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Antidiabetic activity of methanolic extract of bark of *Ficus infectoria* Roxb.

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Abstract

Evaluation of plant products to treat diabetes mellitus is of growing interest as they contain many bioactive substances with therapeutic potential. In recent year several authors evaluated and identified the antidiabetic potential of traditionally used Indian medicinal plants using experimental animals. Previous studies confirmed the efficacy of several medicinal plants in the modulation of oxidative stress associated with diabetes mellitus. The present study showed that the methanolic extract of *Ficus infectoria* possesses hyperglycemic activity.

Keywords: Ficus infectorial, Bark, Antidiabetic activity

Introduction

Diabetes is a group of syndromes characterized by hyperglycemia, altered metabolism of lipids, carbohydrates and proteins and an increased risk of complications from vascular disease. Diabetes is defined as a state in which homeostasis of carbohydrate and lipid metabolism is improperly regulated by insulin. This results primarily in elevated fasting and postprandial blood glucose levels. If this imbalanced homeostasis does not return to normalcy and continues for a protracted period of time, it leads to hyperglycemia that in due course turns into a syndrome called diabetes mellitus. The word "diabetes" is derived from a Greek word that means "to siphon or drain off", the most obvious sign of diabetes being excessive urination. "Mellitus" comes from a Latin word that means "sweet". The urine of a person with diabetes contains extra sugar (glucose). It smells and tastes sweet, thus the name. There is evidence to suggest that diabetes as a disorder was known and recognized by man since the ancient ages. The first mention of diabetes (though it was evidently not known as "diabetes" then), found in Indian literature in the works of the physician Susruta (6th century BC), it also finds a mention in Charaka Samhita.[1-2]

Several comprehensive reviews have been written on the evidence that higher plants are of use in the treatment of diabetes. More than 1000 plants are reported to be used for the treatment of diabetes in various indigenous systems of medicine. Literally hundreds of extracts of higher plants used for diabetes have been screened for their biologic activity in both in vitro and in vivo assays to validate the claimed therapeutic effect.[3] The medicinal plants contain a variety of active constituents that are thought to act on a array of targets by various modes and mechanisms. Therefore, the present work was conceived to evaluate the anti-diabetic activity of the plant.

Material and methods

Collection of Plant

Bark of *Ficus infectoria Roxb.* collected from their natural habitats. The plant was authenticated by comparison with the herbarium and voucher specimen was lodged in the department.

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Processing of plant material

The Bark were shade dried, powdered and extracted/ percolated with hexane, chloroform, methanol, 50% hydroalcohol and water (100 mL x 3 times, 8 h each). The above extracts were pooled and concentrated at reduced temperature (50 °C) on a rotary evaporator (Büchi, Switzerland) and then freeze-dried (Freezone® 4.5, Labconco, USA) under high vacuum (133 x 104 mBar) at a temperature of –40 ±2 °C to obtain yield 3.13 gm, 5.89gm, 31.52gm, 20.50gm and 15.27gm of above mentioned fractions of *F. infectoria* respectively.

Antidiabetic activity[4-6]

Animals

Sprague-Dawley rats (150-200g) were procured from the animal house of Shri Venktesh, Bangalore. They were kept in the departmental animal house at 26 ± 2 °C and relative humidity 44 – 56 %, light and dark cycles of 10 and 14 h respectively for one week before and during the experiments. Animals were provided with standard rodent pellet diet (Amrut, India) and the food was withdrawn 18-24 h before the experiment though water was allowed *ad libitum*.

Toxicological studies[4-6]

Acute toxicity studies

The adult Swiss albino mice of both sexes selected for acute toxicity study. Before the actual LD_{50} determination, a pilot study was made on a small group of mice mainly to select the dose ranges for the subsequent study. The Methanolic extract of *Ficus infectoria* were taken at various dose levels (200, 400, 800, 1000, 2000 mg/kg b. wt.) dissolved in 1 % carboxymethyl cellulose administered 10 ml/kg b.wt. orally to three mice per dose level. The control animals received 1 % carboxymethyl cellulose in distilled water (10 ml/kg) orally. For the actual LD_{50} determination, the extract of *Ficus infectoria* were administered once orally at various dose levels (200 to 2000 mg /kg b. wt.) to group of 3 mice of both sexes about equal in number which have been fasting overnight (about 18 h.). The control animals received 1 % carboxymethyl cellulose in distilled water (10 ml/kg) orally. The animals were observed continuously for 2 hours and then occasionally for further 4 hours and finally overnight mortality recorded. Behavior of the animals and any other toxic symptoms also observed for 72 h. and the animals were kept under observation upto 14 days.

Pharmacological studies[4-6]

Experimental induction of diabetes

Diabetes was induced in rats by tail vein injection of streptozotocin (50 mg/kg, i.v.) dissolved in normal saline. (One group of 6 identical rats was kept without streptozotocin administration as normal control, group I). Forty eight hours after streptozotocin administration blood samples were drawn by retro orbital puncture and glucose levels determined to confirm diabetes. The diabetic rats exhibiting blood glucose levels in the range of 250 and 280 mg/100 ml were selected for the studies.

Experimental Design

Group I - Control rats received vehicle solution (1% gum acacia)
Group II - Diabetic control rats received vehicle solution (1% gum acacia)
Group III - Diabetic rats treated with extract 100 mg/kg body weight in 1% gum acacia
Group IV - Diabetic rats treated with extract 200 mg/kg body weight in 1% gum acacia
Group V - Diabetic rats treated with extract 400 mg/kg body weight in 1% gum acacia
Groups VI - Diabetic rats treated with Glibenclamide 600 µg/kg body weight in aqueous solution

The vehicles and the drugs were administered orally using intra gastric tube daily for three weeks. After three weeks of treatment the rats were fasted overnight, the blood samples were analyzed for blood glucose content. Then the animal was sacrificed by cervical decapitation. The liver and kidney was exposed and perfused with cold phosphate buffer saline of pH 7.4. Blood free liver and kidney were taken out and homogenized in a glass Teflon homogeniser separately (10% w/v). Incubations were done at 37ºC under controlled conditions for biochemical estimations.

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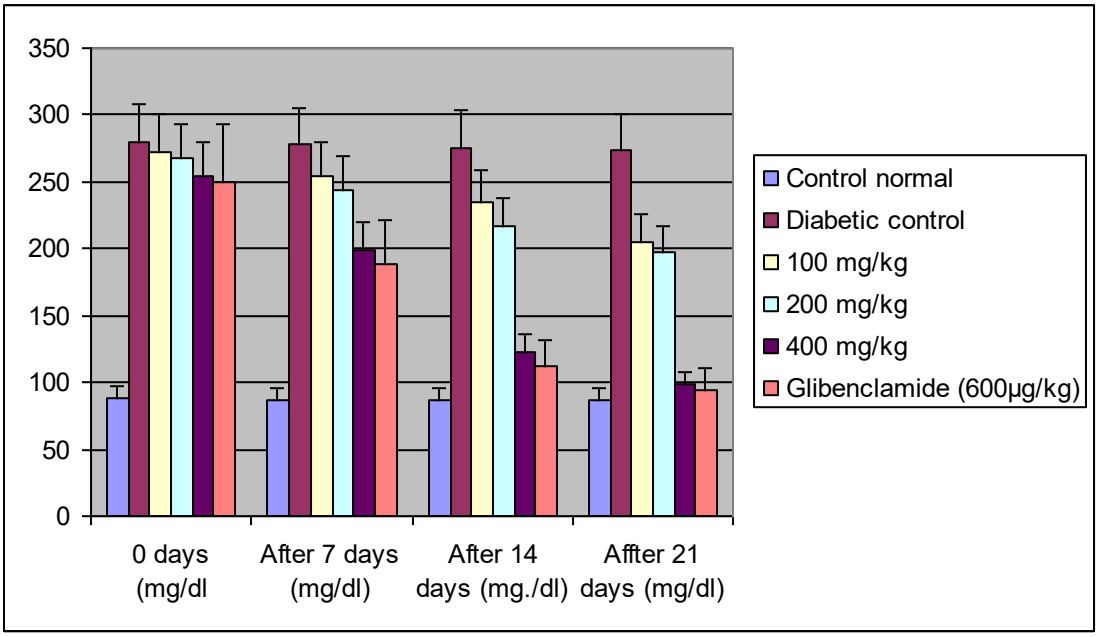
Results and Conclusion

Streptozotocin induced the significant increase in the blood glucose level at 0 day (88.17-250, $p<0.001$), after 7 days the methanolic extract of *Ficus infectoria* at a dose of 100, 200, 400 mg/kg and glibenclamide (600µg/kg) showed the significantly decrease with respect to diabetic control group (272.8-254, 267.17-244.33, 254.17-199.6, 250-188.8, $p<0.001$). After 14 days the treatment showed the significant decrease with respect to diabetic control group at a dose of 100, 200 and 400 mg/kg (254-235, 244.33-216.83, 199.6-123.3, $p<0.001$) and glibenclamide also showed the significant decrease in diabetes (188.8-112.3, $p<0.001$). The methanolic extract of the *Ficus infectoria* showed the significant effect compared with the respective diabetic control group, decrease the blood glucose level at a dose of 100 mg/kg, 200 mg/kg and 400 mg/kg (235-204.83, 216.83-197.6, 123.3-98.3, $p<0.001$), the standard drug glibenclamide also showed the significant decrease the blood glucose level after 21 days (112.3-94, $p<0.001$). Finally the 400 mg/kg and the standard drug showed the significant decrease in the blood glucose level after 21 days treatment ($p<0.001$) were given in table and graph.



Groups	0 day (mg/dl)	After 7 days (mg/dl)	After 14 days (mg/dl)	After 21 days (mg/dl)
Control normal	88.17±1.17	87±1.41	87 ± 0.89	87.5± 1.38
Diabetic control	279.5±1.29	277.5±1.29	275.5± 1.29	273.75± 0.96
100 mg/kg	272.8±1.17	254±1.54	235± 1.41	204.83 ± 1.47
200 mg/kg	267.17±1.47	244.33±1.21	216.83± 1.47	197.6± 1.36
400 mg/kg	254.17±1.47	199.6±1.75	123.3± 1.75	98.3± 1.21
Glibenclamide (600µg/kg)	250±1.4	188.8±1.47	112.3± 1.75	94± 1.41
One-way ANOVA p	<0.001	<0.001	<0.001	<0.001

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Evaluation of plant products to treat diabetes mellitus is of growing interest as they contain many bioactive substances with therapeutic potential. In recent year several authors evaluated and identified the antidiabetic potential of traditionally used Indian medicinal plants using experimental animals. Previous studies confirmed the efficacy of several medicinal plants in the modulation of oxidative stress associated with diabetes mellitus. Effect of methanolic extract of plants on serum glucose, lipid profile and antioxidant status in STZ induced diabetic rats was studied. Based on this, potentiation of dreaded disease like diabetes mellitus may shows a ray for better protocol for future treatment. The efficacy of *Ficus infectoria* in experiment showed the significant decrease in the blood glucose level, increase the antioxidant efficacy in streptozotocin induced diabetes.

The present study showed that the methanolic extract of *Ficus infectoria* possesses hyperglycemic properties in diabetes condition, which was confirmed by glucose level and pancreatic secretion. These observation and description of mechanism of *Ficus infectoria*, which interplay with diabetes biology and pharmacology lead to rapid development in diabetes treatment. In addition to this, studies on molecular aspect of diabetic therapy will give mechanistic information in diabetes therapy and also critical balance should be there between the animal model and clinical research. This holds great promise for future research in human beings.

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