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ANTIDIABETIC POTENTIAL OF METHNOLIC BARK EXTRACT OF FICUS RELIGIOSA L. IN STREPTOZOTOCIN-INDUCED DIABETIC RATS

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ABSTRACT:

Objective: The present study was designed to investigate the hypoglycemic property of a methnolic extract of Ficus religiosa L. which is widely used as a traditional treatment for diabetes mellitus.

Materials and methods: The methanolic extract of Ficus religiosa bark administered orally at a dose of 100 mg/kg, for 15 days to streptozotocin-induced diabetic rats. Fasting blood glucose level and change in body weight assessed in methnolic extract treated diabetic rats, were compared with normal animal, diabetic control and standard drug treated mice.

Results: The yield of methanolic extract in Ficus religiosa bark was found to be 18.17 %. Methanolic extract of Ficus religiosa bark produced a significant reduction in fasting blood glucose level in streptozotocin-induced diabetic rats. Significant differences were also observed in body weight by methnolic extract treated diabetic mice, when compared with diabetic control, normal control and standard drug treated rats.

Conclusion: Methnolic extract of Ficus religiosa exhibit significant anti-hyperglycemic activity in streptozotocin-induced rats. Preliminary phytochemical investigation revealed the presence of phenolic compounds and flavonoids which may be responsible for antidiabetic activity. **Keywords:** Solid lipid nanoparticles, Nateglinide, Cephalin, Diabetes, Stability studies

Introduction:

Ficus religiosa L. belonging to family Moraceae is one of the important plants from traditional system of medicine found all over the world. *Ficus religiosa* is commonly known as “Peepal” or “Ashwattha”, is a fast growing deciduous tree with wide spreading branches and broadly ovate, glossy, leathery, dark green leaves, 5 to 7 inch (12-18cm) long, with unusual tail like tips. The fruits are small (1 to 1.5cm) in diameter, green then purple on ripening. Its bark is light grey and peels in patches. Various chemical constituents like sterols, saponins, coumarins, tannins and amino acid identified in this plant¹. β - sitosteroyl-D-glucoside isolated from the bark of 2 *Ficus religiosa* have shown hypoglycemic activity in normal rabbits.² Traditionally *Ficus religiosa* is used in gout, stomatitis, leucorrhea, ulcers, inflammation and glandular swelling of the neck.³ The literature survey reveals that some work has been done on *Ficus religiosa*. The wound healing⁴, antibacterial⁵, and acetylcholinesterase inhibitory activities⁶ have a scientific justification; still some of the activities are without scientific backing. The present work was an attempt to evaluate antidiabetic activity of this plant and to generate scientifically justified data to support the activity.

MATERIALS AND METHODS**Animals**

Adult albino wistar rats (200 to 250 gm) were used for the study. They were housed in polypropylene cages and fed with a standard diet and water ad libitum. The animals were exposed to an alternating 12 h light and dark cycle. All the experimental procedures and protocols involving animals were reviewed by the Institutional Animal Ethics Committee in accordance with the guidelines of CPCSEA.

Collection and authentication of plant material

Ficus religiosa bark was collected from local area of Meerut, Uttar Pradesh, India in November. The plant was identified and authenticated by Dr. H.B. Singh, Scientist F and Head, Raw Materials Herbarium and Museum at National Institute of Science Communication and Information Resources (NISCAIR), New Delhi. A voucher specimen has been deposited at the NBPGR Herbarium (NISCAIR/RHMD/Consult/2008-09/1091/122 dated 4 November 2008).

Drugs and chemicals

Streptozotocin (CAS no. 18883-66-4) was purchased from Sisco Research Laboratories Pvt. Ltd. Mumbai, India. Oral antidiabetic drug Daonil (batch no. F25898 glibenclamide) was obtained from Aventis Pharma Limited, Goa. Analytical grade chemicals including various organic solvents (Petroleum ether, Methanol) from Rankem, Pvt. Ltd., New Delhi were used for the successive extraction.

Preparation of the Extract

The powdered *Ficus religiosa* bark material (115 g) was extracted using petroleum ether and methanol by hot extraction using Soxhlet apparatus at a temperature of 60°C. The extracts were concentrated under reduced pressure using a rotary vacuum evaporator to constant weight and preserved in desiccator for further studies.⁷ Preliminary phytochemical screening Preliminary phytochemical screening were done to find the presence of the active chemical constituents such as alkaloids, flavonoids, tannins, phenolic compounds, saponins, fixed oils and fats^{8,9}.

Acute toxicity study

The *Ficus religiosa* was administered orally in dose of 50, 100, 200, 300, 400 and 500 mg/kg to groups of mice (n = 6) and percentage mortality was noted 24 h later.

Induction of diabetes

Diabetes mellitus was induced by single intraperitoneal injection of streptozotocin (55 mg/kg in 0.1 M citrate buffer pH 4.5). The normal control group received equivalent amount of citrate buffer only (0.4 ml). The rats were fasted overnight for 16 h with free access to water throughout the duration of the experiment. Diabetes was confirmed by the determination of fasting glucose levels on the third day post administration of streptozotocin¹⁰.

Treatment protocol

The animals were divided into four groups of six rats (n = 6) each.

Group I - Normal control rats, received only distilled water daily.

Group II - Diabetic control rats, received Streptozotocin (55 mg/kg) only.

Group III - Diabetic rats received methanolic extract of *Ficus religiosa* (100 mg/kg, p.o.) for 15 days.

Group IV - Diabetic rats received standard antidiabetic drug glibenclamide (10 mg/kg, p.o.). After 15 days of treatment, experiments were

terminated and observations were made. Blood glucose level was estimated on 1, 4, 7, 10 and 15 day of experiment with the help of glucometer using strip method after taking the blood from tip of the tail.

Statistical analysis

The results are expressed as mean ± S.E.M. Statistical difference was tested by using one-way analysis of variance (ANOVA) followed by post hoc Dunnett’s multiple comparison test. A difference in the mean P value <0.01 was considered as significant.

RESULTS

Yield of plant extract

The 115 gm bark powder of *Ficus religiosa* was taken for extraction by Soxhlet apparatus.

Table 2. Effect of methanolic extract of *F. religiosa* on fasting blood glucose level in diabetic rats.

Group	Blood glucose level (mg/dl)					Reduction in blood glucose level (%)
	Day 1	Day 4	Day 7	Day 10	Day 15	
Normal	86.33±1.2	85.5±1.4	85.83±1.0	87.16±1.1	87.83±0.8	-
Diabetic control	310.83±1.2 ^a	372.33±1.4 ^a	399.33±1.0 ^a	393.83±0.9 ^a	387.83±0.9 ^a	-
Methanolic extract (100mg/kg)	312.33±0.7 ^a	204.5±0.9 ^b	171±0.9 ^b	140±0.5 ^b	123.83±0.8 ^b	54.36
Standard drug (10mg/kg)	287.33±1.4 ^a	198.83±1.2 ^b	168.5±1.0 ^b	138.33±1.2 ^b	125±1.5 ^b	56.49

Values are expressed as mean ± S.E.M. (n=6)
^aP<0.001 as compared to control.

The yield of methanolic extract was found to be 17.17 % w/w.

Phytochemical testing

Phytochemical testing showed that the methanolic extract of *Ficus religiosa* contains tannins, sterols, flavonoids, saponnins, and polyphenolic compound.

Acute toxicity

No toxic effects were observed at a higher dose of 500 mg/kg body weight. Hence, there were no lethal effects in any of the groups. In the study, methanolic extract of *Ficus religiosa* was administered 100 mg/kg dosage, which was determined as the most effective dosage.

Changes in body weight

At the end of 15 days treatment the body weight of diabetic control group decreased whereas treatment with methanolic extract of *Ficus religiosa* (100 mg/kg, p.o.) and GLB (10 mg/kg, p.o.) significantly recovered the body weight towards normal level (Table 1).

Blood glucose level

The effect of methanolic extract on fasting blood glucose in the diabetic rats is shown in Table 2. The

results from the study clearly indicated that the methanolic extract exhibited significant hypoglycemic activity in STZ- diabetic rats. The standard drug glibenclamide also indicated a significant decrease of blood glucose levels.

Table 1. Effect of methanolic extract of *F. religiosa* on body weight in STZ-induced diabetic rats.

Groups	Body weight (g)		Change in body weight (%)
	Day 1	Day 15	
Normal Control	214.83±1.6	219.5±2.2	-
Diabetic Control	214.5±1.4	196.83±1.4 ^a	-
Methanolic extract (100mg/kg)	213.83±1.4	217.66±1.4 ^a	1.79
Standard drug (10mg/kg)	211.83±0.9	215.83±0.9 ^b	1.88

Values are expressed as mean ± S.E.M. (n=6)

^aP<0.01 as compared to control

^bP<0.01 as compared to control

^cP<0.001 as compared to control

DISCUSSION

The fundamental mechanism underlying hyperglycemia involves over-production (excessive hepatic glycogenolysis and gluconeogenesis) and decreased utilization of glucose by the tissues¹¹. Persistent hyperglycemia, the common characteristic of diabetes can cause most diabetic complications. Treatment should aim to lower blood glucose to near-normal levels. In our investigation, the normoglycaemic studies revealed that the methanolic extract of *Ficus religiosa* has the capacity to lower blood glucose levels. The diabetic syndrome in rats administered STZ is characterized by stable moderate hyperglycemia, glucose intolerance and altered but significant glucose stimulated insulin secretion¹². In normoglycaemic study, the data indicates that the *Ficus religiosa* treatment significantly reduced the blood glucose levels in the diabetic rats towards the normal level in the 15 days of study period. The characteristic loss of body weight associated with STZ induced diabetes is due to increased muscle wasting in diabetes¹³. The *Ficus religiosa* treated animals recovered the body weight significantly towards normal level. This may be directly due to the lipid lowering activity of the extract or indirectly to the influence on various lipid regulation systems. Methanol extract showed the presence of tannins, sterols, flavonoids, saponnins, and polyphenolic compound. The anti-diabetic activity of *Ficus*

religiosa may be due to the presence of flavanoid. It is reported that flavanoid constitute the active biological principle of most medicinal plants with hypoglycemic and anti-diabetic properties¹⁴. However the extract should further be subjected to bioactivity guided drug discovery to isolate the lead compound responsible for anti-diabetic and possible mechanism(s) of action.

CONCLUSION

In conclusion, methnolic extract of *Ficus religiosa* exhibit significant anti-hyperglycemic activities in streptozotocin-induced rats. The methnolic extract of *Ficus religiosa* also showed improved in body weight so might be value in treatment of diabetes. However, further phyto pharmacological investigations are needed to identify the lead molecule and to elucidate its exact mechanism of action for anti-diabetic effect.

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