



ANTIDIABETIC ACTIVITY OF ETHANOL EXTRACT OF *FICUS RACEMOSA*. LINN, BARK

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ABSTRACT

The ethanolic extract of the plant *Ficus racemosa* was investigated for its antidiabetic activity. Type-2 diabetes mellitus was induced with standardised doses of alloxan monohydrate. Graded doses of the ethanolic extract was administered to normal and experimental diabetic rats for 12 days. Fasting plasma glucose levels evaluated in diabetic rats. The diabetic groups treated with the ethanolic extract were compared with standard insulin. The findings showed the significant antidiabetic potential of the extract in ameliorating the diabetic conditions in diabetic rats. No significant effects were found in the normal rats.

KEYWORDS: *Ficus racemosa*, antidiabetic effect, alloxan induced diabetes.

INTRODUCTION

Diabetes mellitus is a metabolic disease as old as humankind and its prevalence is considered to be high (4–5%) all over the world.^[1] In spite of the introduction of hypoglycemic agents, diabetes and related issue continue to be a significant medical problem. Since long standing, patients with non-insulin requiring diabetes have been treated orally in folk medicine with a diversity of plant extracts. In India a number of plants are declare in ancient literature (Ayurveda) for the cure of diabetic conditions known as ‘madhumeha’ and some of them have been experimentally evaluated and the active principles isolated.^[2,7] *Ficus racemosa* Linn. (Hindi: *Gular*, Sanskrit: *Udambara*) belongs to the family Moraceae. It is an evergreen spreading tree for average to large size, found in everypart of India in moist localities. It is also found on rocky slopes, sometimes almost gregariously. It is often cultivated around villages for its consumable fruit. The bark of the tree is used in the native systems of medicine for a variety of purposes. The bark is astringent and an infusion of it is employed as a mouth wash for spongy gum condition. The bark is antiseptic, antipyretic, vermifugal and a decoction of the bark is used in treating various skin diseases and ulcers. It is used as a medical plaster in inflammatory swellings and boils. It is described to be effective in the treatment of piles, dysentery, asthma, gonorrhoea, gleet, menorrhagia, leucorrhoea, haemoptysis and urinary diseases.^[8,10] In this study we have attempted to investigate the anti-diabetic activity of ethanolic extract of *Ficus racemosa* bark.

MATERIALS AND METHODS

Plant material

The bark of the plant *Ficus racemosa* were collected from Vidyanagar (Shimoga, Karnataka, India). The plant was authenticated by Professor Kamalakar, Department of Botany, Sahyadri Science College (Shimoga, Karnataka, India). A voucher specimen has been deposited in the Department of Botany, Sahyadri Science College (Shimoga, Karnataka, India).

Preliminary phytochemical screening

Opening phytochemical investigation was conducted by the following standard procedures.^[11,12]

Preparation of extract

The powdered plant material (350 g) was successively extracted in a 2000 mL round bottomed flask with 1500 mL solvents of increasing polarity starting with petroleum ether, chloroform, ethanol and double distilled water. The reflux time for each solvent was 40 cycles. The extracts were cooled at room temperature, filtered and evaporated to dryness under reduced pressure in a rotatory evaporator (Buchi Rotavapor).

Animals

Male wistar albino rats (160–200 g) were used in the experiment. Animals maintained under standard environmental conditions, were fed with a standard diet (Hindustan Lever, India) and water *ad libitum*. The animals were fasted for 18hr before experimentation but allowed free access to water.

Fixation of dose

Acute toxicity study was performed using albino mice and doses were fixed as per OECD guideline No 420 and adopted CPCSEA protocol for the screening of pharmacological activity.

METHODS TO SCREEN ANTIDIABETIC ACTIVITY

Alloxan Induced Hyperglycemia

Hyperglycemia and glycosuria occur after administration of alloxan in several species. Investigators found that alloxan has a selective destructive effect on the β -cells of islet of Langerhans of the pancreas. However, this effect varied with species and the dose.

Experimental Induction of Diabetes in Rats

Diabetes was induced by intraperitoneal injection of alloxan monohydrate in physiological saline at a dose of 60 mg/kg body weight in chilled citrate buffer pH 4.5. Alloxan monohydrate was purchased from the IOBA Chemie Bombay. After 48 hr rats showing blood glucose levels of 250-350 mg/dl were considered as diabetic and were used in the study.

Experimental Design

The rats were housed in polyethylene cages and divided into 5 groups of six animals each. Group-I served as solvent control, group II served as diabetic control, group III received insulin 0.6 u/mg, S.C., group-4 and group-5 received ethanolic extract of *Ficus racemosa* at 100 mg/kg and 50kg/mg., i.p. for 2 weeks respectively. On the 0 week, 1 week and 2 week the animals were fasted for 18 hr and blood samples were drawn by orbital sinus puncture under mild ether anesthesia. The blood samples were collected in Eppendroff's tubes containing 50 μ l of

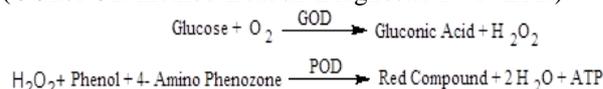
anti-coagulant (EDTA). Plasma was separated by centrifugation at 5000rpm for 10mts and analysed for glucose content in autoanalyser Microlab by enzymatic method (GOD/POD method-Beacon-Diagnostic PVT. LTD). The study was approved by the Institutional Animals Ethics Committee (CPCSEA).

Statistical Analysis

In all the above experiments the results have been expressed as mean \pm S.E.M., six animals in each group. Statistical significance test were performed by Newman-keul's Test and P-values were calculated by comparing with controls. $P < 0.05$ implies significance.

Principle of Estimation of Glucose

Glucose is oxidized by glucose oxidase (GOD) into gluconic acid and hydrogen peroxide. Hydrogen peroxide in presence of Peroxidase (POD) oxidized the chromogen 4-aminophenazone and phenol to a red colored compound. The intensity of this red color produced is proportional to the glucose concentration and is measured at 505nm Microlab by enzymatic method (GOD/POD method-Beacon-Diagnostic PVT. LTD).



RESULTS

Antidiabetic activity of ethanol extract of *Ficus racemosa*, Linn in rats

Alloxan has been shown to destruct beta cells of pancreas producing hyperglycemia. In our experiments the diabetes was characterized by hyperglycemia. The results are shown in below Table1.

Table 1: Antidiabetic activity of crude ethanol extract of *Ficus racemosa*, Linn in rats.

Treatment Groups	O Week	First Week			Second week		
		Mean \pm SEM	Diff	% change	Mean \pm SEM	Diff	% change
I	84.3 \pm 0.9	83.8 \pm 1.2	0.5 \pm 0.9	-0.6	81.8 \pm 1.2	2.5 \pm 1.3	-2.9
II	266.7 \pm 4.0	293.3 \pm 4.2	26.7 \pm 7.0	+10.2	328.3 \pm 6.9	61.7 \pm 7.9	+23.3
III	245.0 \pm 3.4	162.0 \pm 1.0	83.0 \pm 3.4	-33.8	128.2 \pm 1.9	116.8 \pm 4.0	-47.6
IV	269.2 \pm 4.0	187.0 \pm 2.4	82.2 \pm 3.4	-30.5	157.5 \pm 2.5	111.7 \pm 3.6	-41.5
V	276.7 \pm 3.1	235.8 \pm 6.4	40.8 \pm 5.2	-14.8	228.3 \pm 6.5	48.3 \pm 5.9	-17.5
ANOVA	----	F=72.9 P < .001, HS			F=186.5 P < .001, HS		

MEAN \pm SEM

Between groups one way ANOVA, followed by Newman-keul's Test.

$P < 0.05$, $P < .001$, Sig. $P < .001$, HS. $n = 6$

Antidiabetic activity of the coloured fractions of *Ficus racemosa*

The ethanolic extract of the bark of *Ficus racemosa* has shown to possess a wide spectrum of activity. TLC of the crude extract was carried out using solvents and solvent combinations of varying polarities. It was observed that there was clear separation. Therefore the ethanol extract was subjected to column chromatography. Out of all the following fractions only two major fractions were

subjected to antidiabetic activity the results were shown in Table. 2.

Table 2: Antidiabetic activity of coloured fractions of *Ficus racemosa*, Linn in rats.

Treatment Groups	O Week	First Week			Second week		
		Mean \pm SEM	Diff	% change	Mean \pm SEM	Diff	% change
I	80.6 \pm 0.40	81.0 \pm 0.31	0.5 \pm 0.9	0.4	80.6 \pm 1.2	2.5 \pm 1.3	-2.9
II	260.8 \pm 0.58	301.80 \pm 0.86	26.7 \pm 7.0	-15.8	350.20 \pm 0.20	61.7 \pm 7.9	+23.3
III	260.60 \pm 0.24	123.60 \pm 0.40	83.0 \pm 3.4	52.6	110.40 \pm 0.40	116.8 \pm 4.0	57.6
IVEA:MeOH8:2	261.60 \pm 0.87	141.6 \pm 0.40	86.2 \pm 7.7	+45.9	123.6 \pm 0.40	124.2 \pm 5.3	52.8
V EA:MeOH6:4	260.60 \pm 0.24	123.60 \pm 0.40	83.0 \pm 3.4	52.6	110.40 \pm 0.40	116.8 \pm 4.0	57.6

Between groups one way ANOVA, followed by Newman-keul's Test Test
 $P < 0.05$ $P < .001$, Sig. $P < .001$, HS. $n = 6$

Effect of experimental plant on Serum glucose levels

The effect of ethanolic extracts from two medicinal plants on the blood glucose levels of experimental animals was determined at various time interval for 2 weeks after oral administration at 50, 100 mg dose kg^{-1} b.wt. (Table 1). There was a significant elevation in the blood glucose level by 2 times during experimental time period in alloxan-induced diabetic rats, when compared to normal rats. The administration of *Ficus racemosa* extract caused the blood glucose levels of diabetic rats to -30.5, -14.8 (1 week), 41.5, 17.5 (2-week) at the dose of 50, 100 mg dose kg^{-1} body weight. ($p < 0.05$).

Effect of coloured fractions of experimental plant on Serum glucose levels

The effect of coloured fractions from two medicinal plants on the blood glucose levels of experimental animals was determined at various time interval for 2 weeks after oral administration at 50 mg dose kg^{-1} body weight. (Table 2). The EA: MeOH (8:2) fraction from *Ficus racemosa* showed reduction in serum glucose level to +45.9 (1 week), 52.8 (2 week) respectively.

DISCUSSION

Although the accurate devise of alloxan-induced diabetes remains uncertain, there is increasing evidence that it involves the degeneration of islet b-cells by accumulation of cytotoxic free radicals. The pharmacological investigations of the alcohol and aqueous extracts of the root tuber of *Ficus racemosa* indicated that the plant extracts caused significant reduction in blood glucose levels in diabetic rats from day 14 onwards. Alloxan lead to permanent destruction of the pancreatic β -cells.^[13] The observed hypoglycemic effect of the drug extracts in alloxan-diabetic rats sharp to pancreatic and extrapancreatic device of drug action. Hence, improvement of peripheral utilization of glucose and increased insulin release may be cited as the possible mechanisms involved in the hypoglycemic action of *Ficus racemosa*.

CONCLUSION

The *Ficus racemosa* bark showed significant hypoglycemic effect, comparable with the antidiabetic drug insulin, in diabetic rats. Thus, the claim made by the traditional Indian system of medicine regarding the use of bark of this plant in the treatment of diabetes is substantiated. Further investigation is hereby recommended to demonstrate cellular mechanisms and

structural components of the active ingredients of this bark extract in order to standardize them.

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