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IN VITRO AND *IN VIVO* STUDY ON *TINOSPORA CORDIFOLIA* EXTRACT AS AN ANTIDIABETIC AGENT IN RAT

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ABSTRACT – Clinical trials have shown that some plants are useful as antidiabetic agents. One such plant is *Tinospora cordifolia.* Oral administration of the organic extract of *T. cordifolia* roots for 6 weeks resulted in a significant reduction in blood and urine glucose in alloxan diabetic rats. *Tinospora cordifolia* extract interferes with cellular metabolic oxidative mechanisms .In all diabetic patients, treatment should aim to lower blood glucose to near normal level. The present investigation fulfills this statement by producing a significant fall in blood glucose levels in organic extract administered STZ diabetic rats.

Keywords : *Tinospora cordifolia,* antidiabetic agent, rat.

INTRODUCTION

In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin, less side effects, more effective, low cost, etc (Das, 1990) . Many traditional medicines in use are derived from medicinal plants, minerals and organic matter (ADA, 1997; Baynes, 1991; Bailey *et al,* 1989) . *Tinospora cordifolia* is a large, glabrous, deciduous climbing shrub belonging to the family Menispermaceae (Nadkarni and Nadkarni, 1954; Anonymous, 1976). It is widely distributed throughout India and commonly known as Guduchi. Oral administration of the organic extract of *Tinospora cordifolia* roots for 6 weeks resulted in a significant reduction in blood and urine glucose in alloxan diabetic rats. The extract also prevented a decrease in body weight (Hu *et al,* 2003; Branstrup *et al,* 1957; Lewis *et al,* 1949). *T. cordifolia* is widely used in Indian ayurvedic medicine for treating diabetes mellitus. In this paper we have studied extensively about i*n vitro* and *in vivo* study of this extract against diabetic animal model.

MATERIALS AND METHODS

Streptozotocin was purchased from Sigma-Aldrich, USA. All chemicals used in present study are of analytical grade and purchased from Sigma. All the solvents were used after distillation. TLC was run on the silica gel coated aluminium sheets (silica gel 60 F254, E Merck, Germany) and visualized under UV light.

Plant materials: The roots of *T. cordifolia* were collected in winter season (Nov - Dec, 2009) from the botanical garden of M.M.H. College Campus, Ghaziabad. The plant was taxonomically identified by the Department of Botany, M.M.H. College, Ghaziabad, U.P.(India).The roots of matured *T. cordifolia* were freshly collected and chopped, shade dried and coarsely powdered. The organic extraction were done at the powder was defatted with petroleum ether (60 -80°C) then extracted with hexane using Soxhlet extractor. The extracts were dried under reduced pressure using a rotary vacuum evaporator. The percentage yield was 7% w/w and the extracts were kept in refrigerator for further use. A dose determination process was carried out by administering 100 mg/kg b.w.p.d, 150 mg/kg b.w.p.d, 200 mg/kg b.w.p.d, 250 mg/kg b.w.p.d, 300 mg/kg b.w.p.d and 350 mg/kg b.w.p.d dissolved in 1 ml 0.3% carboxy methyl cellulose.

To demonstrate the antidiabetic property of TCS and its effect on blood glucose levels, male albino wistar rats aged 7 to 8 weeks (150 - 200 g) bred in the animal division were used. Male albino wistar rats are being maintained as per the guidelines issued by the concerned authorities. These animals were provided by Central Animal House, Maulana Azad Medical College, Delhi and were housed at 22, Sham Nath Marg. Animals were kept in animal house at an ambient temperature of 25 - 30°C and 45 - 55 % relative humidity with a 12 h each of dark and light cycle. The experimental protocol has been approved by the institutional animals ethics committee and by the regulatory body of the government.

Experimental

Induction of experimental diabetes

Table1

S.N.	Group	Glucose (mg/100 ml)
1	Normal	76.5 ± 9.5
2	Diabetic Control	275.5 ± 21.3
3	Diabetic + TCR Et (2.0 g/Kg, p.o.)	116.5 ± 8.3
4	Diabetic + TCR Et (4.0 g/Kg, p.o.)	111.6 ± 15.8
5	Diabetic + TCR Et (6.0 g/Kg, p.o.)	254.2 ± 19.1
6	Diabetic + glibenclamide (0.5mg/Kg, p.o.)	156.5 ± 12.4
7	Diabetic + Insulin (5 U/Kg, i.p.)	86.2 ± 10.5

Values are given as mean±S.D. in each group.
Diabetic control is compared with normal;
Experimental groups are compared with diabetic control;
Values are statistically significant at
P<0.001 as compared with normal;
P<0.001 as compared with diabetic control;
Treatment duration is 50 days.

The animals were fasted overnight and diabetes was induced by a single intraperitoneal injection of a freshly prepared solution of streptozotocin (55 mg/kg b.w.p.d) in 0.1 M citrate buffer (pH 4.5) (Sekar *et al,* 1990). Control rats were injected with citrate buffer alone. On the third day of STZ-injection, the rats were fasted for 6 h and blood was taken from tail artery of the rats (Brucelin *et al,* 1995). Rats with moderate diabetes having hyperglycemia (i.e. with blood glucose of 250 - 400 mg/dl) were taken for the experiment. The blood was collected from sinocular puncture. The rats were kept for 15 days to stabilize the diabetic condition. In the experiment, a total of 36 rats (30 diabetic surviving rats and 6 normal rats) were used.

Biochemical analysis

Fasting blood glucose was estimated by the oxidase/peroxidase method. Glycosylated hemoglobin was estimated using the diagnostic kit from Biosystems. Hexokinase and glucose-6-phosphatase were assayed by standard protocols.

RESULT AND DISCUSSION

The organic extract gives a great change in all groups of animal model as in table1.

For all the parameters studied, TCREt at doses of 2.0 and 4.0 g kg-1 body weight showed significant effect. TCREt at higher doses (6.0g kg-1) did not show any significant effect.

The effect of TCREt was more effective than glibenclamide. Insulin brought back all the parameters to near normal.The possible mechanism by which organic extract brings about its hypoglycemic action may be by induction of pancreatic insulin secretion from cells of islets of Langerhans or due to enhanced transport of blood glucose to peripheral tissue. This is a clear evidenced from the data with significant (p- value < 0.001) decrease in plasma glucose level of diabetic rats treated with organic extract.

Acute toxicity studies revealed the non-toxic nature of the organic extract of *T. cordifolia*. Experiment was carried out on normal healthy male rats. No mortality was observed in the organic extract-treated rats and behaviour of the treated rats also appeared normal. There was no lethality or toxic reaction found at any dose selected until the end of the study.

Administration of extracts to normal animals does not alter the blood glucose level which is evidenced .The increased blood glucose in the diabetic condition is gradually reduced and almost nearer to normal after 50 days by the administration of TCS extracts.

CONCLUSIONS

Root extract of *Tinospora cordifolia* has insulin-like effects in targets tissues, increases insulin secretion *in vitro*, and improves glucose tolerance *in vivo*. These results support the traditional use of *Tinospora cordifolia* as an antidiabetic herb. However, further and specific studies are needed for the identification of the active constituents/compounds found in *Tinospora cordifolia.* The root extract of *Tinospora cordifolia* extract may be the basis for the development of new antidiabetic drugs.

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