Hypoglycemic activity of *Ficus hispida* (bark) in normal and diabetic albino rats

R. Ghosh*, Kh. Sharatchandra, S. Rita, I. S. Thokchom

**ABSTRACT**

**Objective:** To find out the hypoglycemic activity of *Ficus hispida* Linn. (bark) in normal and diabetic albino rats and to evaluate its probable mechanism of hypoglycemic activity if any.

**Material and Methods:** Albino rats were divided into groups (n=6) receiving different treatments consisting of vehicle, water-soluble portion of the ethanol extract of *Ficus hispida* bark (FH) (1.25 g/kg) and standard antidiabetic drugs, glibenclamide (0.5 mg/kg) and 0.24 units of insulin (0.62 ml of 0.40 units/ml). Blood glucose was estimated by the glucose oxidase method in both normal and alloxan-induced diabetic rats before and 2 h after the administration of drugs. To find out the probable mechanism of action of FH as a hypoglycemic agent, i) the glycogen content of the liver, skeletal muscle and cardiac muscle, and ii) glucose uptake by isolated rat hemi-diaphragm were estimated.

**Results:** FH showed significant reduction of blood glucose level both in the normal (P<0.01) and diabetic (P<0.001) rats. However, the reduction in the blood glucose level was less than that of the standard drug, glibenclamide. FH also increased the uptake of glucose by rat hemi-diaphragm significantly (P<0.001). There was a significant increase in the glycogen content of the liver (P<0.05), skeletal muscle (P<0.01) and cardiac muscle (P<0.001). The amount of glycogen present in the cardiac muscle was more than the glycogen present in the skeletal muscle and liver.

**Conclusion:** FH has significant hypoglycemic activity. Increased glycogenesis and enhanced peripheral uptake of glucose are the probable mechanisms involved in its hypoglycemic activity.

**KEY WORDS:** Antidiabetic, diabetes mellitus

**Introduction**

Diabetes mellitus is one of the common metabolic disorders and 1.3% of the population suffers from this disease throughout the world. Insulin and oral hypoglycemic agents like sulphonylureas and biguanides are still the major players in the management of the disease. However, complete cure of the disease has been eluding physicians for centuries and the quest for the development of more effective antidiabetic agents is pursued relentlessly. Many herbal products, including several metals and minerals have been described for the cure of diabetes mellitus in ancient literature. Herbal preparations alone or in combination with oral hypoglycemic agents sometimes produce a good therapeutic response in some resistant cases where modern medicines alone fail. Currently available treatment is far from satisfactory and is expensive. *Ficus hispida* Linn. (Family: Moraceae) is a small tree variety found throughout India including the state of Manipur. It is used by the ‘Maaiba’ (indigenous medicine-man of Manipur) in the treatment of diabetes mellitus. All parts of *Ficus hispida* (FH) are reported to be bitter, cooling, acrid, astringent to the bowels, antidysentric and useful in “Kapha”, ulcers, biliousness, psoriasis, anemia, piles, jaundice, hemorrhage of the nose and mouth, and diseases of the blood. The fruit acts as a coolant, aphrodisiac, tonic, lactagogue and emetic; also causes “Vata” and constipation. Charaka advised that the juice obtained from the fig be taken with jaggery as a Sramsana (mild purgative) in the treatment of Switra (vitiligo). A mixture of honey and the juice of these fruits is a good antihemorrhagic. The hypoglycemic effects of different compounds obtained from *F. bengalensis* have been reported by different workers. However, no scientific data are available regarding the effect of FH on blood glucose levels. The present study was undertaken to explore the effect of FH bark extract on the blood glucose level.
of experimental animals and to determine the probable mechanism of action.

The effect of the aqueous suspension of a water-soluble portion of the alcoholic extract of FH on fasting blood sugar level was evaluated as compared to the standard drug glibenclamide, both in normal and diabetic albino rats. The effects of FH extract on glucose uptake by rat hemi-diaphragm and the glycogen content of the liver, skeletal muscle and cardiac muscle were evaluated to study its probable mechanism of action as a hypoglycemic agent.

Material and Methods

**Material:** *Ficus hispida* Linn. (Manipuri-Ashee-Haiboang; Sanskrit-Kakadumbura; Hindi – Konéa-dumber) was authenticated by Dr. S.C. Sinha, Professor of Botany, Manipur University. Fresh barks of FH were collected during April-May from the Imphal area and dried under sunlight. The method as described by Dr. S.C. Sinha, Professor of Botany, Manipur University. Fresh barks of FH were collected during April-May from the Imphal area and dried under sunlight. The method as described by Prema et al. was adopted for the isolation of the chemical constituents. Fifty grams of the powdered bark was extracted with double distilled ethanol and the water-soluble fraction of the extract was isolated. The yield was 4.6%.

**Animals and experimental set-up:** Colony bred, healthy Wistar albino rats (NIN strain) of either sex weighing 100-200 g were taken for the study. The animals were fed on standard laboratory diet with water *ad libitum* and housed at room temperature. The rats were kept fasting overnight with free access to water during the experiment in the same ambiance. The animals were divided into three groups of six animals each unless mentioned otherwise. One ml of blood was taken from the orbital sinus of each rat with the help of a capillary tube for the estimation of blood sugar. The Institutional ethics committee approved all experimental protocols.

- **Group A (Control):** Received 3% aqueous Tween-80 (Loba Chem) suspension at a dose of 10 ml/kg.
- **Group B (Test):** Received aqueous suspension of water-soluble portion of alcoholic extract of FH 6% w/v with 3% Tween-80 at a dose of 1.25 g/kg.
- **Group C (Standard):** Received aqueous suspension of glibenclamide (Hoechst) 0.01% w/v with 3% Tween-80 at a dose of 0.5 mg/kg.

All drugs were administered with the help of a stomach tube. No adverse effect or mortality was observed in the albino rats with oral FH (4 g/kg) observed for 24 h during preliminary toxicity testing. The dose of glibenclamide was calculated from human dose by extrapolation based on the surface area.10

1. **Hypoglycemic effect of FH in normal rats:** Fasting blood glucose levels of the rats were estimated by glucose oxidase method.11 The blood glucose levels of different groups were estimated again after 2 h of drug administration. The maximum hypoglycemic effect of glibenclamide has been found around 2 h of its administration.

2. **Hypoglycemic effect of FH in diabetic rats:** The albino rats were made diabetic by intravenous injection of sterile, freshly prepared 1% alloxan monohydrate solution at a dose of 40 mg/kg. After 24 h, when the condition of diabetics had stabilized, rats with a blood glucose level ranging from 350 to 450 mg% were selected for the experiment. Fasting blood glucose levels before and 2 h after administration of drugs were estimated by the same procedure as described above.

3. **Glycogen estimation of the liver, skeletal muscle and cardiac muscle in normal rats:** Two hours after administration of drugs into different groups of animals, they were sacrificed by decapitation. The glycogen content of the liver, skeletal (soleus) muscle and cardiac muscle was estimated as described by Carroll et al.12

4. **Glucose uptake by isolated rat hemi-diaphragm:** Glucose uptake by rat hemi-diaphragm was estimated by the methods described by Walaas13 and Chattopadhyay14 with some modification. Four sets containing six numbers of graduated test tubes (n=6) each, were taken as follows:

- **Group 1:** 2 ml of Tyrode solution with 2% glucose.
- **Group 2:** 2 ml of Tyrode solution with 2% glucose and regular insulin (Nova Nordisk) 0.62 ml of 0.4 units per ml solution.
- **Group 3:** 2 ml of Tyrode solution and 1.38 ml of FH (0.1%) regular insulin 0.62 ml of 0.4 units per ml solution and 1.38 ml of FH (0.1%).

The volumes of all the test tubes were made up to 4 ml with distilled water to match the volume of the test tubes of Group 4. Twelve albino rats were fasted overnight and killed by decapitation. The diaphragms were dissected out quickly with minimal trauma and divided into two halves. Two diaphragms from the same animal were not used for the same set of experiment. Six numbers of diaphragms were used for each group. The hemi-diaphragms were placed in test tubes and incubated for 30 min at 37°C in an atmosphere of 100% oxygen with shaking at 140 cycles/min. Glucose uptake per gram of tissue was calculated as the difference between the initial and final glucose content in the incubated medium.

**Statistics:** The data were analyzed using one-way ANOVA followed by Dunnett’s test. The level of significance was set at 0.05.

**Results**

FH and glibenclamide significantly reduced the fasting blood sugar level in normal albino rats at 2 h with a % decrease of 7.3 and 14.1 respectively. In alloxan-induced diabetic rats, the % decrease recorded at 2 h was 14.75 and 25.37 for FH and glibenclamide respectively (Table 1).

The glycogen content of the liver, skeletal muscle and cardiac muscle in both FH and glibenclamide-treated groups after 2 h was significantly higher as compared to the control group. The glycogen uptake by rat hemi-diaphragm was significantly more in all the groups tested when compared to the control group. The effect was more in FH and FH+insulin treated groups than in the animals treated with insulin alone (Table 2).

**Discussion**

The results of the present study show that a water-soluble fraction of the alcoholic extract of FH significantly decreases fasting blood glucose levels both in the normal (P<0.01) and
alloxan-induced diabetic (P<0.001) rats at 2 h as compared to controls. However, the reduction in the blood glucose level is less than that brought about by the standard drug, glibenclamide. Observations were made at 2 h after the administration of the drugs to compare the effect of FH with the hypoglycemic activity of glibenclamide which peaks at around 2 h after its administration. The basal blood sugar level of normal albino rats corresponds with the findings of previous workers.7,8 The percentage reduction in blood sugar level following glibenclamide treatment (14.14% in normal and 25.37% in diabetic rats) is comparable to the findings of Cherian et al.8 The glycogen concentration in the liver, skeletal muscle and cardiac muscle was significantly increased following treatment with FH. This may be due to the enhancement of glycogen synthesis by FH. The concentration of glycogen was found to be higher in the cardiac muscle than in the liver and skeletal muscle. The rise in the glycogen content of the liver, skeletal muscle and cardiac muscle correlates with the fall in blood glucose level at 2 h. The estimation of glucose content in rat hemi-diaphragm is a commonly employed and reliable method for in vitro study of peripheral uptake of glucose. FH also enhances the uptake of glucose by isolated rat hemi-diaphragm significantly (P<0.001) and was found to be more effective than FH alone but significantly higher than insulin-treated group (P<0.001). It appears that drug interaction could have occurred between FH and insulin when given together. The control value of the glucose uptake by rat hemi-diaphragm (5.70±0.69 mg/g/30 min) corresponds with the findings of Chattopadhyay et al.14 Dimethoxy derivative of leucocyanidin 3-O-β-D-galactosyl celllobioside15 and dimethoxy derivative of pelargonidin 3-O-α-L-rhamnoside16 isolated from the bark of F. bengalensis Linn. have demonstrated anti-diabetic activity. FH, which belongs to the same family as F. bengalensis Linn., is likely to contain such glycosides. The present study demonstrates that a water-soluble fraction of the ethanol extract of FH decreases blood glucose level in normal and alloxan-induced diabetic albino rats. The hypoglycemic activity of FH involves increased glycogen synthesis in the liver and muscles and also enhanced uptake of glucose in the peripheral tissues. Further studies are needed to identify the chemical constituent of FH responsible for the hypoglycemic activity.

References
2. Anturlikan SD, Gopumadhavan S, Chauhan BL, Mitra SK. Effect of D-400, a


Announcement

IPS Members please note

The Executive Committee of IPS which met at New Delhi on 3/7/2004 decided that “the Organizing Secretary (of annual conference of IPS) in coordination with the Chief Editor should publish the supplement issue of the Indian Journal of Pharmacology on conference abstracts and copies of the same will be given to the registered delegates only”.

Henceforth, the conference abstracts will not appear in regular issues and only those members attending the conference will be eligible to receive the supplement of IJP on conference abstracts. If any member needs further clarification, he/she may please email the President (skgupta@hotmail.com) and the General Secretary (goyalrk@rediffmail.com) of IPS.