

## Effect of *Tinospora cordifolia* as an add-on therapy on the blood glucose levels of patients with Type 2 diabetes

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### ABSTRACT

**Background:** Type 2 diabetes is a fast growing epidemic affecting people globally. Good glycemic control helps in reducing the risk of macro and microvascular complications in diabetics. Alternative medicines have been used since ancient times in India to achieve good glycemic control. *Tinospora cordifolia* (Tc) is a well reported plant possessing anti-diabetic property. Therefore, we undertook this study to evaluate the effectivity of Tc in reducing the blood glucose levels of Type 2 diabetic patients in the form of add-on therapy.

**Methods:** In the present study, we enrolled 100 Type 2 diabetic patients who met our inclusion criteria. These patients were then randomly divided into two Groups, A and B. Patients in Group A were treated as controls and they continued with their anti-diabetic medications. In Group B, Tc was added to the conventional treatment at a dose of 500 mg 3 times daily along with meals. The fasting and postprandial blood glucose levels and glycosylated hemoglobin (HbA1c) were recorded baseline and after 6 months.

**Results:** During the course of study, we observed a decrease in the fasting, postprandial, and HbA1c levels of the patients. However, this decrease was found to be more statistically significant ( $p \leq 0.005$ ) in Group B.

**Conclusion:** The results obtained from the present study conclude that Tc, when given in the form of add-on therapy, was found to be synergistic and effective in the better management of Type 2 diabetes. The drug was well tolerated by the patients and no adverse drug event was recorded.

**Keywords:** Type 2 diabetes, *Tinospora cordifolia*, Oral hypoglycemic agents

### INTRODUCTION

Type 2 diabetes mellitus is one of the most common disorders seen all over the world. It is a complex and progressive disease characterized by hyperglycemia resulting from defects in insulin sensitivity and insulin secretion.<sup>1</sup> Adequate control of hyperglycemia helps in reducing the risk of microvascular (nephropathy, retinopathy, and neuropathy)<sup>2-4</sup> and macrovascular (stroke, myocardial infarction, and cardiovascular death) complications.<sup>5-7</sup> Diet and exercise also help in achieving glycemic control<sup>8</sup> and are important aspects of Type 2 diabetes management,<sup>9,10</sup> however, individualized pharmacotherapy is required to meet glycemic goals.<sup>11</sup> Due

to the progressive nature of Type 2 diabetes,<sup>12</sup> failure to maintain euglycemia with oral agent monotherapy over the long term is common,<sup>11,13,14</sup> and therefore patients require two or more agents to achieve their glycemic goals.

Combination therapy using agents with complementary, but different mechanisms of action that address different pathophysiologic defects of Type 2 diabetes may improve glycemic control to a greater extent than monotherapy.<sup>15</sup> Combination therapy may also allow the use of lower doses of concomitant antihyperglycemic agents, which may minimize unwanted side effects.<sup>16</sup> For example, weight gain and hypoglycemia are associated with some

antihyperglycemic agents,<sup>17</sup> occur more frequently with higher doses,<sup>16</sup> and may hinder achievement of glycemic and metabolic goals.<sup>18,19</sup>

Over the centuries, herbs have served as a major source of medicines for prevention and treatment of diseases including diabetes mellitus. *Tinospora cordifolia* (Tc) (Guduchi) is reported to be one such herb in Ayurvedic system of medicine. It is incredibly versatile and safe<sup>20-23</sup> herbaceous vine and is indicated to combat various diseases and is proved to be a highly potent anti-diabetic herb<sup>24-26</sup> Hence, we undertook this study to see the effect of Tc as an add-on therapy in controlling blood glucose levels of Type 2 diabetic patients.

## METHODS

The present study included 100 Type 2 diabetic patients recruited from the Medicine and Diabetic OPD of King George Medical University, Lucknow (Uttar Pradesh). The study protocol was approved by the Institutional Ethics Committee and written informed consent was taken from all the participants. The procedures followed were in accordance with the Institutional Ethical Committee standards responsible for human experimentation and with the Helsinki Declaration. The subjects who were included in this study met the following inclusion criteria:

- A known case of Type 2 diabetes mellitus on oral hypoglycemic drugs
- Patients of age between 30 and 60 years, of either sex.

Subjects with the following conditions were excluded from the study:

- Type 2 patients on insulin.
- Type 1 diabetic and gestational diabetic patients.
- Patients above 60 years of age.
- Patients with Diabetic nephropathy, neuropathy, retinopathy or any other chronic complications.

Patients fulfilling the aforementioned inclusion criteria were selected. The selected patients were divided randomly into two Groups A and B. The patients in Group A were treated as controls and they continued their oral hypoglycemic drugs, while in Group B Tc was given as an add-on therapy along with their anti-diabetic medications. Tc was given in the form of immumod tablets which contains extract of Tc. One tablet of 500 mg was given three times daily along with meals for 6 months. The baseline characteristics of the patients like age, height, weight, body mass index (BMI), blood pressure were also recorded.

### Collection of blood samples

Total 5 ml of blood was drawn from each patient under aseptic conditions from the antecubital vein. The drawn blood was collected in fluoride vials and plasma was separated and stored at  $-20^{\circ}\text{C}$ .

### Estimation of blood glucose levels

The fasting and postprandial blood glucose levels were estimated by kit using glucose oxidase peroxidase method.

### Estimation of glycosylated hemoglobin (HbA1c)

The HbA1c was estimated by using the high performance liquid chromatographic method.

The normal values of fasting blood glucose, postprandial blood glucose, and HbA1c were taken according to WHO guidelines. These biochemical parameters were repeated after 3 months and 6 months.

### Statistical analysis

The statistical analysis was carried out using “paired t-test” using Graph pad statistical computer software package. Level of significance (p value) was considered  $<0.05$ .

## RESULTS

### Baseline parameters

Table 1 shows the baseline parameters of Groups A and B. These parameters included the age, height, weight, BMI, systolic and diastolic blood pressure, fasting and postprandial blood glucose levels, HbA1c, serum urea, serum creatinine, aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase of the subjects. We did not find any significant difference ( $p \geq 0.05$ ) in these parameters between the two groups. Hence, we can say that Groups A and B were statistically similar at the beginning of the study.

### Fasting blood glucose levels

Figure 1 shows the decrease in the fasting blood glucose levels of the patients. In Group A, the mean values decreased from  $149.42 \pm 6.87$  mg/dl to  $120.32 \pm 4.97$  mg/dl. While in Group B it decreased from  $150.21 \pm 7.32$  mg/dl at baseline to  $115.93 \pm 3.42$  mg/dl after 6 months. This reduction in the fasting blood glucose level was statistically significant in Group A ( $p \leq 0.05$ ) and highly significant ( $p \leq 0.005$ ) in Group B.

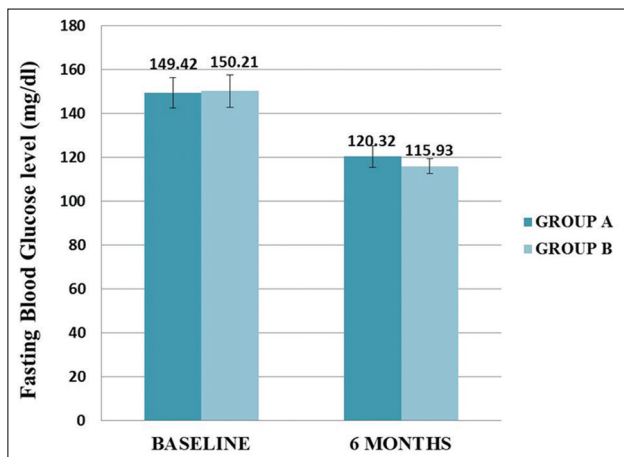
### Post prandial blood glucose levels

As shown in Figure 2, the mean baseline postprandial blood glucose levels recorded were  $255.53 \pm 17.38$  mg/dl and  $248.71 \pm 15.42$  mg/dl in Groups A and B, respectively. After 6 months, the values decreased to  $184.94 \pm 6.97$  mg/dl in Group A and  $176.89 \pm 5.37$  mg/dl in Group B. The reduction in the postprandial blood glucose level was found to be statistically significant in both the groups ( $p \leq 0.05$ ).

**Table 1: A comparative table showing baseline parameters of Groups A and B.**

Baseline Parameters	Mean±SD		p value
	Group A	Group B	
Age (years)	49.5±8.25	50.37±9.87	0.6685
Height (cm)	155.1±13.25	159.2±10.95	0.1356
Weight (Kg)	67.29±21.17	63.52±11.03	0.3214
BMI (kg/m <sup>2</sup> )	26.21±4.58	25.29±4.56	0.5391
Fasting blood glucose (mg/dl)	149.42±6.87	150.20±7.32	0.7364
Postprandial blood glucose (mg/dl)	255.53±17.38	248.71±15.42	0.8571
HbA1c (%)	8.17±0.25	8.24±0.27	0.9651
Systolic blood pressure (mm Hg)	132.75±14.4	134.9±15.6	0.5235
Diastolic blood pressure (mm Hg)	86.1±8.64	85.65±9.16	0.8219
Serum urea (mg/dl)	31.22±8.89	28.36±8.73	0.1512
Serum creatinine (mg/dl)	0.90±0.19	0.82±0.22	0.1015
AST (IU/L)	32.13±16.2	28.92±15.8	0.2550
ALT (IU/L)	34.20±12.06	35.72±14.31	0.0983
ALP (IU/L)	108.67±25.70	119.71±28.42	0.5828

AST: Aspartate aminotransferase, ALP: Alkaline phosphatase, ALT: Alanine aminotransferase, BMI: Body mass index, SD: Standard deviation, HbA1c: Glycosylated hemoglobin



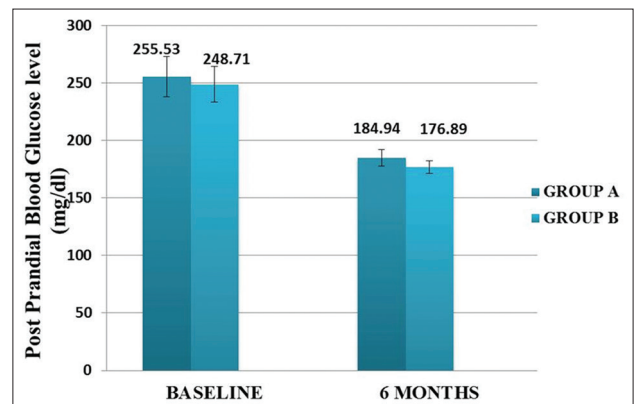
**Figure 1: Decrease in the fasting blood glucose levels of Groups A and B.**

**Glycosylated hemoglobin**

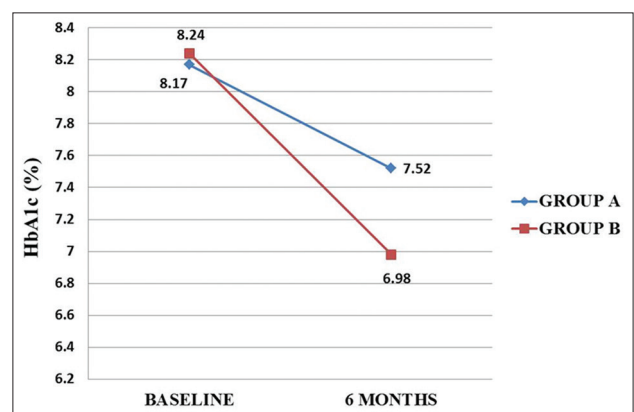
The mean HbA1c recorded at baseline in Group A was 8.17±0.254% while in Group B was 8.24±0.256%. With the decrease in the fasting and postprandial blood glucose levels, the HbA1c also decreased to 7.52±0.181% in Group A and 6.98±0.130% in Group B Figure 3. This reduction in HbA1c was found to be more statistically significant in Group B as the p<0.005 as compared to Group A.

**DISCUSSION**

In this study, both the groups displayed similar clinical and biochemical characteristics, which enabled us to compare metabolic variables, as well as the possible influence of Tc as an add-on intervention in these patients. The results obtained from the present study showed a decrease in the



**Figure 2: Decrease in the postprandial blood glucose levels of Groups A and B.**



**Figure 3 : Decrease in the glycosylated hemoglobin levels of Groups A and B.**

fasting and postprandial blood glucose levels as well as HbA1c levels within the groups. This reduction was found

to be more significant in Group B. Earlier studies conducted by Rout in 2006 and Sudha et al. in 2011 have reported its anti-diabetic potential through a large number of biologically active phytoconstituents derived from different parts of the plant including alkaloids, tannins, cardiac glycosides, flavonoids, saponins, steroids, etc.<sup>27,28</sup> Similar studies conducted on Tc suggest that the hypoglycemic activity is possibly due to inhibition of salivary and pancreatic amylase and glucosidase.<sup>29</sup>

Due to its blood glucose lowering activity Tc is also reported to be used as an important constituent in many polyherbal formulations prepared for the treatment of diabetes. One Ayurvedic polyherbal formulation "Ilogen-Excel," which contains *T. cordifolia* as one of the constituents, when administered at the dose of 50 and 100 mg/kg for 60 days has shown significant decrease in blood glucose levels and increase in plasma insulin, hepatic glycogen, and total hemoglobin. The root extract of plant lowered the levels of HbA1c, plasma thiobarbituric acid reactive substances, hydroperoxides, and ceruloplasmin in diabetic rats.<sup>30</sup> Similarly, another herbomineral formulation "Hyponidd" is reported for its hypoglycemic potential as well as antioxidant activity and the results are comparable with earlier reports on this plant.<sup>31</sup> Hypoglycemic activity of polyherbal formulation "Trasina" is reported due to the superoxide dismutase (SOD) activity of pancreatic islet cells in the rats. The formulation induces a dose-related decrease in hyperglycemia and augments islet SOD activity.<sup>32</sup> Another polyherbal Ayurvedic formulation of the plant, "Dihar," showed significant antihyperglycemic, antihyperlipidemic and antioxidant effects in rats. There was a significant decrease in reduced glutathione, SOD, catalase levels and increase in thiobarbituric acid reactive species levels in the liver.<sup>33</sup> Therefore, from the results obtained from this study we can conclude that Tc can play a beneficial role in the form of alternative therapy in the treatment of Type 2 diabetes.

## CONCLUSION

The findings of the present study suggested that Tc demonstrated a significant reduction in the blood glucose as well as HbA1c levels of the patients. In conclusion, we can say that Tc helps in maintaining good glycemic control in the form of adjunctive therapy. The drug was well tolerated and was found safe on hepatic and renal markers.

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*Conflict of interest: None declared*

*Ethical approval: The present study was approved by the Institutional Ethical Committee (Ref No-291/R- Cell-12)*

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