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Hypoglycemic and Hypolipidemic Activities of *Trianthema portulacastrum* Linn. Plant in Normal and Alloxan Induced Diabetic Rats

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Abstract: The present study was designed to evaluate the hypoglycemic and hypolipidemic activity of methanol extract of *Trianthema portulacastrum* Linn. whole plant in normal and alloxan-induced diabetic rats. Alloxan was used to induce diabetes in rats and the blood glucose, lipid levels were estimated using commercial kits available in the market. The methanol extract of *T. portulacastrum* was administered for 7 days to normal and alloxan induced diabetes rats at a dose of 100, 200 and 300 mg kg⁻¹. The extract produced significant reduction (p<0.001) in blood glucose at a doses of 100, 200 and 300 mg kg⁻¹ in normal and diabetic rats. It also produced beneficial effects on the lipid profile in normal as well as alloxan induced diabetic rats at the end of the treatment period (7th day). The methanol extract of *Trianthema portulacastrum* produced a dose dependent hypoglycemic, antihyperglycemic and hypolipidemic activity in rats and were comparable with standard oral hypoglycemic agent, glibenclamide.

Key words: *Trianthema portulacastrum*, diabetes mellitus, arteriosclerosis, hypolipidemic, hypoglycemic, glibenclamide

INTRODUCTION

Trianthema portulacastrum Linn. is plant of the family Aizoaceae, found almost throughout India as a weed in cultivated and wastelands. The local (telugu) name of the plant is Galijeru and national (Hindi) name is santhi. The plant is bitter and used as analgesic, stomachic, laxative and serves as alterative cure for bronchitis, heart disease, blood anemia and inflammation. The plant is used in the treatment of edema in the liver and spleen (Javed *et al.*, 2000) uteralgia and cough. The plant is lithotriptic for the kidney and bladder. In the Indian traditional medicine system, the plant is considered as a diuretic. Previously, it was reported the hepatoprotective activity (Kumar *et al.*, 2004) of *Trianthema portulacastrum* (TP) against paracetamol thioacetamide intoxication in albino rats and antifungal activity of *T. portulacastrum*. Sharmila-Banu *et al.* (2009) reported that ethanolic leaves extract of *T. portulacastrum* ameliorates AFB1-induced hepatotoxicity in rats due to its combined antioxidant potential as well as hepatoprotective action. Kumar *et al.* (2005) also reported the *in vivo* antioxidant activity of *T. portulacastrum* plant extract in relation to paracetamol and thioacetamide intoxication in rats.

Diabetes mellitus is a disease in which homeostasis of carbohydrates, protein and lipid metabolism is improperly regulated by the insulin resulting in elevation of fasting and post prandial blood glucose levels (Tiwari and Madhusudana-Rao, 2002). Diabetes mellitus is heterogeneous disorder with multiple etiological factors; it generally involves absolute or insulin resistance, or both and it has also been associated with an increased risk for premature arteriosclerosis due to increased in triglycerides and low density lipoprotein levels. Diabetes mellitus is an independent predictor of high risk for Coronary Heart Disease (CHD). About 70-80% of deaths in diabetic patients are due to vascular disease. Glucose control is essential, but this provides only minimal benefit with respect to CDH prevention. An ideal treatment for diabetes would be a drug that are not only controls the glycemic levels but also prevents the development of arteriosclerosis and other complications of diabetes (Halliwell and Gutteridge, 1985). Nowadays, the use of complementary and alternative medicine and especially the consumption of botanicals have been increasing rapidly worldwide, mostly because of the supposedly less frequent side-effects when compared to modern Western medicine (Hu *et al.*, 2003).

The objective of the present study was to evaluate the hypoglycemic and hypolipidemic activity of methanolic extract of *Trianthema portulacastrum* L. whole plant in normal and alloxan-induced diabetic rats.

MATERIALS AND METHODS

Extraction of plant material: The plant *Trianthema portulacastrum*, was collected in the month of October, 2007 and the plant was taxonomically identified and authenticated as *Trianthema Portulacastrum* Linn. by Prof. Chelladurai, Research Botanist, Palayamkottai, Tamil Nadu, India. The whole plant was dried under shade and ground to a fine powder in a mechanical blender. The powder of the plant was initially extracted in a Soxhlet apparatus with petroleum benzene (60-80°C) to remove the chlorophyll followed by methanol by the method of continuous hot extraction to get the methanol extract of *Trianthema portulacastrum* (METP). This methanolic extract was stored at 2-8°C and used for subsequent experiments.

Phytochemical screening: The methanolic extract was screened for the presence of various phyto-constituents. Phytochemical properties of the extract were tested using the following chemicals and reagents. Alkaloids with Mayer and Dragendorff's reagents, terpenoids, glycosides (NaCl and Fehling's solution A and B), flavonoids (NaCl and HCl), saponins (frothing test), tannins (FeCl₃), phenolic compounds (FeCl₃ and K₃Fe(CN)₆) and carbohydrates (Molisch's test) (Kokate, 1994; Harborne, 1998).

Acute toxicity studies: Acute toxicity studies were conducted in mice and rats using various doses of methanolic extract of TP up to 4000 mg kg⁻¹ and observed for the mortality and behavioral changes.

Animals: Wistar albino adult male rats, weighing 200-220 g were selected and housed in polypropylene cages in a room where the congenial temperature was 27±1°C and 12 h light and dark cycles were maintained. The animals were allowed to acclimatize to the environment for 7 days and supplied with a standard pellet diet (Hindustan Lever Ltd., Bangalore) and water *ad libitum*.

Activity in normoglycemic animals: A total of 30 normal overnight fasted rats were divided into five equal groups. The animals of group I served as an untreated control, group II was treated with glibenclamide (1 mg kg⁻¹) and group III, IV and V were treated with methanolic extract of

T. portulacastrum (METP) at a dose of 100, 200 and 300 mg kg⁻¹ (single dose day⁻¹), respectively. Plasma glucose levels were estimated using a commercial kit (GOD-POD kit of Span Diagnostics, India) at 0th, 1st, 3rd and 7th day from the start of treatment and compared with untreated control. At the end of the study i.e., on 7th day, serum lipid levels were estimated in all untreated and treated groups of rats.

Activity in alloxan induced hyperglycemic (diabetic) animals: Diabetes mellitus/hyperglycemia was induced in Wistar rats by single intraperitoneal injection of 120 mg kg⁻¹ b.wt. of alloxan monohydrate (Sigma, USA), dissolved in normal saline (Ragavan and Krishnakumari, 2006). After 5 days, blood samples were collected by retro-orbital puncture under mild anesthesia and blood glucose levels were monitored. Rats showing serum glucose level above 200 mg dL⁻¹ were used for the antihyperglycemic evaluations and randomly divided into groups four groups of 6 animals each. Group I served as untreated diabetic control, group II diabetic rats treated with a standard oral hypoglycemic agent, glibenclamide (1 mg kg⁻¹) while group III, IV and V diabetic rats received 100, 200 and 300 mg kg⁻¹ of methanolic extract of TP. Blood samples were collected at 0th, 1st, 3rd and 7th day from the start of treatment for the estimation of blood glucose levels in all overnight fasted rats. At the end of the study i.e., on 7th day, serum lipid levels were estimated in all untreated and treated groups of rats.

Collection of blood samples and estimation of glucose and lipid profiles: The blood samples were collected from orbital plexus centrifuge tubes and serum was separated by immediate centrifugation of blood samples using REMI ultra cooling centrifuge at 3000 rpm for 5 min at room temperature and was directly used for estimating glucose, triglyceride, total cholesterol, HDL-cholesterol by using respective span diagnostic kits.

Statistical analysis: The results were expressed as Mean±SD. Statistical analysis were carried out using paired t-test and one-way ANOVA followed by Bonferroni's test. Differences below p<0.05 implied statistically significance.

RESULTS

Preliminary phytochemical screening of the methanolic extract of *T. portulacastrum* reveals the presence of alkaloids, flavonoids, saponins, phenolic compounds and terpenoids. Different doses of methanolic extract were screened for their oral toxicity. No mortality

Table 1: Effect of METP on plasma glucose levels of normoglycemic rats (mean±SD)

Treatment	0 day	1st day	3rd day	7th day
Untreated control	82.2±3.7	83.5±3.9	85.3±4.1	82.6±3.4
Normal + Glibenclamide (1 mg kg ⁻¹)	79.5±3.3	73.1±3.6 ^b	67.9±3.1 ^c	60.6±2.8 ^c
Normal + METP (100 mg kg ⁻¹)	79.6±3.8	76.5±3.2 ^a	72.4±2.6 ^c	69.6±3.4 ^c
Normal + METP (200 mg kg ⁻¹)	82.7±2.6	77.9±2.3 ^a	72.3±3.1 ^c	65.6±3.9 ^c
Normal + METP (300 mg kg ⁻¹)	82.2±2.9	74.3±2.8 ^b	63.4±3.4 ^c	55.6±3.9 ^c

Values are in Mean±SD; n = 6; a: p<0.05, b: p<0.005, c: p<0.0001 vs. 0th day

Table 2: Effect of administration with *T. portulacastrum* and glibenclamide on serum lipid parameter level in normal rats (on 7th day)

Groups	TC	TG	HDL-C
	----- (mg dL ⁻¹) -----		
Normal control	106.3±4.92	72.10±3.52	54.80±2.82
Normal + Glibenclamide (1 mg kg ⁻¹)	95.4±3.90 ^b	58.20±2.55 ^b	59.10±2.24
Normal + METP (100 mg kg ⁻¹)	101.8±2.40 ^b	65.20±2.61 ^b	57.40±2.18 ^b
Normal + METP (200 mg kg ⁻¹)	96.9±3.22 ^b	60.51±2.81 ^b	58.43±2.42 ^a
Normal + METP (300 mg kg ⁻¹)	90.7±3.41 ^b	56.55±2.49 ^b	60.33±2.12 ^a

Values are in Mean±SD; n = 6; a: p<0.01, b: p<0.0001 vs. normal control; (TC: Total Cholesterol; TG: Triglycerides; HDL-C: HDL cholesterol)

was recorded till 4000 mg kg⁻¹ with methanolic extract, hence, the extracts were found to be safe up to the dose levels of 4000 mg kg⁻¹.

Effect of methanolic extract of *T. portulacastrum* on normal rats: The hypoglycemic effect of methanolic extract of *T. portulacastrum* in normal rats was shown in Table 1. A significant reduction (p<0.05) in blood glucose levels was observed at 24 h post-administration of methanolic extract (100, 200 and 300 mg kg⁻¹ b.wt.) of *T. portulacastrum* in the normal rats; this was further lowered after 3, 5, 7 days of treatment. The maximum reduction in blood glucose level was seen at a dose of 300 mg kg⁻¹ b.wt. of *T. portulacastrum* extract administration. However, the hypoglycemic effect of methanolic extract of *T. portulacastrum* was comparable with that of standard oral hypoglycemic agent, glibenclamide.

As the blood glucose-lowering effect of METP was observed with both 100, 200 and 300 mg kg⁻¹, the effect of these doses on the lipid profile of normal rats were estimated and the results were shown in Table 2.

Similar to glibenclamide, administration of the methanolic extract led to a significant fall in the level of triglycerides, total cholesterol and improved the HDL levels in normal rats after 7 days of METP treatment.

Table 3: Effect of METP on plasma glucose levels of hyperglycemic rats (Mean±SD)

Treatment	0 day	1st day	3rd day	7th day
Diabetic control	286.3±3.2	281.4±1.2	275.3±2.9	269.2±3.2
Diabetic + Glibenclamide (1 mg kg ⁻¹)	287.9±5.7	264.8±3.9 ^b	233.4±5.2 ^b	201.2±4.2 ^b
Diabetic + METP (100 mg kg ⁻¹)	289.2±4.8	270.6±4.1 ^a	242.5±2.1	234.7±3.4
Diabetic + METP (200 mg kg ⁻¹)	288.1±3.9	268.9±3.3 ^b	239.3±4.1 ^b	209.6±3.7 ^b
Normal + METP (300 mg kg ⁻¹)	289.5±3.4	260.4±3.5 ^b	219.3±3.7 ^b	181.6±3.2 ^b

Values are in Mean±SD; n = 6; a: p<0.005, b: p<0.0001 vs. 0th day

Table 4: Effect of administration with *T. portulacastrum* and glibenclamide on serum lipid parameter level in diabetic rats (on 7th day)

Groups	TC	TG	HDL-C
	----- (mg dL ⁻¹) -----		
Diabetic Control	136.3±4.43	132.1±4.67	29.5±2.12
Diabetic + Glibenclamide (1 mg kg ⁻¹)	98.9±4.26 ^a	87.2±3.72 ^a	43.8±2.64 ^a
Diabetic + METP (100 mg kg ⁻¹)	121.4±3.94 ^a	119.2±3.73 ^a	35.4±2.84 ^a
Diabetic + METP (200 mg kg ⁻¹)	105.3±4.12 ^a	95.8±4.27 ^a	41.4±2.62 ^a
Normal + METP (300 mg kg ⁻¹)	99.1±4.53 ^a	88.8±3.72 ^a	43.5±2.02 ^a

Values are in Mean±SD; n = 6; a: p<0.0001 vs. normal control; (TC: Total Cholesterol; TG: Triglycerides; HDL-C: HDL cholesterol)

Effect of methanolic extract of *T. portulacastrum* on alloxan induced diabetic rats: In alloxan induced diabetic rats, the methanolic extract (METP) and glibenclamide produced significant antihyperglycemic effects (p<0.05) from day 1 onwards of their continuous administration and this antihyperglycemic effect was pronounced after 3, 5, 7 days of treatment (Table 3). In untreated diabetic rats, the plasma glucose levels on different days were significantly more (p<0.0001) than that of treated groups (group III, IV and V).

In alloxan-induced diabetic rats, there was a significant increase in the level of triglycerides (TG), total cholesterol (TG) and decreased HDL-C was observed. Continuous administration of the methanolic extract (300 mg kg⁻¹) of *T. portulacastrum* led to significant decrease in the level of triglycerides, total cholesterol in the diabetic rats, while increasing the level of HDL-C (Table 4).

DISCUSSION

Diabetes mellitus is possibly the world's largest growing metabolic disease and as the knowledge on the heterogeneity of this disorder is advanced, the need for more appropriate therapy increases (Bailey and Day, 1989). Considerably, large number of hypoglycemic/antidiabetic plants and herbs are known through folklore but their introduction into modern

therapy waits pharmacological testing by modern methods. The Study of such medicines might offer a natural key to unlock a diabetologist's pharmacy for the future.

The present study results suggest that the methanolic extract of TP whole plant exhibited significant hypoglycemic, antihyperglycemic and hypolipidemic activities in normal and alloxan induced diabetic rats. Fasting blood glucose level in diabetic rats is an important basal parameter for monitoring diabetes (Rajkumar *et al.*, 2005) and it has shown that the METP causes the hypoglycemic and antihyperglycemic effect by reducing the fasting blood glucose level (Table 1, 2). The significant decrease in the levels of fasting blood glucose in diabetic rats treated with the METP may be by stimulation of the residual pancreatic mechanism, probably by increasing peripheral utilization of glucose (Erah *et al.*, 1996).

Prolonged administration of methanolic extract of *T. portulacastrum* lead to significant reduction in blood glucose levels. The hypoglycemic activity of the METP was due to the regeneration of pancreatic cells that were partially destroyed by alloxan and potentiation of insulin secretion from surviving b-cells of the islets of Langerhans (Suba *et al.*, 2004).

The methanolic extract may increased secretion of insulin from b-cells of pancreas and results in of this increased secretion of insulin stimulates fatty acid biosynthesis and also the incorporation of fatty acids into triglycerides in the liver and adipose tissue (Best and Taylor, 1989).

Diabetes is associated with hyperlipidemia (De-Sereday *et al.*, 2004). Alteration in the serum lipid profile is known to occur in diabetes and this is likely to increase the risk for coronary heart disease. A reduction in serum lipids, particularly of the LDL and VLDL fraction and triglycerides, should be considered as being beneficial for the long-term prognosis of these patients (Chattopadhyay and Bandyopadhyay, 2005). Lowering of blood glucose and plasma lipid levels through dietary modification and drug therapy seems to be associated with a decrease in the risk of vascular disease.

Moreover, supplementation of methanolic extract of *T. portulacastrum* produced significant beneficial effects in the lipid profile in normal and diabetic rats by reducing triglycerides, total cholesterol and increasing HDL levels significantly (Table 2, 4). This effect may be due to low activity of cholesterol biosynthesis enzymes and or low level of lipolysis which are under the control of insulin (Sharma *et al.*, 2003).

It is widely accepted that reduction in plasma HDL is a risk factor for developing atherosclerosis. HDL facilitates the translocation of cholesterol from the peripheral tissue, such as arterial walls to liver for

catabolism. The increase in HDL may slow down the atherosclerotic process (Nofer *et al.*, 2002). Increased levels of HDL (cardio protective lipid) after administration of TP extract concluded the cardio protective effect of METP.

The higher lipid levels seen in diabetic rats was due to increased mobilization of free fatty acids from peripheral depots and also due to lipolysis caused by hormones (Ei-Soud *et al.*, 2007; Nikkila and Kekki, 1973). The methanolic extract may cause the regeneration of the b-cells of the pancreas and potentiation of insulin secretion from surviving b-cells; the increase in insulin secretion and the consequent decrease in blood glucose level may lead to inhibition of lipid peroxidation and control of lipolytic hormones. In this context, a number of other plants have also been reported to have antihyperglycemic, antihyperlipidemic and insulin stimulatory effects (Fernandes *et al.*, 2007; Ramalingam and Pari, 2005).

In conclusion, the methanolic extract of *T. portulacastrum* produced significant hypoglycemic, antihyperglycemic and antihyperlipidemic activities in normal and alloxan induced diabetic rats. Further studies, are needed to identify the chemical constituents of the methanolic extract of *T. portulacastrum* that may be responsible for the hypoglycemic and hypolipidemic activity.

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