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Original Research Article

Improvement in Glucose Tolerance due to Tinospora Cordifolia (Willd.)

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ABSTRACT

Background: As an alternative medicine to treat diabetes mellitus, many herbal drugs are being studied throughout the world. In the present study, an attempt was made to investigate the effect of *Tinospora cordifolia* (Willd.) on glucose tolerance in streptozotocin diabetic albino rats as well as type II diabetic patients. **Primary study objective:** To study the effect of aqueous extract of *Tinospora cordifolia* on glucose tolerance in type II diabetic patients and streptozotocin diabetic albino rats to explore the probable mechanism by which it acts as an anti diabetic drug, by measuring serum insulin levels and by studying histology of endocrine pancreas. **Methods:** Oral glucose tolerance test and serum insulin concentration was studied in twenty four non-insulin dependent diabetics and same number of streptozotocin induced diabetic albino rats. An aqueous extract of *Tinospora cordifolia* in two different dosages (200 mg/ kg b.w and 400 mg/ kg b.w) was given orally to the different groups of animals and the diabetic patients before giving the glucose load. **Participants:** Twenty four non-insulin dependent diabetics and same number of streptozotocin induced diabetic albino rats. **Intervention:** Glucose tolerance test in type II diabetic patients and streptozotocin diabetic albino rats to explore the probable mechanism by which *Tinospora cordifolia* acts by measuring serum insulin levels and histology of endocrine pancreas. **Results:** The present study clearly showed that the *Tinospora cordifolia* treatment has significantly ($p < 0.05$) reduced the blood glucose concentration during a 50 g oral glucose tolerance test in diabetic patients and 2 g/ kg b.w. oral glucose tolerance test in diabetic rats. However, serum insulin levels were unchanged due to *Tinospora cordifolia* treatment in diabetic animals. **Conclusions:** Our results indicated an improvement in glucose tolerance in diabetic patients as well as in diabetic animals due to *Tinospora cordifolia,* though this improvement in glucose tolerance was not associated with an increase in serum insulin responses in the diabetic animals.

Key words: *Tinospora cordifolia*; Diabetes mellitus; Anti-diabetic; Streptozotocin; Glucose tolerance.

INTRODUCTION

Diabetes mellitus is a metabolic disorder, which affects the human beings all over the world and yet to be understood fully the management of diabetic complications. Impairment in glucose

tolerance is the hallmark in diabetes mellitus. [1] In recent years, the herbal remedy for the unsolved medical problems is gaining importance in research field. Thus, this study was undertaken to explore the effect of aqueous extract of *Tinospora cordifolia* on oral glucose tolerance test in non-insulin dependent diabetic patients as well as in streptozotocin induced diabetic rats.

Tinospora cordifolia (Willd.) Miers ex Hook. F. & Thoms. (TC) belongs to the Menispermaceae family and known as Gulancha in English, Guduchi in Sanskrit, and Giloya in Hindi. It is a large, glabrous, deciduous climbing succulent shrub, commonly found in hedges. It has been known for long in Ayurvedic literature as a tonic, vitalizer and as a remedy for diabetes and other metabolic disorders. [2]

MATERIALS AND METHODS

Patients and experimental animals

We studied glucose tolerance during a 50 g of oral glucose load in twenty four non-insulin dependent diabetic outpatients (sixteen men and eight women) of age group 48 to 56, who are visiting Ayurvedic clinic, seeking the supplementary herbal drugs in addition to their routine oral anti-hyperglycemic drugs.

Twenty four albino rats of inbred *Wistar* strain (body wt. 180-210 g) were used in this study. Animal ethical committee clearance was obtained from Institutional Animal Ethics Committee (IACE No. 08/004/02). The animals were fed on pellet diet (Hindustan Lever Ltd. Bangalore) and water ad libitum during the study period.

Experimental induction of diabetes in rats

To induce diabetes, the rats were fasted for 16 hours and injected with freshly prepared streptozotocin (STZ) (Sigma chemicals, USA) at the dose of 55 mg / kg b.w. intravenously in 0.1 M Citrate buffer of pH 4.5. [3] Control animals were received citrate buffer alone. Diabetes status was confirmed by estimating the fasting blood glucose levels and urine glucose (Benedict's test) after 72 hours of STZ injection. Diabetic animals showing fasting blood glucose levels above 250 mg/dl were selected for this study.

Plant material

Tinospora cordifolia stem was collected fresh from forest areas in Udupi-district, Karnataka state, South India and dried in shade and then powdered. The plant was identified by Professor and Head, Department of Botany, Mangala Gangothri, Mangalore University. A specimen (Voucher No. 31) was deposited in the botany department museum of University. The powdered materials were kept in an air tight container in a refrigerator until the time of use.

Extraction

Aqueous extract of *Tinospora cordifolia* was prepared according to the standard extract procedure. [4] The yield of extracts was approximately 8.5%.

Experimental protocol

Patients, who were selected for this study, have omitted their routine anti-hyperglycemic drugs for 48 hours and were fasted and did not smoke on the day before test. These patients were divided in to three groups consisting of eight in each group. First group was considered as untreated diabetic control group. Second group received 200 mg/ kg b.w. of *Tinospora cordifolia* aqueous extract orally, dissolved in 50 ml of water and third group with 400 mg/ kg b.w. of aqueous extract. Control group received 50 ml of water alone. All these patients (Group second and third) received this extract 30 minutes before giving 50 g of oral glucose load. Fasting blood glucose levels were estimated before giving drug and glucose load (zero hour) as well as after giving glucose load in venous

blood sampled every half hour for two hours.

All the experimental animals were divided into three groups with each group consists of eight animals as follows: Group 1- Untreated diabetic control, Group 2- Diabetic rats received with 200 mg /kg b.w. of aqueous extract of TC. Group 3- Diabetic rats received with 400 mg/kg b.w. of aqueous extract of TC. All these animals were fasted over night and fasting blood glucose and serum insulin levels were estimated. Oral glucose load of 2 g/ kg b.w. [5] was given 30 minutes after giving TC extract (Group- 2 and 3) and water alone (Group-1) through oral intubations. Blood glucose and serum insulin levels were estimated in all these experimental animals at different intervals as above. Sodium pentathol was used as an anesthetic agent for blood sampling from jugular vein.

Fasting blood glucose was estimated by glucose oxidase method. [6] Serum insulin levels were assayed by using standard Mercodia Rat Insulin ELISA enzyme immunoassay kit by Mercodia, Sweden, Cat. No-10-1124-01.

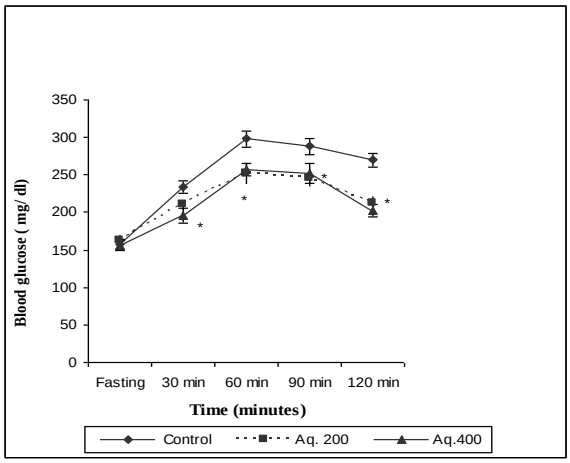
Statistics analysis

Statistical significance between the different groups was determined by One way Analysis of Variance (ANOVA) followed by Tukey's multiple comparisons by fixing the P value as $p< 0.05$.

RESULTS

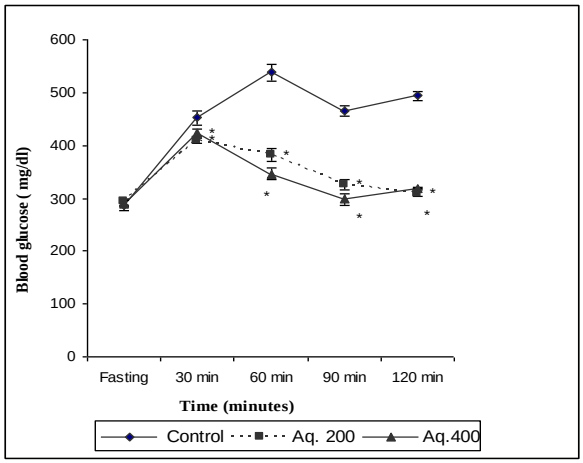
Aqueous extract of *Tinospora cordifolia* in both the dosages (200 mg and 400 mg/kg b.w) significantly reduced the blood glucose levels and improved the glucose tolerance in diabetic patients 60 to 120 minutes after giving glucose load compared to untreated control group, who received the water alone (Fig.1). Maximum reduction in blood glucose levels was observed with 400 mg/ kg b.w. dosage 120 minutes after giving the glucose load. Similar results were also observed in *Tinospora cordifolia* treated diabetic rats (Fig. 2). Here, the maximum reduction in blood glucose levels was observed with 400 mg/ kg b.w. dosage 90 minutes after giving the glucose load. This fall in blood glucose levels was persisting. However, serum insulin levels in these treated rats did not change significantly due to treatment, when compared to untreated animals (Table. 1).

Fig.1. Effect of aqueous extract of *Tinospora cordifolia* on oral glucose tolerance test in diabetic patients.



Data expressed as Mean ± SD. (n=8) $p< 0.05$.
* Control Vs Tinospora treated groups.

Fig.2. Effect of aqueous extract of *Tinospora cordifolia* on oral glucose tolerance test in STZ diabetic rats.



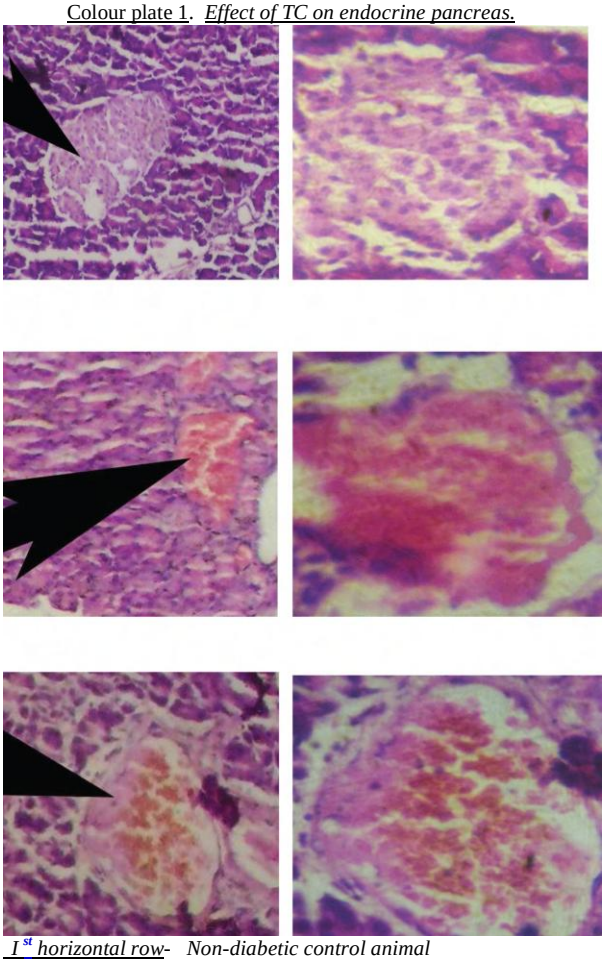
Data expressed as Mean ± SD. (n=8) $p< 0.05$.
* Control Vs *Tinospora* treated groups

Table.1. Effect of *Tinospora cordifolia* on serum insulin (pmol/L)

	Fasting	*30 minutes*	*60 minutes*	*90 minutes*	*120 minutes*
Control	147.50 ± 7.89	156.88 ± 5.1	152.04 ± 2.9	145.89 ± 4.4	149.90 ± 5.7
Aq. 200	139.66 ± 9.31	151.34± 4.8	150.01 ± 3.8	148.23 ± 3.9	154.21 ± 8.2
Aq. 400	144.55 ± 8.66	152.32 ± 3.2	147.59± 4.5	147.10 ± 6.9	143.34 ± 4.6

Data expressed as Mean ± SD. (n=8) p< 0.05.
* Control Vs *Tinospora* treated groups

Colour plate 1. *Effect of TC on endocrine pancreas.*



1st horizontal row- Non-diabetic control animal treated with 400 mg/kg b.w. of T C extract [10 X & 45 X].
2nd horizontal row- Untreated diabetic control [10 X & 45 X].
3rd horizontal row- Diabetic animal treated with TC [10 X & 45 X].

DISCUSSION

We have confirmed in our previous study, the anti- diabetic activity of *Tinospora cordifolia* in streptozotocin diabetic rats. Our study also shown that this anti-hyperglycemic potentiality of *Tinospora cordifolia* is not due to hyperinsulinaemia caused by its treatment. This novel finding was very much evident in the serum insulin essay and histological examination of endocrine pancreas in TC treated diabetic rats. [7] Histological study did not reveal any evidence of regeneration of beta cells of islets of Langerhans in diabetic animals (Colour plate 1). The present study has clearly shown that the *Tinospora cordifolia* improves glucose tolerance in diabetic patients as well as in diabetic animals. Though, the different dosages of aqueous extract of *Tinospora cordifolia* has improved the glucose tolerance in both the diabetic patients as well as in the diabetic animals, the efficacy of this anti-hyperglycemic effect can't be compared since there is a substantial differences in these two groups as per etiology, signs and symptoms and line of treatment of diabetes mellitus are considered.

As serum insulin concentrations were not increased after this treatment in diabetic rats, *Tinospora cordifolia* may directly influence hepatic or peripheral glucose disposal. *Tinospora cordifolia* has been used extensively in fringe medicine without serious side effects and merits further study.

CONCLUSION

The present study has clearly showed that the aqueous extract of *Tinospora cordifolia* improves glucose tolerance in both diabetic patients as well as in streptozotocin diabetic rats during an oral glucose load. However, this improvement in glucose tolerance is not due to its ability to increase the insulin secretion, which was evident by animal study. For Ayurvedic physicians, who are treating diabetics with herbal drugs, it is desirable to aware this property of *Tinospora cordifolia*.

Conflict of interest

The authors have no conflicts of interest.

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