ANTIDIABETIC ACTIVITY OF TINOSPORA CORDIFOLIA (FAM: MENISPERMACEAE) IN ALLOXAN TREATED ALBINO RATS

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ABSTRACT

The antidiabetic (hypoglycemic) activity of Tinospora cordifolia (Menispermaceae) investigated in alloxan treated albino rats. The rats weighing 150-190gm were administered intraperitoneally with 180mg/kg body weight dose of alloxan monohydrate for the induction of diabetes. The oral dose of alcoholic extract of Tinospora cordifolia, 20ml/kg of body weight from day 2 to 30 given to the animals; twice a day half an hour prior to feeding. Significant decrease in blood sugar level of animals was noticed after the treatment. The results showed that the extract of Tinospora cordifolia is antidiabetogenic and possess hypoglycemic effects.

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1. INTRODUCTION

Glucose is the major energy source of cells. A stable blood glucose level is necessary since energy must be supplied to all cells at all times despite intermittent food intake and variable demands, such as the level of physical activity. The major regulatory hormone for intermediary metabolism is insulin, produced and secreted by the β-cells of the islets of Langerhans of the pancreas. Impaired control of blood glucose concentrations by insulin leads to diabetes mellitus. In patients with diabetes, an increased blood glucose concentration (hyperglycemia) causes an increased thirst, hunger and urine volume, but it is the chronic complications of diabetes that are the major health issues [1, 2, 3, and 4]. Diabetes was first recognized around 1500 B.C.E. by the ancient Egyptians, who considered it a rare condition in which a person urinated excessively and lost weight. The term diabetes mellitus was first used by the Greek physician Aretaeus, (80 to 138 C.E.) reflecting the fact that the urine of those affected had a sweet taste. However, [5] actually measured the concentration of glucose in the urine of such patients and found it to be increased. In the past 200 years, dramatic advances in our understanding of the regulation of normal glucose metabolism have been made. Von Mering and Minkowski investigated that the removing the pancreas produce fatal diabetes in dogs, providing the first clue that the pancreas plays a key role in regulating glucose concentrations [6, 7]. In 1910, Edward Albert Sharpey-Schafer hypothesized that diabetes was due to the deficiency of a single chemical produced by the pancreas; he called this chemical insulin, from the Latin word insula, meaning island and referring to the pancreatic islet cells of Langerhans. In 1921, Banting and Best actually discovered insulin when they reversed diabetes that had been induced in dogs with an extract from the pancreatic islet cells of healthy dogs [8]. Diabetes is a complex, heterogenous disorder characterized by selective autoimmune destruction of pancreatic β cell leading to insulin deficiency. Many patients with diabetes have insulin resistance rather than insulin deficiency [9]. Diabetes results from both insulin resistance and impaired β cell function [10]. Diabetes mellitus is reaching epidemic proportion in developed countries [11]. It is estimated that 366 million people had diabetes mellitus in 2011; by 2030 this should have risen to 552 million. The International Diabetes Federation (IDF) estimates the total number of diabetic subjects to be

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around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025 [12]. In patients with diabetes, an increased blood glucose concentration (Hyperglycemia) causes an increased thirst, hunger and urine volume. Diabetes dramatically increases the risk of various cardiovascular problems including coronary artery disease, heart failure, angina pectoris, heart attack, stroke, narrowing of arteries and high blood pressure. Although several therapies are in use for the treatment of diabetes, there are certain limitations due to high cost and side effects such as development of hypoglycemia, weight gain, gastrointestinal disturbances, liver toxicity etc. [13]. Medicinal plants are being looked up once again for the treatment of diabetes. Current study is performed to evaluate the antidiabetic potential of Tinospora cordifolia; Family: Menispermaceae. This family is a rich source of alkaloid and terpenes [14]. All parts of this plant are documented to be useful in ethno botanical surveys [15]. Present investigation was carried out on albino rat Rattus norvegicus due to its metabolic relatedness with human.

Management of diabetes without any side effect is still a challenge in the medical field, as presently available drugs for diabetes have one or more adverse effects. Since the existing drugs for the treatment of diabetes mellitus do not satisfy our need completely, the search for new drugs continues. In recent years herbal remedies for the unsolved medical problems have been gaining importance in the research field. Thus, this study was undertaken to explore the efficacy of anti-diabetic activity of Tinospora cordifolia in diabetic rats.

2. MATERIAL AND METHODS

The plant material Tinospora cordifolia was identified and collected from hygienic habitats from in and around Nagpur city of Central India. The plant material was washed with water in order to make it free of dirt and other impurities and was shade dried. The whole plant material was grind with mortar and pastel into the fine powder; alcoholic and aqueous extract of Tinospora cordifolia was prepared.

Healthy albino rats (9 months old) of both the sexes, weighing 150-190gm were used for the experiment. Animals were free to access drinking water and food. Animals were cared for and used in accordance with the Institutional Animal Ethics Committee (IAEC), P.G.T. Department of Zoology, RTM Nagpur University, Nagpur (Registration No: 478/01/a/CPCSEA). For experimental induction of diabetes alloxan monohydrate (A74/3 Sigma Aldrich was used). Diabetes was induced in 16 hrs fasted albino rats with single intraperitoneal dose of alloxan monohydrate. Alloxan injection was prepared in 0.9% normal saline. Rats with fasting blood glucose more than 220 mg/dl was considered for study. During dose standardization study it was found that 180 mg /kg intraperitoneal dose of alloxan monohydrate was suitable for diabetes induction with the 6-12 month old rats. For this study the animals were divided into three groups (n=6).

Group-I (NC): Kept as normal control, the animals of this group was free to access drinking water and food they neither injected by alloxan nor feed on plant extract.

Group- II (DC): These group of animals were injected with alloxan monohydrate (180 mg/kg bw) and kept as diabetic control. They were not feed on extract.

Group-III (DC+TCE): This group was injected with alloxan monohydrate (180mg/kg bw) and from day 2 to 30 half an hour prior to feeding, orally administrated with Tinospora cordifolia Extract TCE (20ml/kg bw) twice a day. The blood samples were collected from retro orbital plexus of each rat for the determination of blood glucose with GOD-POD Assay kit.

3. RESULTS

This study was undertaken to explore the efficacy of antidiabetic activity of Tinospora cordifolia whole plant extract in alloxan induced diabetic rats. The study of antidiabetic activity of the Tinospora cordifolia whole plant part extract was carried out on albino rats of both the sexes. The rats were grouped into three group i.e., normal control, diabetic control and treatment group respectively. Experimental diabetes was induced with alloxan 180 mg/kg intraperitoneal dose.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Blood Glucose (mg/dl)</th>
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</thead>
<tbody>
<tr>
<td>NC</td>
<td>89.1± 2.14</td>
</tr>
<tr>
<td>DC</td>
<td>298.3±3.68</td>
</tr>
<tr>
<td>DC + TCE</td>
<td>96.7±1.74*</td>
</tr>
</tbody>
</table>

where, NC- Normal control; DC- Diabetic control; TCE- Tinospora cordifolia extract. Values are expressed as mean ± standard error mean, (n=6); *P<0.001 when DC compared with NC and DC+TCE compared with DC.

In present study we have observed that the whole plant extract of Tinospora cordifolia very significantly (p<0.001) reduces the blood glucose towards the normal blood glucose value may be either due to insulin like behavior of the plant extract or due to its activating effect on the insulin secretion which further makes
the glucose available to the fasting tissue this may results into decrease of the blood glucose towards the normal value.

4. CONCLUSION AND DISCUSSION

Diabetes mellitus is a metabolic disorder that affects people of all age groups and from all walks of life. Management of diabetes without any side effects is still a challenge in the medical field, as presently available drugs for diabetes have one or more adverse effects. Since the existing drugs for the treatment of diabetes mellitus do not satisfy our need completely, the search for new drugs continues.

Glucose is the most important carbohydrate fuel in the body. In the fed state, the majority of circulating glucose comes from the diet; in the fasting state, gluconeogenesis and glycogenolysis maintain glucose concentrations. Very little glucose is found in the diet as glucose; most is found in more complex carbohydrates that are broken down to monosaccharides through the digestive process. About half of the total carbohydrates in the diet are in the form of polysaccharides and the remainder as simpler sugars. About two thirds of the sugar in the diet is sucrose, which is a disaccharide of glucose and fructose.

In recent years, herbal remedies for the unsolved medical problems have been gaining importance in the research field. Although many researchers have studied the anti-diabetic activity of *Tinospora cordifolia* parts such as stem and root, no satisfactory study was conducted to investigate its efficacy in alloxan induced diabetic rats or to explore how this drug acts as an anti-diabetic agent. Thus, this study was undertaken to explore the efficacy of anti-diabetic activity of *Tinospora cordifolia* whole plant extract in alloxan induced diabetic rats. The possible mechanism by which this drug may act is discussed.

Sangeetha *et al.*, [16] examined in vitro mechanism of action of *Tinospora cordifolia* and its active compound in differentiated myocytes, L6 cells. They noticed that the key marker of diabetes in cells is the insulin dependent glucose transporter-4 (Glut-4) which also responds to exogenous chemicals, and is over expressed up to 5- and 4-fold, by *Tinospora cordifolia* and palmatine, respectively. Next to Glut-4, the predominant protein influencing glucose metabolism is PPARs and γ whose expressions were also positively modulated. Further, the inhibitors of insulin pathway prevented glucose uptake mediated by *Tinospora cordifolia* and palmatine which shows that the activity is majorly mediated through insulin pathway.

Grover *et al.*, [17] reported maximum antihyperglycemic effect after oral feeding of aqueous extract of *Tinospora cordifolia* with 400 mg/kg body weight after six weeks. Stanly *et al.*, [18] used the *Tinospora cordifolia* aqueous root extract on alloxan-induced diabetic rats. They used very high concentration of aqueous extract 2.5, 5 and 7.5 g/kg body weight for 42 days. Only 2.5 and 5 gram crude extracts were antihyperglycemic.

The *Tinospora cordifolia* whole plant part extract shows hypoglycemic activity in the alloxan induced diabetes. This hypoglycemic activity of the plant extract is not because of the insulin mimicking activity. *Tinospora cordifolia* whole plant part extract stimulate the pancreatic islets regeneration as observed during the histological photomicrograph. The plant extract induced regeneration of the islets responsible for the increase in the serum insulin. In addition to these activities the *Tinospora cordifolia* extract shows protective activity in reactive oxygen species induced damage tissues.

To confirm the antidiabetic property of the extract blood glucose analysis by GOD–POD method was performed for each animal of every group. From glucose analysis it is observed that the whole plant extract of the *Tinospora cordifolia* very significantly (P<0.001) reduces the blood glucose towards normal significantly in alloxan diabetic rats.

From this report it is concluded that the *Tinospora cordifolia* whole plant extract possess antidiabetic activity which is not by insulin mimicking activity of bioactive compound instead, it is mediated by regeneration of islets of Langerhans. Beside its antidiabetic and regeneration stimulating activity on damaged pancreatic Islets, the plant extract found to contain the bioactive principle which prevents reactive oxygen species mediated oxidative damage.

5. REFERENCES


