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# Hypoglycemic Activity of *Ficus racemosa* L. (Moraceae) Leaves in Streptozotocin-induced Diabetic Rats

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**Abstract** – The hypoglycemic effect of the extract of *Ficus racemosa* leaves was studied on streptozotocin-induced diabetic rats. Petroleum ether (60-80℃) extract of the plant obtained by soxhlet extraction from coarsely pulverised leaves was used. In the $LD_{50}$ determination of the extract no abnormalities were observed at the dose range of 3 g/kg (p.o.) of the extract. The extract (200 mg/kg and 400 mg/kg orally) caused a reduction of blood glucose levels in streptozotocin-induced diabetic rats by 28.9% ($P<0.001$) and 34.6% ($P<0.001$) respectively at the end of 9 days. The results of this study indicate that the petroleum ether (60-80℃) extract of the leaves possesses significant hypoglycemic activity in hyperglycemic animals compared with glybenclamide as standard drug.

**Keywords** – *Ficus racemosa*, leaves, hypoglycemic activity, streptozotocin diabetic rats.

## Introduction

Ficus racemosa Linn. Syn. *Ficus glomerata* Roxb. (Family-Moraceae) commonly known as 'Gular', 'Umbar' or 'Jagya-dumbar' (Anonymous, 1966) is found everywhere throughout India. Almost all parts of the plant are used by traditional medical practitioners in many parts of India for the treatment of various diseases. The leaves are used in dysentery, billious affection, mouth wash in spongy gum and in dysmenorrhoea (Nadkarni *et al.*, 1976). The barks, roots and fruits has been found to possess hypoglycemic activity. Hypoglycemic activity of the root barks of Ficus racemosa has been reported (Balaji *et al.*, 1996). In view of the above information the present study was undertaken to evaluate the hypoglycemic effect of the petroleum ether (60-80℃) extract of *F. racemosa* in hypoglycemic rats util- izing the Glucozyme kits (Johnson & Johnson, Bombay, India) and UV spectrophotometer (Beckman DU-64).

## Experimental

**Plant Material** – The leaves of *Ficus racemosa* were collected from Hetyasole, Bankura district of West Bengal, India, during the month of July and August. Taxonomic identification of the plant (Reference No. CNH/7-3(20)/Tech.II/95/239) was established by Central National Herbarium, Botanical Survey of India, Shibpur, Howrah. A specimen sample has been kept in our laboratory for future reference. The leaves were shade

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dried, pulverised by a mechanical grinder and passed through 40 mesh sieve.

**Preparation of petroleum ether extract** – The powdered leaves were extracted in a soxhlet extractor with petroleum ether (60-80℃). On evaporation of solvent in vacuo a greenish residue was obtained (yield 6.43 w/w in terms of dry starting material), and was stored for the pharmacological experiments. On preliminary screening the extract showed the presence of steroidal compound (Trease and Evans 1985) which was confirmed by TLC with the solvent system Hexane: Ethylacetate (1:1) over silica gel G (Stahl 1969). Further separation of the specific compound is under process. The dried petroleum ether extract was suspended in a 2% (w/v) aqueous Tween 80 solution and administered to the animals in specific doses on and after each alternate day of starting the experiment.

**Animals** – Adult albino rats (Wistar strain) weighing 180-200 g and mice (25-30 g) were used. The animals were housed in standard metal cages and provided with food and water *ad libitum*.

**Chemicals** – All chemicals were of analytical grade. Streptozotocin was obtained from Upjohn Company (Kalamazoo, MI, USA). Glybenclamide from Hoechst India Ltd., Bombay, and Glucozyme Kits for blood glucose estimation was obtained from Johnson & Johnson Ltd., Bombay, India.

**Study on streptozotocin (STZ) induced diabetic rats** – The $LD_{50}$ of the extract was determined in albino mice following the method of Lorke, D.A. (1983).

To evaluate the hypoglycemic activity, studies were carried out on the variations of blood glucose level after the administration of streptozotocin and then a petroleum ether (60-80℃) extract of leaves. The blood glucose concentration of each rats were determined on the 1st day of the experiment before administration of either standard drug or the extract. The extract and standard drug were administered on every alternative day and blood samples were taken for glucose estimation on every 24 h after administration of drug upto 9th day of the experiment. Owing to the instability of streptozotocin in aqueous media, the solution was made in citrate buffer (pH 4.5) immediately before administration (Karunanayake *et al.*, 1974). For the induction of diabetes this streptozotocin solution was injected intraperitoneally at a dose of 70 mg/kg. A rest period of 2 days was allowed for the blood glucose level to stabilise. During this period the animals had free access to both food and water. Blood sugar levels of the animals were determined, 48 h after injection of STZ. Animals were divided into five groups, each containing ten animals. Petroleum ether extract (200 mg/kg and 400 mg/kg) was administered orally as a suspension in 2% (w/v) aqueous Tween 80 to two groups of animals. The third group received glybenclamide at a dose of 1 mg/kg orally (Jimenez *et al.*, 1995) as a suspension in aqueous Tween 80. The control animals received the control vehicle only (Ho *et al.*, 1985).

**Statistical analysis** – For hypoglycemic activity in rats, the results has been expressed as mean ± SEM, and the significance of the results were analysed by student's t-tests, comparing with control.

## Results

In the $LD_{50}$ determination no animal death or any other abnormalities were observed at

**Table I.** Toxicity study of *Ficus racemosa* leaves extract in mice

| Treatment | Dose (mg/kg) | No. of animals | No. of survival | No. of death | $LD_{50}$ |
|---|---|---|---|---|---|
| Control | Tween 80 solution | 20 | 20 | 0 | - |
| | 100 | 20 | 20 | 0 | - |
| | 200 | 20 | 20 | 0 | - |
| | 400 | 20 | 20 | 0 | - |
| | 800 | 20 | 20 | 0 | - |
| | 1600 | 20 | 20 | 0 | - |
| | 3200 | 20 | 20 | 0 | >3 g/kg |

**Table 2.** Effect of petroleum ether extract of *Ficus racemosa* leaves (200 mg/kg, 400 mg/kg) and glybenclamide (1 mg/kg) on streptozotocin-induced diabetic rats (each group contains ten animals)

| Time after administration of drug (day) | Control (Normal) | Control (STZ) | Blood sugar level (mg/100 ml) Petroleum ether extract 200 mg/kg | Petroleum ether extract 400 mg/kg | Glybenclamide |
|---|---|---|---|---|---|
| | | X±SEM | X±SEM | X±SEM | X±SEM |
| 0 | 80±4 | 228±6.5 | 225±5.6 | 221±4.9 | 219±5.2 |
| 1 | 78±5.2 | 225±5.8 | 198±6.1[b] (12.0) | 183±5.2[b] (13.3) | 180±4.8[a] (17.8) |
| 3 | 76±4.1 | 226±5.1 | 175±5.2[a] (22.2) | 162±5.5[a] (23.2) | 162±5.1[a] (26.0) |
| 5 | 73±3 | 218±5.6 | 169±4.7[a] (24.9) | 151±4.9[a] (28.4) | 149±4.7[a] (31.9) |
| 7 | 70±4.3 | 215±4.8 | 161±4.9[a] (28.4) | 145±4.7[a] (31.3) | 135±4.7[a] (38.3) |
| 9 | 73±3.8 | 218±4.5 | 160±5.2[a] (28.9) | 138±4.6[a] (34.6) | 136±4.8[a] (37.9) |

[a]$p<0.001$, [b]$p<0.01$ compared with control, student's t-test.

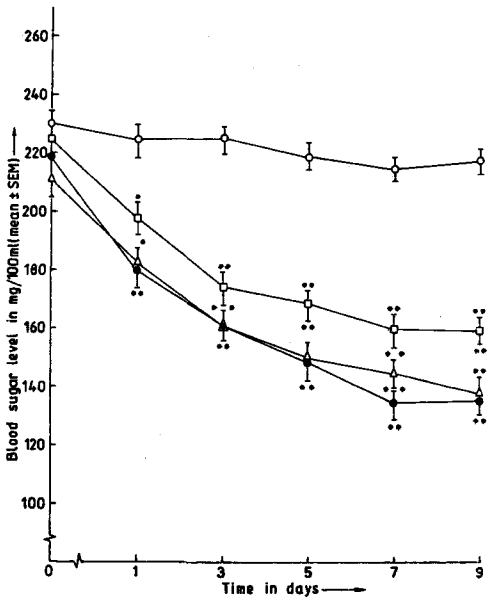


**Fig. 1.** Effect of mean blood sugar level of petroleum ether extract (□, 200 mg/kg. △, 400 mg/kg) and ●, glybenclamide (1 mg/kg) on streptozotocin-induced diabetic rats, ○, control.

the dose range of 3 g/kg (p.o.). The results has been shown in Table 1.

The effects of the petroleum ether (60-80℃) extract of *Ficus racemosa* leaves on blood glucose levels in streptozotocin induced diabetic animals has been shown in Table 2 and Fig. 1. Hypoglycemic activity was produced in a dose related fashion with the doses of 200 and 400 mg/kg in rats. At a dose of 200 mg/kg the extract significantly lowered the blood glucose concentration in rats within 1 day by 12% ($p<0.01$) with a peak activity at 9th day by 28.9% ($p<0.001$). At a dose of 400 mg/kg, the extract significantly lowered the blood glucose concentration in rats within 1 day by 13.3% ($p<0.01$) with a peak activity at 9th day by 34.6% ($p<0.001$). Glybenclamide at a dose of 1 mg/kg also produced significant hypoglycemia within 1 day by 17.8% ($p<0.001$) with a peak activity at 7th day by 38.3% ($p<0.001$).

The mean hypoglycemia (with SEM and % change) induced by the petroleum ether extract (200 mg/kg and 400 mg/kg) and glybenclamide (1 mg/kg) in streptozotocin induced diabetic rats has been shown in Table 2. These results are also represented in Fig. 1.

## Discussion

In the $LD_{50}$ determination it has been observed that the extract is safe to use in animal even at a dose of 3 g/kg (p.o.). The petroleum ether extract, like the sulphonylurea derivative, glybenclamide produced dose related hypoglycemia in rats. In experiments with many animal species streptozotocin produced permanent diabetes with extrapancreatic lesions that mimic the pathological status found in human diabetes (Arison *et al.*, 1967). So streptozotocin diabetes is reproducible, convenient and induced a diabetic state of graded severity suitable for experimental studies (Junod *et al.*, 1969).

The hypoglycemic activity exhibited by the extract was statistically significant with both the doses, having a gradual onset and longer duration of action. The action of the extract and the sulphonyl urea, glybenclamide on rats suggests that both might be acting in a similar manner, at least in part by stimulating the release of insulin. The extract was more potent with a maximum decrease of blood glucose levels of 34.6% at a dose of 400 mg/kg. Further studies concerning the mechanism for the observed hypoglycemic effect as well as the isolation of the active principles responsible for such activity are underway in our laboratory.

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