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RESEARCH ARTICLE

# Antihyperlipideamic effect of *Solanum trilobatum* L. leaves extract on streptozotocin induced diabetic rats

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**ABSTRACT**

The present study was undertaken as antihyperlipidaemic effect of an aqueous leaves extract of *Solanum trilobatum* L. on streptozotocin (STZ)-induced diabetic rats. Repeated administration of the leaves extract of *S.trilobatum* (100mg and 200mg/kg b.w) for 21 days resulted in significant reduction in serum and tissue triglycerides, cholesterol, free fatty acids and phospholipids in STZ diabetic rats. In addition to that, significant ($P<0.05$) decrease in high density lipoprotein (HDL) whereas significant increase ($P<0.05$) in low density lipoprotein (LDL) and very low density lipoprotein (VLDL) were observed in STZ diabetic rats, which were normalized after 21 days of leaves extract treatment. The leaves extract at a dose of 200mg/kg.body wt. showed much significant antihyperlipidaemic effect than at the dose of 100mg/kg-body wt. The study was compared with a standard drug, tolbutamide (100mg/kg b.w).

**Keywords:** Antihyperlipidaemic effect, cholesterol, Lipoprotein levels, Solanum trilobatum, Streptozotocin.

## 1. INTRODUCTION:

Diabetes mellitus (DM) is a metabolic disorder, which affects carbohydrate, fat and protein metabolism. They are representing as a various group of disorders having hyperglycemia, which is due to impaired carbohydrate consumption resulting from a defective or lacking insulin secretory response [1]. Along with hyperglycemia and aberration in serum lipids [2], [3], diabetes is associated with other complicated diseases like micro and macrovascular disorder, which are the most important causes of morbidity and death in diabetic subjects [4]. Now a- days, there are different groups of various oral hypoglycemic agents for clinical use, having characteristic profiles of side effects [5], [6]. Hence, management of diabetes without any side effects is still being a challenge to the medical system. This leads to rising demand for natural products with antidiabetic activity and less side effects. Indian traditional medicines belong to one of the richest medicinal systems among those available in the world. In accordance with the recommendations of the WHO expert committee on Diabetes mellitus [7], an investigation of hypoglycemic agents of plant origin used in traditional medicine seems important.

*Solanum trilobatum* (Solanaceae) is a common shrub, called as 'Tuduvelai', used in various diseases distributed over Gujarat, Deccan, Ceylon, North Circars, Carnatic and Malay Peninsula [8]. In Indian Ayurveda and Siddha medicinal system, the roots and leaves are bitter and prescribed in consumptive cases of acute and chronic bronchitis [8], [9], asthma [10], [11], cough [12], and analgesic action [13]. The herbs are useful in treating indigestion, spermatorrhoea, tuberculosis and disease of ear [14].

Pharmacological investigations have demonstrated that S. trilobatum possess an antibacterial, antifungal & anticancer activity [15]-[22], antioxidant activity [23], hepatoprotective activity [19], anti-ulcerogenic activity [24] and anti-inflammatory activity [25], [26]. The leaves of the plant possess calcium, iron, phosphorus, fat,



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carbohydrates, crude fibre and minerals [27]. The whole plant contains alkaloids, phenolics, flavanoides, sterols, saponins and their glycosides [24], solasodine and β-solamarine [28].

In the current literature, there is not much data concerning the effect of *S.trilobatum* on the lipid parameters and their activities, which are abnormally altered due to DM. Therefore, the present study has been planned to investigate the leaves of *S.trilobatum* influences lipid parameters in STZ induced diabetic rats and to compare it with tolbutamide as a reference standard.

## 2. MATERIALS AND METHODS

### Plant Material

The leaves of *Solanum trilobatum* L. was collected during Jan-Feb 2003 from Local Market, Namakkal, Tamilnadu. The plant was authenticated and comparison with reference specimens preserved at the Rapinat Herbarium, St. Joseph's College, Tiruchirapalli. Voucher Herbarium specimens are kept in the Herbarium for future references.

### Animals

Albino rats of Wister strain weighing about 150-200gms were used in the study. Animals were obtained from Animal house, Bharathidasan University, Tamilnadu and kept under standard laboratory conditions in 12h light/dark cycles at 25-280C and 60-80% relative humidity. Animals were reared with robust health by providing pellet diet (Lipton, India) and water ad libitum. Six rats were housed per cage, to provide them sufficient space and to avoid unnecessary morbidity and mortality. All studies were conducted in accordance with the National Institute of Health guide [29]. The study was approved by the ethics committee CPCSEA and ethical norms were strictly followed during all experimental

**procedures.**

### Preparation of plant extract

Fresh leaves of *Solanum trilobatum* (500g) were washed and homogenized in a waring blender with 2 litres of distilled water. The extraction was carried out in a cold room (20o ± 1oC) with constant stirring over night. The homogenate was then squeezed through cheese cloth and centrifuged at 1200g for 10 min at 4oC. The supernatant being the S. trilobatum leaves extract (yield 210 w/w) was decanted and kept at 4oC until used**.**

### Chemicals

Streptozotocin (STZ) was obtained from Sigma Chemical Co, (St. Louis, MO, USA). All other chemicals used were of analytical grade.

### Induction of diabetes

STZ (Sixty mg/kg) dissolved in saline was injected to tail vein of animals intraperitoneally. After a fortnight rats with moderate diabetes having glycosuria (indicated by Benedict's test for urine) and hyperglycemia, i.e. with blood glucose levels of 200-280 mg per 100ml were used for the investigation. Blood was collected from eyes (venous pool).

### Assessment of antihyperlipidaemic response of extract in STZ induced diabetic rats

The diabetic rats were divided in to 5 groups of 6 animals each. Group I received vehicle alone and served as control. Group II received STZ (60mg/kg/i.p) dissolved in 0.1M-citrate buffer. Group III & Group IV received the aqueous leaves extract of *S.trilobatum* (100mg, 200mg/kg/p.o) suspended in vehicle followed by single intra-peritonial administration of STZ. Group V received Tolbutamide (100mg/kg/p.o) followed by single intraperitonial administration of STZ.

### Blood and tissues collection

After 21 days of treatment, the animals were killed by cervical dislocation. Blood was collected in heparinized tubes, and the serum was separated by centrifugation. The liver, kidney, pancreas and cardiac tissues were quickly removed, washed in ice cold, isotonic saline and blotted individually on ash-free filter paper and organ weights were measured. The tissues were then homogenized in 0.1M Tris – HCl buffer, pH 7.4. The homogenate was used for the estimations of lipid profile and other parameters.

### Biochemical analysis

The extraction of serum lipids was measured by Folch et al. [30] and phospholipid was estimated by Zilversmit and Davis [31]. The serum and tissue free fatty acids were measured by Falholt et al. [32]. The total cholesterol is measured using diagnostic kits, Boehringer Mannheim, Germany. The triglycerides were estimated by the method of Foster and Dunn [33] and HDL Cholesterol was estimated by the method of Wilson and Spiger [34] & Perekh and Jung [35]. The VLDL Cholesterol was calculated using the formula (TG/5) mg/dl. The serum LDL Cholesterol was estimated by the method of Friedewald et al. [36] and the total lipids was estimated by Phillips et al. [37].

### Statistical analysis

Values were presented as Means ± SD. Data were analyzed using analysis of variance (ANOVA) and group means were compared with Duncan's multiple range test (DMRT) using SPSS (Statistical Package for Social Science).

## 3. RESULTS

The present investigation was carried out to evaluate the effect of *S.trilobatum* leaves extract on lipid content in the serum, liver, pancreas, kidney and cardiac tissues of control and streptozotocin (STZ) induced diabetic rats (Table 1-5).



 

| Groups | Cholesterol (mg/dl) | Free fatty acid (mg/dl) | Phospholipids (mg/dl) | Triglycerides (mg/dl) |
|---|---|---|---|---|
| I | 105.68 ± 12.35[a] | 65.3 ±6.29[c] | 139.52 ± 9.68[a] | 62.33 ± 7.56[a] |
| II | 346.35 ± 17.56[b] | 144.2 ± 9.48[b] | 242.3 ± 11.98[b] | 178.36 ± 9.56[b] |
| III | 168.28 ± 11.67[c] | 79.39 ± 5.39[c] | 177.3 ± 10.54[c] | 118.56 ± 6.49[c] |
| IV | 126.22 ± 9.11[d] | 66.25 ± 5.78[a] | 155.56 ± 9.98[d] | 89.4 ± 6.14[d] |
| V | 109.68 ± 9.9[a] | 64.59 ± 6.43[a] | 140.2 ±8.2[a] | 69.56 ± 7.56[a.] |

**Table 1: Effect of leaves extract of *Solanum trilobatum* on serum lipid profile in control and experimental animals**

Values are given as Mean ± SD for groups of six animals each. Values not sharing a common superscript (a, b, c and d) differ significantly at P< 0.05, Duncan's Multiple Range Test (DMRT).

| Groups | Cholesterol (mg/g wet wt of tissue) | Free fatty acid (mg/g wet wt of tissue) | Phospholipids (mg/g wet wt of tissue) | Triglycerides (mg/g wet wt of tissue) |
|---|---|---|---|---|
| I | 4.16 ± 1.33[a] | 10.22 ± 2.89 | 28.46 ± 6.98[a] | 19.69 ± 3.69[a] |
| II | 8.98 ± 1.56[b] | 19.36 ± 3.23[b] | 62.51 ± 7.8[d] | 40.39 ± 4.89[b] |
| III | 6.15 ± 1.67[c] | 14.87 ± 3.22[c] | 39.56 ± 5.67[c] | 25.73 ± 4.28[c] |
| IV | 4.4 ± 1.12[d] | 10.07 ± 2.94[a] | 29.67 ± 4.67[a] | 20.18 ± 3.46[a] |
| V | 4.26 ± 1.18[a] | 9.98 ± 2.33[a] | 28.69 ± 6.22[a] | 19.05 ± 3.26[a] |

**Table 2: Effect of leaves extract of *Solanum trilobatum* on lipid content in liver of control and experimental animals**

Values are given as Mean ± SD for groups of six animals each. Values not sharing a common superscript (a, b, c and d) differ significantly at P< 0.05, Duncan's Multiple Range Test (DMRT).

| Groups | Cholesterol (mg/g wet wt of tissue) | Free fatty acid (mg/g wet wt of tissue) | Phospholipids (mg/g wet wt of tissue) | Triglycerides (mg/g wet wt of tissue) |
|---|---|---|---|---|
| I | 6.29 ± 1.1[a] | 6.24 ± 2.83[a] | 15.89 ± 4.5[a] | 6.59 ± 1.29[a] |
| II | 12.49 ± 2.39[b] | 17.29 ± 3.79[b] | 34.56 ± 6.87[b] | 14.23 ± 2.43[b] |
| III | 7.29 ± 2.69[c] | 9.54 ± 2.56[c] | 24.6 ± 5.17[c] | 10.53 ± 2.22[c] |
| IV | 6.43 ± 2.74[a] | 7.23 ± 2.46[d] | 16.23 ± 3.79[d] | 7.82 ±2.12[d] |
| V | 6.18 ± 2.56[a] | 6.56 ± 2.15[a] | 15.55 ± 3.4[a] | 6.94 ± 2.43[a] |

**Table 3: Effect of leaves extract of *Solanum trilobatum* on lipid content in kidney of control and experimental animals**

Values are given as Mean ± SD for groups of six animals each. Values not sharing a common superscript (a, b, c and d) differ significantly at P< 0.05, Duncan's Multiple Range Test (DMRT).

| Groups | Cholesterol (mg/g wet wt of tissue) | Free fatty acid (mg/g wet wt of tissue) | Phospholipids (mg/g wet wt of tissue) | Triglycerides (mg/g wet wt of tissue) |
|---|---|---|---|---|
| I | 2.16 ± 0.95[a] | 7.28 ± 2.14[a] | 9.23 ± 2.24[a] | 5.45 ± 1.91[a] |
| II | 5.13 ±1.35[b] | 19.46 ± 3.53[b] | 28.23 ± 4.18[b] | 9.07 ± 2.67[b] |
| III | 3.45 ± 1.01[c] | 12.4 ± 2.39[c] | 16.23 ± 4.22[c] | 6.83 ± 2.65[c] |
| IV | 2.43 ± 0.96[d] | 8.0 ± 2.38[d] | 11.53 ± 3.12[d] | 5.05 ± 2.33[a] |
| V | 2.16 ± 0.9[a] | 7.55 ± 3.44[a] | 11.75 ± 2.94[d] | 5.02 ± 1.89[a] |

**Table 4: Effect of leaves extract of *Solanum trilobatum* on lipid content in cardiac tissue of control and experimental animals**

Values are given as Mean ± SD for groups of six animals each. Values not sharing a common superscript (a, b, c and d) differ significantly at P< 0.05, Duncan's Multiple Range Test (DMRT).



 

| Groups | Cholesterol (mg/g wet wt of tissue) | Free fatty acid (mg/g wet wt of tissue) | Phospholipids (mg/g wet wt of tissue) | Triglycerides (mg/g wet wt of tissue) |
|---|---|---|---|---|
| I | 7.33 ± 1.63[a] | 24.19 ±2.36[a] | 135.2 ± 11.52[a] | 3.3 ± 0.9[a] |
| II | 15.49 ± 3.5[b] | 49.52 ± 5.76[b] | 229.5 ± 12.97[b] | 6.6 ± 1.2[b] |
| III | 10.5 ± 3.79[c] | 39.54 ± 5.74[c] | 166.39 ± 10.1[c] | 4.8 ± 1.9[c] |
| IV | 7.69 ± 2.36[d] | 28.2 ± 4.37[d] | 145.33 ±9.69[d] | 3.6 ± 0.9[d] |
| V | 7.12 ± 2.56[a] | 26.6 ± 4.94[ad] | 139.55 ± 9.22[a] | 3.3 ± 0.4[a] |

**Table 5: Effect of leaves extract of *Solanum trilobatum* on lipid content in pancreas of control and experimental animals**

Values are given as Mean ± SD for groups of six animals each. Values not sharing a common superscript (a, b, c and d) differ significantly at P< 0.05, Duncan's Multiple Range Test (DMRT).

Serum and tissue cholesterol, triglycerides, phospholipids and free fatty acids were significantly higher in the STZ treated rats compared to those in normal rats. The continuous treatment with the leaves extract of *S.trilobatum* brought down the above lipid parameters in the diabetic rats to almost normal levels.

The effect of leaves extracts of *S.trilobatum* on serum HDL, LDL, VLDL and lipoprotein of control and STZ induced diabetic animals are shown in Table-6.

| Groups | HDL-C | LDL-C | VLDL-C | Serum total lipids |
|---|---|---|---|---|
| I | 35.25 ± 5.21[a] | 44.33 ± 6.49[a] | 11.55 ± 2.96[a] | 236.45 ± 12.9[a] |
| II | 19.32 ± 4.6[b] | 145.32 ± 10.26[b] | 19.53 ± 3.76[b] | 690.4 ± 39.53[b] |
| III | 26.5 ± 5.28[c] | 72.56 ± 10.5[c] | 14.89 ± 3.33[c] | 365.22 ± 14.5[c] |
| IV | 31.3 ± 4.89[d] | 52.33 ± 5.21[d] | 11.22 ± 3.80[a] | 277.35 ± 25.46[d] |
| V | 32.4 ± 5.69[d] | 51.56 ± 6.46[d] | 11.16 ± 2.49[a] | 269.36 ± 19.22[a] |

**Table 6: Effect of leaves extract of *Solanum trilobatum* on serum lipoprotein of control and experimental animals**

Values are given as Mean ± SD for groups of six animals each. Values not sharing a common superscript (a, b, c and d) differ significantly at P< 0.05, Duncan's Multiple Range Test (DMRT).

Serum HDL levels were significantly lowered in STZ induced diabetic rats. But LDL, VLDL and lipoproteins were significantly elevated in the STZ treated rats compared to those in control rats. The treatment with *S.trilobatum* leaves extract carried down these lipoproteins in the diabetic rats to nearly normal levels.

The effect of leaves extract of *S.trilobatum* on erythrocyte lipid content in control and experimental animals are shown in Table-7.

| Group | Cholesterol (µg/mg protein) | Phospholipids (µg/mg protein) | C/PL ratio |
|---|---|---|---|
| I | 155.77 ± 11.12[a] | 292.3 ± 14.45[a] | 0.53 ± 0.05[a] |
| II | 98.46 ± 9.23[b] | 208.54 ± 19.47[b] | 0.47 ± 0.19[b] |
| III | 125.25 ± 9.23[c] | 255.46 ± 13.74[c] | 0.49 ± 0.20[c] |
| IV | 139.52 ± 9.45[d] | 282.86 ± 16.44[d] | 0.49 ± 0.16[a] |
| V | 138.25 ± 10.9[d] | 283.58 ± 15.92[d] | 0.48 ± 0.11[a] |

**Table 7: Effect of leaves extract of *Solanum trilobatum* on erythrocyte lipid content in control and experimental animals**

Values are given as Mean ± SD for groups of six animals each. Values not sharing a common superscript (a, b, c and d) differ significantly at P< 0.05, Duncan's Multiple Range Test (DMRT).

Cholesterol and phospholipids levels were significantly lowered in STZ induced diabetic rats. But the treatment of *S.trilobatum* leaves extract significantly increased these erythrocyte cholesterol and phospholipids levels in the diabetic rats, which were normalized after 21 days of treatment. The ratio of cholesterol and phospholipid was significantly higher in STZ induced diabetic rats. The treatment of leaves extract reversed the increased levels of these lipid ratios and normalized soon after.

## 4. DISCUSSION

Diabetes is associated with profound alterations in the plasma lipid, triglycerides and lipoprotein profile and with an increased risk of coronary heart disease [38- 40]. High level of total cholesterol is one of the major factors for coronary heart diseases (National Cholesterol Education Program Expert Panal 1994) and it is well known that hyperlipidemia and the incidence of atherosclerosis is increased in diabetes [41]. The liver and some other tissues participate in the uptake, oxidation and metabolic conversion of free fatty acids, synthesis of cholesterol and phospholipids and secretion of specific classes of plasma lipoprotein. Lowering of serum lipid levels through dietary or drug therapy seems to be associated with a decrease in the risk of vascular disease and related complications [42], [43].



 

Many herbs and plant products have been shown to have antihyperglycemic and antihyperlipidemic properties [44, 45]. Diabetes is generally associated with hyperlipidemia, which has been found to be mainly due to overproduction of VLDL-triglycerides in type 2 diabetes [46-49], besides abnormalities in lipid metabolism, characterized by severe hypertriglyceridemia and hypercholesterolemia [50-53]. The present studies show that the leaves extract possesses definite hypotriglyceridemic and antiatherogenic properties in STZ diabetic rats after 3 weeks of treatment.

The repeated administration of leaves of *S.trilobatum* extract for a period of 21days resulted in a significant decrease in lipid parameter levels of various tissues when compared to the diabetic control. It is not known whether *S.trilobatum* has a direct effect on lipids or the present hypolipidemia is achieved due to controlled hyperglycemia.

Many studies have shown that the increase in fatty acid delivery to the liver leads to increased triglyceride synthesis accompanied by increases in VLDL secretion [54-56]. It is an important factor in controlling the hepatic triglyceride secretion, and inhibition of protein synthesis has been shown to reduce VLDL, triglyceride secretion [57], [58]. Additionally, insulin is a well-known acute inhibitor of VLDL secretion [59], [60], and insulin resistance is associated with increased VLDL, triglyceride secretion [46], [61], [62].

## 5. CONCLUSION

From this study it has been concluded that the aqueous extract of the leaves of *Solanum trilobatum* benefits for hyperlipidaemia due to diabetes. Further works are needed to identify the active principle(s) present in the plant and elucidate its possible mode of action and that is in progress.

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