1. Introduction

Diabetes mellitus is characterized by hyperglycemia together with biochemical alterations of glucose and lipid metabolism. Liver is an insulin dependent tissue, which plays a pivotal role in glucose and lipid homeostasis and is severely affected during diabetes [2] liver participates in the uptake, oxidation and metabolic conversion of free fatty acids, synthesis of cholesterol, phospholipids and triglycerides. During diabetes a profound alteration in the concentration and composition of lipid accurs [3]. Decreased glycolysis, impeded glycogenesis and increased gluconeogenesis are some of the changes of glucose metabolism in the diabetic liver [4]. Many traditional plant treatments for diabetes mellitus are used throughout the world [5] few of the traditional plant treatments for diabetes has received scientific scrutiny, and the World Health Organization has recommended that this area warrants attention [6].

In the present study attempts were made to study detail phytochemical and pharmacological, particularly anti-hyperglycemic activity of the leaves of Ficus racemosa belonging to family

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Moraceae. The root sap is used for treating diabetes; both the root and fruit are credited with hypoglycemic activity. The root juice is reportedly useful for treating dysentery. The stem bark is used to treat menorrhagia, leucorrhoea, gonorrhoea, urinary diseases, haemorrhage and skin diseases. Both the fruits and bark are used extensively in Ayurvedic and Unani medicine [7-8]. The following phytoconstituents have been isolated from the plant tannins, [9] leucoanthocyanins, leucocyanidin-3-0-β-D-glucopyranoside and leucopelargonodine-3-0-α-L-rhamnopyranoside, β-sitosterol, stigmasterol, lupeol,ceryl behenate, α-amyrin acetate [10].

Ficus racemosa documented to possessed anti-inflammatory [11-13], anti-pyretic [14], antidiuretic [15]. The bark of Ficus racemosa is reported to possess the Antidiabetic activity [16]. The bark and leaves of this group used as astringent, haemostatic, anti-inflammatory, antiseptic, prescribed in diarrhea, dysentery and in treatment of skin disease ulcers vaginal disorder leucorrhoea monorrhagia deficient lactation and act as urinary astringent and reduce sugar in diabetic [17]. Still no scientific study has been carried out on the leaves of this plant for diabetes. Our aim to evaluate efficacy of this plant in diabetes mellitus.

2. Materials and Methods

2.1 Plant Material

Fresh leaves of the plant were collected from our university campus, North Maharashtra University, Jalgaon, India. It was authenticated by Dr.P.S.N.Rao Joint Director from the Botanical Survey of India, Pune. Voucher No. is (VVP1) dated 09/11/2005. and letter No.BSI/WC/Tech/2005/728.

2.2 Preparation of the extract

Leaves were dried under normal environmental condition. The completely dried leaves were powdered with an electric grinder and used for the extraction. Since ethanol is the common solvent for extracting most of the constituents present in herbal material, the powdered leaves were extracted by percolation at room temperature with 80% ethyl alcohol. The extract was concentrated under reduced pressure (bath, temperature 50°C) and dried in a vacuum desiccator (yield 15% w/w). Samples were then suspended in 5% gum acacia at a concentration of 100mg/ml and used in all experiments. Preliminary phytochemical screening was carried out on the extract.

2.3 Animals

Normal healthy Albino rats (200-250 g) of Wistar strain of either sex obtained from Yash Farms, Pune were used in the study. They were divided in to 10 groups of five each and were provided with standard pellet diet (Goldmuhar Brand, Lipton India Ltd., Mumbai.) and water ad libitum. All the rats were kept in cages with wide square mesh at the bottom to avoid coprophagy and maintained in a well ventilated animal house with 12 h light and dark cycle. They were fasted for 18 h prior to the experiment, allowing access to water only, and were deprived of both food and water during the 12 h monitoring period of the experiment after the treatment either with the drug (or) vehicle. The experimental protocol and animal house has been approved by the institutional animal ethics committee and by the animal regulatory body of the Indian Government (Registration No.652/02/a/ CPCSEA, dated 25/01/1999).

2.4 Chemicals used

Glibenclamide was a generous gift sample from Themis laboratories wagle estate, Thane. Alloxan monohydrate was purchased from Sigma-Aldrich Himedia. The glucose oxidase/peroxidase reagents kit was purchased from Dr. Reddy’s Laboratories Hyderabad. All other reagents used were of analytical grade.
Table 1. Effect of *Ficus racemosa* leaves extract on blood glucose levels after oral administration in normal rats.

<table>
<thead>
<tr>
<th>Group (n=5)</th>
<th>Dose</th>
<th>Blood glucose levels at different hours after the treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>Control</td>
<td>-</td>
<td>110.05±4.10</td>
</tr>
<tr>
<td><em>F. racemosa</em> 100mg/kg</td>
<td>110.56±2.10</td>
<td>108.35±3.40</td>
</tr>
<tr>
<td><em>F. racemosa</em> 200mg/kg</td>
<td>106.70±5.25</td>
<td>105.08±6.11</td>
</tr>
<tr>
<td><em>F. racemosa</em> 300mg/kg</td>
<td>98.60±4.20</td>
<td>96.83±3.25</td>
</tr>
<tr>
<td>Glibenclamide 10mg/kg</td>
<td>101.20±1.90</td>
<td>95.78±2.63</td>
</tr>
</tbody>
</table>

All blood glucose values were expressed as Mean ± S.E.M of five animals.

All blood glucose values were compared with corresponding values of control groups by using one way ANOVA Dunnett's test.

Statistical significant difference were expressed as *p<0.05, **p<0.01, ***p<0.001.

Table 2. Effect of *Ficus racemosa* leaves extract on blood glucose levels after oral administration in diabetic rats.

<table>
<thead>
<tr>
<th>Group (n=5)</th>
<th>Dose</th>
<th>Blood glucose levels at different hours after the treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>Control</td>
<td>-</td>
<td>261.20±3.10</td>
</tr>
<tr>
<td><em>F. racemosa</em> 100mg/kg</td>
<td>301.16±2.50</td>
<td>294.70±3.48</td>
</tr>
<tr>
<td><em>F. racemosa</em> 200mg/kg</td>
<td>271.85±2.65</td>
<td>262.38±2.65*</td>
</tr>
<tr>
<td><em>F. racemosa</em> 300mg/kg</td>
<td>291.56±1.60</td>
<td>278.29±2.50***</td>
</tr>
<tr>
<td>Glibenclamide 10mg/kg</td>
<td>288.20±2.49</td>
<td>275.38±2.13***</td>
</tr>
</tbody>
</table>

All blood glucose values were expressed as Mean ± S.E.M of five animals.

All blood glucose values were compared with corresponding values of control groups by using one way ANOVA Dunnett's test.

Statistical significant difference were expressed as *p<0.05, **p<0.01, ***p<0.001.
2.5 Acute oral toxicity

Healthy Swiss albino mice of either sex, starved and divided into 5 groups and orally fed the MEMI in increasing dose level of 250, 500, 1000, 1500, 2000 mg/kg body weight. Mice were observed for 24 hours for any lethality [18].

2.6 Effect on normal rats

Group I, II, III were given the ethanolic extract of Ficus racemosa leaves (suspended in 5% gum acacia) orally following a standard procedure19, at doses of 100, 200, 300 mg/kg body weight respectively. Animals in group IV received Glibenclamide at a dose of 10mg/kg body weight and served as standard. Group V served as a normal control and received appropriate volumes of vehicle orally.

2.7 Induction of diabetes

Group VI-X were rendered diabetic by injecting a freshly prepared aqueous solution of alloxan monohydrate (110 mg/kg, i.p.) after a base line blood glucose estimation was done [20]. After two weeks when the condition of diabetes was stabilized, animals with blood glucose levels above 250 mg/dl were selected for the study.

2.8 Effect on diabetic rats

Group VI-VIII were treated with ethanolic extract of Ficus racemosa leaves (suspended in 5% acacia) in the form of mucilage orally by gavage at doses of 100, 200, 300 mg/kg body weight, respectively. Group X served as a diabetic control and received appropriate volume of the vehicle orally while group IX received Glibenclamide at a dose of 10mg/kg body weight and served as a standard.

2.9 Collection of blood and determination of blood glucose

Blood samples were collected from the retro-orbital plexus under light ether anesthesia before and at 0.5, 1, 2, 4, 6, 8 and 12 h after drug administration. The samples were analyzed for blood glucose content by using glucose-oxidase method [21] with optical density measured by visible spectrophotometer at 520 nm.

2.10 Statistical analysis

All values were expressed as means ± standard error of means. Statistical comparisons were made by using one way ANOVA and Dunnett’s t-test [22] by using graph pad prism 4.0 software. P values p<0.05 were considered as significant.

3. Results

Acute toxicity study revealed the non toxic nature of extract of F. racemosa leaves upto 2000 mg/kg. There was no lethality or any toxic reactions found at any of the doses selected until the end of the study period.

Preliminary phytochemical screening revealed the presence of alkaloids, glycosides flavonoids, phenolic compounda and tannins.

3.1 Effect of leaves extract on blood glucose levels in normal rats

The mean blood glucose concentration of control and drug-treated animals (after oral administration of different doses of F. racemosa leaves extract) at various time intervals are shown in Table I a dose dependent hypoglycemia was observed in animals treated with F. racemosa leaves extract. A significant reduction (p<0.001) in blood glucose of 20.82%, 24.28% and 26.33% was observed at the 6 h with doses of 100, 200 and 300 mg/kg body weight respectively. The present study ethanolic extract of the F. racemosa leaves suppressed blood glucose levels in normal and alloxan induced diabetic rats, when compared to control animals. The hypoglycemic potential of the extract was comparable with that of the Glibenclamide in normal and diabetic rats. On the other hand, Glibenclamide caused significantly (p<0.001) more hypoglycemia in comparison with the plant extract at 300 mg/kg body weight (p<0.001).
There were also significant reductions starting 1 h following treatment. The maximum reduction was observed 6 h after treatment.

3.2 Effect of leaves extract on blood glucose levels in diabetic rats

The mean blood glucose concentration of control, *Fracemosa* treated (100, 200 and 300 mg/kg, p.o.) and Glibenclamide were treated (10 mg/kg, p.o.) rats are shown in Table II dose dependent Antihyperglycemic activity was also observed *Fracemosa* in alloxan induced diabetic rats. The percentage reduction of blood glucose was higher in the diabetic state compared to the normal state by the three doses of *Fracemosa*. a significant reduction (p<0.001) in blood glucose of 35.06%, 38.03% and 47.92% was observed at 6 h with the doses of 100, 200 and 300 mg/kg body weight, respectively. There were also significant reductions starting 2 h following treatment. The maximum reduction was observed 6 h after treatment. Glibenclamide produced a significant reduction (p<0.001) in blood glucose compared to diabetic control at the 6 h (53.56%).

4. Discussion

*Diabetes* mellitus is possibly the world’s largest growing metabolic disease, and as the knowledge on the heterogeneity of this disorder is advanced, the need for more appropriate therapy increases [23]. Traditional plant medicines are used throughout the world for a range of diabetic presentations. The study of such medicines might offer a natural key to unlock a diabetologist's pharmacy for the future. The treatment goal for patients with type 2 diabetes mellitus is generally to achieve normal glycemic control in patient with type 2 diabetes mellitus. Type-II diabetes is characterized by reduced circulating concentration of insulin; poor insulin sensitivity or insulin resistance and poor glucose tolerance resulting in high blood glucose level. Diabetes mellitus of long duration is associated with several complications such as atherosclerosis, myocardial infarction, and neuropathy etc. These complications have long been assumed to be related to chronically elevated glucose levels and subsequent oxidative stress. There is a need for drugs, which lower the elevated blood glucose levels and also reduce oxidative stress to prevent long term complications [24].

Alloxan causes a massive reduction in insulin release by the destruction of β cells of the islets of Langerhans and induces hyperglycemia. Alloxan exerts its diabetogenic action when it is administered parenterally, intravenously, intraperitoneally or subcutaneously [25].

Flavonoids, steroids/triterpenoids, alkaloids and phenolics are known to be bioactive antidiabetic principles [26]. Flavonoids are known to regenerate the damaged beta cells in alloxan diabetic rats. *Fracemosa* reported to be possessed alkaloid, flavonoids, phenolic compounds and tannins which confirmed by phytochemical analysis. On the basis of above evidence it seems possible that the presence of alkaloid, flavonoids, phenolic compounds and tannins may be responsible for the observed antidiabetic activity.

5. Conclusion

Our results have showed that leaves of *Fracemosa* possess blood glucose lowering effect in normoglycemic and in alloxan induced hyperglycemic rats. Thus the folk use of this plant may be validated by this study.

6. Acknowledgement

The authors wish to thanks Themis Laboratories (Thane India) for providing gift sample Glibenclamide by Mr. H.S. Bonde. The authors are thankful to the plant material was identified and authenticated by Dr.P.S.N. Rao Joint Director from the Botanical Survey of India, Pune. The authors also wish to thank the management of the college for encouraging and providing research facilities.


### References


10. *Indian herbal pharmacopoeia* (2002);223-232.


