test: Mean with superscripts Statistically significant, diabetic rats compared to normal and treated rats compared to diabetic control. [a]$P < 0.001$, [b]$P < 0.01$, [c]$P < 0.05$, [#] NS, non significant.

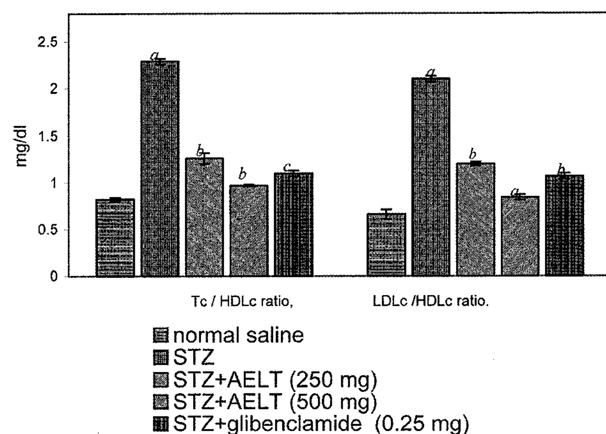

Fig. 3. Effect of AELT on serum Tc/HDLc and LDLc/HDLc ratios in rats.

Each values represents mean ± S.E.M, (n = 8). ANOVA followed by Dunnett multiple comparison Test: Mean with superscripts Statistically significant, diabetic rats compared to normal and treated rats compared to diabetic control. [a]$P < 0.001$, [b]$P < 0.01$, [c]$P < 0.05$, [#] NS, non significant.

The hyperlipidemic activity of *L.tuberosa* attributed to the decrease in serum TC and TG levels after the administration of the extract to the diabetic rats. This effect may be due to decreased activity of the enzymes involved in the biosynthesis of cholesterol and or decreased level of lipolysis, which are under the regulation of insulin (Sharma *et al.*, 2003). The treatment of extract also resulted in significant decrease in the level of LDLc and HDLc in serum towards the control levels, showing the antihyperlipidemic efficiency of extract. Above this

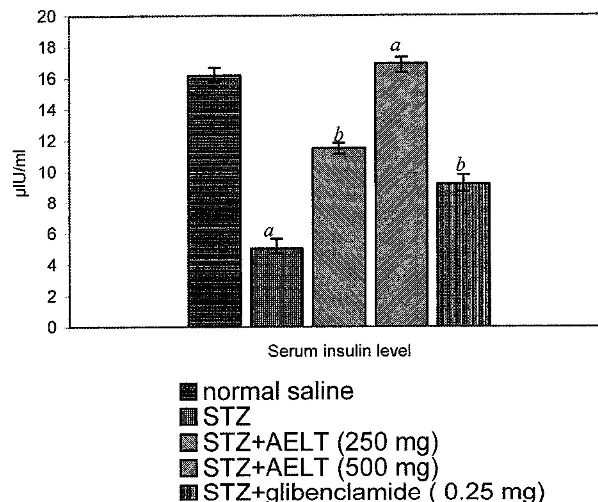

Fig. 4. Effect of AELT on serum insulin levels in rats.

Each values represents mean ± S.E.M, (n = 8). ANOVA followed by Dunnett multiple comparison Test: Mean with superscripts Statistically significant, diabetic rats compared to normal and treated rats compared to diabetic control. [a]$P < 0.001$, [b]$P < 0.01$, [c]$P < 0.05$, [#] NS, non significant.

the extract also decreased the dyslipidemia (Elisaf *et al.*, 1995), which is confirmed by decrease in the elevated rates of LDLc/HLc and TC/HDLc ratio. The extra pancreatic effects of the extract are focused by significant recovery of glucose-6-phosphatase activity in liver and the modulation of glucose absorption from the intestine.

The phytochemical studies carried out on the extract has shown the presence of glycosides, alkaloids and phenolic compounds which have been reported to have major role in reducing oxidative stress associated with diabetes, which in turn helps in the regulation of plasma glucose concentration (Kako *et al.*, 1997; Abdel-Hassan *et al.*, 2000; Olmedilla *et al.*, 1991). Thus the significant antidiabetic and antihyperglycemic activity of aqueous extract of *L.tuberosa* fruits in our studies are attributed to the phytoconstituents present in the fruits. We are in a process of isolation of active constituents responsible for antidiabetic activity of *Luffa tuberosa.*

Acknowledgement

The first author Veerendra C.Yeligar, Senior Research Scholar is grateful to AICTE New Delhi, for providing financial facilities and Jadavpur University for laboratory facilities.

References

Abdel-Hassan, I.A., Abdel-Barry, J.A., and Tariq Mohammed, S., The

hypoglycaemic and antihyperglycaemic effect of *citrullus colocynthis* fruit aqueous extract in normal and alloxan diabetic rabbits. *J. Ethnopharmacol.* **71**(1-2) 325-330 (2000).

Akhtar, M.S., Athar, M.A., and Yaqub, M., Effect of *Momordica charantia* on the blood glucose level of normal and alloxan diabetic rabbits. *Planta Med.*. **42**, 205-212 (1981).

Anitha Devi, B., Kamalakkannan, N., Stanely, P., and Prince, M., Supplementation of fenugreek leaves to diabetic rats. Effect on carbohydrate metabolic enzymes in diabetic liver and kidney. *Phytother. Res*, **17**(10), 1231-1233 (2003).

Augusti, K.T., Reji, S.D., Sheeja, C., Sheela, C.G., and Sudhakaran, N.C.R., Effect of leucopelargonin derivative from *Ficus bengalensis* Linn. on diabetic dogs. *Indian J. Med Res.* **99**, 82-6 (1994).

Barger, S., Incidence of severe side effects during therapy with sulfonylureas and biguanides. *Horm. Metab. Res.* **17**, 111-115 (1985).

Bolkent, S., Yanardag, R., Tabakoglu-Oguz, A., and Ozsoy-Sacan, O., Effects of chard (*Beta vulgaris* L. var. cicla) extract on pancreatic B cells in streptozotocin-diabetic rats: a morphological and biochemical study *J. Ethnopharmacol.* **73**, 251-259 (2000).

Burstein, M., Scholnick, H.R., and Morgin, R., Rapid method for the isolation of lipoproteins from human serum by precipitation with polyanions. *J. Lipid Res.* **11**, 1583-1586 (1970).

Chakravarty, H.L., Rec. Bot. Survey of India **17**, 1, 81, 1959. *Wealth of India*. C.S.I.R New Delhi, Vol VI, L-M, 412 VI, 1962.P.P.412.

Choi, J.S., Yokozawa T., and Oura H., Improvement of hyperglycemia and hyperlipidemia in streptozotocin-diabetic rats by a methanolic extract of *Prunus davidiana* stems and its main component pruning. *Planta Medica*: **57**, 208-211 (1991).

Elisaf, M., Bairaktari, H., Tzaiallas, C., Germanos, N., and Siamopoulos, K., *Dial. Transplant.*, **24**, 642-650 (1995).

Erah, P.O., Osuide, G.E., and Omogbai, E.K.I., Hypoglycemic effect of the extract of *Solenostemon monostachys* leaves. *J. West Afr Pharm.* **10**, 21-27 (1996).

Friendwald, W.T., Levy, K.J., and Frederickson, D.S., Estimation of concentrations of low density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. *Clin. Chem.* **18**(6), 499-502 (1972).

Ghosh, M.N., Fundamentals of experimental pharmacology. 2nd ed. Scientific Book Agency, Calcutta **26**, 153-158 (1984).

Ghosh, S. and Suryawanshi, S.A., Effect of *Vinca rosea* extracts in treatment of alloxan diabetes in male albino rats. *Ind. J. Exp. Biol.* **39**, 748-759 (2001).

Grover, J.K., Yadav, S., and Vats, V., Medicinal plants of India with antidiabetic potential. *J. Ethnopharmacol.* **81**, 81-100 (2002).

Job, D., Eschwege, E., Gyet. G., and Tobobrontsky, J., Effect of multiple insulin daily injection on the course of retinopathy, Diabetes, *DIAEAZ.* **24**(suppl. 2), 393 (1975).

Kako, M., Miura, T., Nishiyama, Y., Ichimaru, M., Moriyasu, M., and Kato, A., Hypoglycemic activity of some triterpenoid glycosides. *J. Nat Prod.* **60**(6), 604-5 (1997).

Kameshwar Rao, B., Kesavulu, M.M., Giri, R., and Appa Rao, C., Antidiabetic and hypolipidemic effects of *Momordica cymbalaria* Hook. Fruit powder in alloxan-diabetic rats. *J. Ethnopharmacol.* **67**, 103-109 (1999).

Kameshwar Rao, B., Kesavulu, M.M., and Apparao, C., Evaluation of antidiabetic effect of *Momordica cymbalaria* fruit in alloxan-diabetic rats. *Fitoterapia* **74**, 7-13 (2003).

Karunanayake, E.H., Wehilendra, J., Sirimanne, S.R., and Gowri S., Oral hypoglycaemic activity of some medicinal plants of Sri Lanka. *J. Ethnopharmacol.* **11**, 223-231 (1984).

Leatherdale, B.A., Pavesar, R.K., Singh, G., Atcius, T.W., Baliley, C.J., and Bignell, A.H.C., Improvement in glucose tolerance due to *Momordica charantia* (Karela). British Medical Journal **282**, 1823-1824 (1981).

Litchfield, J.T. and Wilcoxon, F., A simplified method of evaluating dose-effect experiments. *J. Pharmacol. Exp Ther.* **96**, 99-113 (1959).

Marles, R.J. and Farnsworth, N.R., Antidiabetic plants and their active constituents. *Phytomedicine.* **2**, 137-189 (1995).

Mukharjee, S.K., Indigenous drugs in diabetes mellitus. *J. Diabet Assoc Ind.* **21**, 97-106 (1981).

Nicholas, V.C., Robert, W.L., and Joseph, H.R., The determination of glycogen of liver and muscle by use of anthrone reagent. *J. Biol Chem.* **220**, 583-593 (1956).

Olmedilla, M.N., Reference value for retinal, tocopherol and main carotenoids in serum of control and insulin dependent diabetic Spanish subjects. *Clin. chem.* **43**, 1066-1071 (1999).

Panneerselvam, R.S. and Govindaswamy, S., Effect of sodium molybdate on carbohydrate metabolizing enzymes in alloxan-induced diabetic rats *J. Nut. Biochem.* **13**, 21-26 (2002).

Parvathi, S. and Kumar, V.J.F., Studies on chemical composition and the utilization of wild edible vegetable Athalakkai (*Momordica tuberosa*) *Plant foods for human nutrition.* **57**, 215-222 (2002).

Piters, K., Goodman, J., and Bossman, A., Treatment of diabetic ketoacidosis dose intravenous insulin diabetes. *DIAEAZ* (suppl.2) **24**, 393 (1975).

Rai, M.K., A Review on some antidiabetic plants of India. *Ancient Sci Life.* **14**, 42-54 (1995).

Rang, H.P., Dale, M.M., and Ritter, J.M., Pharmacology, Logman Group LTD U.K. 1991. pp. 504-508.

Riyad, A., Abdul-Ghani, Abdul-Salam, S., and Auleiman, S.M., Effect of fenugreek and lupine seeds on the development of experimental diabetes in rats. *Planta med.* **54**, 286-290 (1988).

Sharma, S.B., Nasir, A., Prabhu, K.M., Murthy, P.S., and Dev, G., Hypoglycaemic and hypolipidemic effect of ethanolic extract of seeds of Eugenia jambolana in alloxan-induced diabetic rabbits *J. Ethnopharmacol.* **85**, 201-206 (2003).

Sharma, S.R., Dwivedi, S.K., and Swarup, D., Hypoglycemic and hypolipidemic effects of *Cinnamum tamala* nees leaves. *Indian J. Exp. Biol.* **34**, 372-374 (1966b).

Swanson, M.A., Methods in Enzymology, Vol. II, ed. by Colowick SP, Kaplan N O, Academic Press, New York: 1955, pp. 541-543.

Tarfa, S.P., Joseph, P.K., and Augusti. K.T., Preliminary studies on the antidiabetic effects of cabbage (*Brassica oleracea* Van *Capitata* L.) oil streptozotocin-diabetic rats. *Curr.Sci.* **57**, 32-33 (1988).

(Accepted November 28, 2006)