

Antidiabetic Potential of *Tinosporacordifolia* in Streptozotocin (STZ) induced diabetic wistar albino rats.

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Abstract

Background: *Tinosporacordifolia* is an important medicinal plant containing different classes of phytochemicals with medicinal significance. The aim was to evaluate the antidiabetic potential of *T. cordifolia* in STZ induced diabetic mice in comparison with a currently used oral antidiabetic agent glimepride.

Materials and Method: There were 30 rats with fasting blood glucose (FBG) in the range 70-110 mg/dl were used for the study five groups each containing six mice, were induced diabetes with STZ (0.5mg/kg). The diabetic control group (0.5ml normal saline), Standard control group (2mg/kg glimepride), test group I (200mg/kg *T. cordifolia* extract), test group II (200 mg/kg *T. cordifolia* extract). Fasting glucose levels were recorded on day 0, 1, 7, 14 and 21. Statistical analysis was done by using MATLAB software and data were presented as mean \pm SEM

Results: *Tinosporacordifolia* extract showed that dependent antidiabetic action in both low dose (200 mg/kg) and high dose group (400 mg/kg). Antidiabetic action with high dose of *Tinosporacordifolia* is comparable to that of standard drug glimepride.

Conclusion- Ethanolic extract of *T. cordifolia* possesses antidiabetic potential. Therefore, *T. cordifolia* can be used as therapeutic agent to manage type 2 diabetes mellitus.

Keywords: *Tinosporacordifolia*, Glimepride, Streptozotocin, antidiabetic potential.

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I. Introduction

Diabetes mellitus is a chronic disorder in metabolism of carbohydrates, proteins, and fats due to absolute or relative deficiency of insulin secretion with/without varying degree of insulin resistance¹. DM is a common metabolic disorder which affects all the vital organs/ systems of the body including eyes, kidneys, heart, nerves, blood vessels etc²

Diabetes mellitus is now seen as heterogeneous group of diseases characterised by hyperglycemia resulting from various causes³. The prevalence of diabetes is increasing mostly in the world's middle income countries and India is going to become the diabetic capital of the world by 2030⁴. Diabetes mellitus affects more than 422 million adults globally and it is raising from 4.7% to 8.5% compared to 1980⁵. Hyperglycemia and its attendant metabolic complications lead to various biochemical changes leading to complications like nephropathy, retinopathy and peripheral neuropathy. Type II diabetes mellitus (Non insulin dependent diabetes mellitus) is treated mainly by oral antidiabetic drugs and gliptins which lead to various complications like hypoglycaemia, weight gain, water retention, diarrhoea, malabsorption, necrotising pancreatitis, etc.,^{2,6,7} India has emerged as one of the major epicentre of the global diabetes mellitus pandemic. Rapid development in socioeconomic status and demographic changes has led the Indian population with increased susceptibility for explosive prevalence of diabetes mellitus in past four decades⁸. The chronic diabetes is associated with long term damage and dysfunction of eye, heart, kidney, blood vessels and others⁹. As per ancient literature, more than 800 plants are reported to have antidiabetic activities. Ethnopharmacological survey indicate that more than 1200 plants are used in traditional medicine for their hypoglycemic activity¹⁰. Many antidiabetic drugs are being used in the treatment of diabetes mellitus but search for more effective drug with less or no side effects¹¹. So the present study is to investigate the antidiabetic potential of stem extract of *Tinosporacordifolia* and its comparison with currently used oral antidiabetic drug glimepride.

II. Materials And Method

Wistar albino rats : The albino rats are excellent model for present study. Adult albino rats weighing around 150-200 gram were selected for experiments. The relative humidity of the room was maintained between 50 and 55 percent 12 hours of lighting and 12 hours of darkness was provided in the rooms for optimal growth and reproduction.

Plant materials : Preparation of plant stem extract : The powder of *T cordifolia* (weighted 940 gram) after the grinding is kept in the separate preculator and filled up with about 3 litres commercial alcohol (95% ethanol and 5% water) more than 1 inch than powder and left it 24 hours. After 24 hours, the whole dissolved solution is drained out in a 5000 ml conical flask. About 50 ml dissolved solution is taken in 3000 ml Round bottle flask from the 5000 ml conical flask and evaporated under reduced pressure and low temperature (60°C) in Rotavapour. In Rotavapour, the commercial alcohol is vapourised and plant extract remains in the round bottle flask the remaining plant extract is collected from the saptula from round bottle flask and kept in plastic jar.

Instruments and chemicals: Glucometer (Acucheck-Sensor) Mumbai, India) was used to measure the fasting blood glucose level { GOD-POD method (Glucose oxidase-peroxidase method)}. Glimepride was obtained from IPCA Laboratories, Mumbai, India. It was used as the standard drug in the dose of 0.1 mg/kg/day¹² Streptozotocin monohydrate was purchased from Sigma chemicals, USA, and used to induce diabetes mellitus.

Induction of diabetes:

Streptozotocin was used to induced diabetes mellitus. After an overnight fasting, the rats were injected with freshly prepared 0.5 ml of this solution is injected to each mouse intraperitoneal by insulin syringe. rats were developed hyperglycemia with fasting blood glucose of more than 200 mg/dl were selected for the study.

Experimental design

The study was conducted for 21 days. The standard drug glimepride and the test drug ethanolic extract of *Tinosporacordifolia* were given orally for all the 21 days. The animals were grouped as below-

Group- 1	:	Normal control (NC)
Group- 2	:	Diabetic Control (DC)
Group- 3	:	<i>T cordifolia</i> (200 mg/dl) (TC 200)
Group-4	:	<i>T cordifolia</i> (400 mg/dl)(TC 400)
Group- 5	:	Glimepride (0.1 mg/day)

In all the groups the blood glucose levels were recorded on day- 0, 1, 7, 14 and 21. By tail blood withdrawal technique, 12 hour after the overnight fasting.

Statistical analysis

The results were expressed in mean standard deviation the results were analysed using one way ANOVA with post Hoc analysis. The statistical significant value for any measure was set to $P < 0.05$ at a confidence interval of 95%.

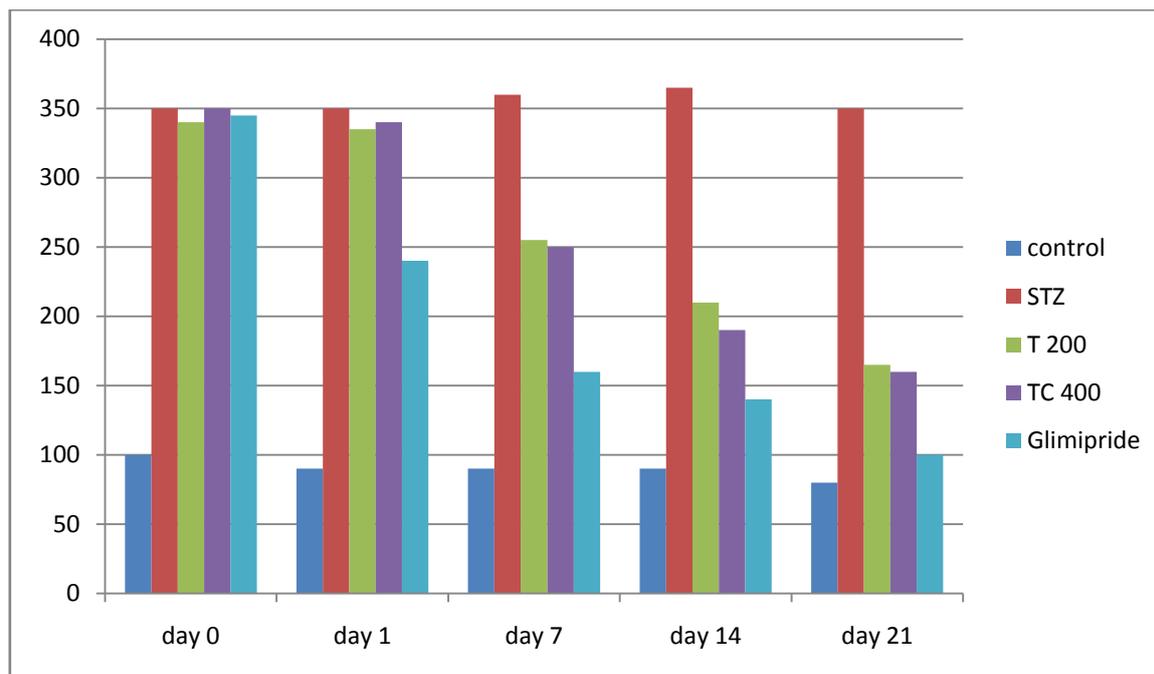
III. Results

Effect on fasting Blood Glucose (FBG) Levels

Induction of diabetes with STZ increases the blood glucose level in the rats by a factor of 3.5, when compared to the control. The changes in the blood glucose levels before and after receiving the treatment in normal and diabetic rats are listed in Table 1. Treatment with *T. cordifolia* extract at two different concentrations (200 and 400 mg/kg body weight) significantly decreases the blood glucose levels when compared to the control. The FBG level of the diabetic control was significantly higher than that of normal control ($p < 0.01$).

The standard drug glimepride significantly decreased the blood glucose level from day 1 onwards (247 ± 1.32 mg/dl, $p < 0.01$) on the 21st day glimepride reduced the blood glucose to almost normal (103.141 mg/dl) level. Test drug TC (200mg/kg/day reduced the blood glucose level significantly on day 7 onwards (265.5 ± 1.12 mg/dl, $p < 0.01$). the fasting blood glucose level of TC 200 mg/kg/day was 212.3 ± 7.2 ($P < 0.001$) on 14th day and 183.4 ± 3.6 mg/dl on 21st day ($p < 0.001$).

Test drug in the dose of 400 mg/kg/day reduced the blood glucose level significantly on day 7 (255 ± 2.3) mg/dl $p < 0.001$) onwards and 14th day fasting glucose level was 195.2 ± 7.1 mg/dl ($p < 0.001$), 21st day blood glucose level to normal when compared to normal control group.



[Fig-1];
Fasting blood glucose levels (mg/dl)
TC = *Tinosporacordifolia*.

[Table-1]
Comparison of fasting blood level within and in between the groups.

Groups	Drugs	Fasting blood glucose (mg/dl)				
		Day 0	Day 1	Day 7	Day 14	Day 21
Group I	Control	103.5±2.4	97.8±3.2	99±2.5	98.5±9.3	97.3±2.3
Group II	STZ	357.2±11.0	360.2±15.2	363±13.6	377.7±5.2	362.2±11.2
Group III	TC 200	343.1±12.2	329.2±11.2	265.5±1.12**	212.3±7.2***	183.4±3.6***
Group IV	TC 400	357.6±5.5	352±5.7	255±2.3***	195.2±7.1	162.5±6.3***
Group V	Glimepride	346.1±12.1	247.1±1.32***	171.7±7.8***	136.3±3.3***	103.41±3.4***

Expressed as Mean ± SEM

*p<0.05, **p<0.01, ***p<0.001, TC = *Tinosporacordifolia*

IV. Discussion

The ethanolic extract of stem of *Tinosporacordifolia*(TC), commonly known as Guduchisattwa in Ayurveda, is recommended for the treatment of diabetes mellitus.¹³ Authors, therefore, preferred the ethanolic extract of the stem and it has been evaluated and its efficacy is compared with that of standard oral hypoglycaemic drug glimepride. The extract met with all the analytical specifications of the standardized herbal extract as per the international standards.

In this study, low dose *T. cardifolia*(200mg/kg) decreased blood glucose level (BGL) from 265.5±1.22mg/dl on day 7 to 183.4±3.6mg/dl on day 21 and high dose (400mg/dl) *T.cardifolia*BGL from 357.6±5.5mg/dl to 162.5±6.3mg/dl on day 21. The results show that the stem extract of *T. cardifolia* has definitive hypoglycaemic activity. The present study is in accordance with the previous studies done by who reported the hypoglycaemic action of *T. cardifolia*.¹⁴

In this study *T. cardifoliadid* not produce hypoglycaemic in non-diabetic test group (BGL-103.5±2.4mg/dl on day 1, 97.3±2.3mg/dl on day 21), which suggests that it might have anti-hyperglycaemic activity and no hypoglycaemic activity in normal rats. Studies show that *T.cardifolia* induces secretion only in the presence of high plasma glucose level which supports our above observation. This can be a huge advantage in the therapy of diabetes mellitus, since one of the important adverse effect of using conventional anti diabetic drugs in hypoglycaemia.

V. Conclusion

Treatment with *T.cordifolia* extract at two different concentrations significantly decreases the blood glucose levels in diabetic rats when compared to the control. This decrease is comparable to the effect shown by the Glimepride. These results indicate that *T.cordifolia* extract acts in significant reduction in blood levels in diabetic rats.

In conclusion, the present study indicates that *T.cordifolia* extract show high potential for the treatment of diabetes and that the improvement of insulin resistance might be the underlying mechanism of the pharmacological actions.

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Conflict Of Interest

Authors declare no conflict of interest regarding publication or any other activity related to this article.

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