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EVALUATION OF ANTIDIABETIC POTENTIAL OF ETHANOLIC EXTRACT OF LEAVES OF *FICUS BENGALENSIS* LINN.

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ABSTRACT

The aim of the present study was to evaluate the antidiabetic potential of ethanolic extract of *Ficus bengalensis* Linn. leaves in alloxan induced diabetic rats. The effect of different concentrations of ethanolic extract on glucose, heamoglobulin, urea, creatinine, uric acid, cholesterol, LDL, VLDL, HDL, protein, albumin, globulin, ALP and ACP level in diabetic rats was studied. Oral administration of ethanolic extract decreases the level of heamoglobulin, sugar, urea, uric acid, cholesterol, TGL ,LDL, VLDL, albumin, ALP, ACP and increase the level of HDL. Optimum dasage of 1ml/Kg/day was arrived on the basis of our experimental results.

KEY WORDS

Antidiabetic, Alloxan, *Ficus bengalensis* Linn.

INTRODUCTION

Diabetes mellitus is one of the major metabolic disorders currently associated with considerable morbidity, mortality and several long term complications in the affected individuals [1]. It is a clinical syndrome characterized by inappropriate hyperglycemia caused by a relative or absolute deficiency of insulin or by a resistance to the action of insulin at the cellular level [2]. It is the most common endocrine disorder, affecting 16 million individuals in the United States and as many as 200 million worldwide. It has been known since ages and the sweetness of diabetic urine has been mentioned in Ayurveda by Sushruta. Its pharmacotherapy however is over 80 years old. The word diabetes was coined by the Greek physician Aerates in the first century A.D. In the l7th century, Willis observed that the urine of, diabetics as wonderfully sweet as if imbued with honey or sugar. The presence of sugar in the urine of diabetics was demonstrated by Dobson in 1755. Diabetes is a chronic disease affecting around 2-3 % of the population worldwide.

The World Health Organization estimated that about 30 million people suffered from diabetes in 1985 and the number increased to more than 171 million in 2000. It is estimated that the number will increase to over 366 million by 2030 and that large increase will occur in developing countries, especially in people aged between 45 and 64 years.

India has a rich heritage of knowledge on plant based drugs both for use in curative and preventive medicine. First medicinal use of plants is found in Rig Veda, which is approximately 8000 years old. In Atharvanaveda, remarkable description of Indian medicinal plants has been given by ancient Indian scholars. An Upaveda, Ayurveda composed around 2500 BC, deals with medicine, healthcare and treatment of disease from indigenous drugs. From Veda it is learnt that Indo-Aryans used the 'Soma' (A Plant product) as a medicinal agent, which exhibits an amazing stimulating effect [3].

India has a rich source of biodiversity (both flora and fauna) possessing tremendous medicinal properties. The biodiversity of *Ficus* species ecosystem have attracted scientific attention throughout the world.It was observed from the literature that *Ficus bengalensis* Linn. Possesses mutidimentional curative properties [4].

Ficus bengalensis Linn.(*Moraceae)* is native to India where it grows from low altitudes to 2000 ft (610 m) , especially in dry regions. It is native to a wide area of Asia from India through Myanmar (Burma), Thailand, Southeast Asia, Southern China and Malaysia.This tree is considered to be sacred in some places. It is used in traditional system of medicine like Ayurveda,Siddha,Unani and Homeopathy.The active compounds isolated from this plant are considered to be very effective in various treatments such as dysentery,diarrhoea, diabetes,leucorrhoea,menorragia,nervous disorders, tonic and astringent [5].

Leaves are broadly ovate ,obtuse, the base cordate; lamina 10-30 cm long, 7-20 cm wide, very coriaceous, puberulous beneath; lateral veins 5-7 pairs, the basal pair prominent, reaching 1/3 of lamina length; petiole 1.5-7 cm long, 5mm wide, puberulous, stipules thick, 1-1.5 cm long and wide, puberulous. Figs paired sessile, puberulous, depressed-globular, 1.5-2 cm diam., maturing orange to red; ostiole broadly unbonate, enclosed by 3 flat apical bracts; basalbracts3, foliaceous, obtuse, 3-7

mm long, 10-15mm wide puberulous. Extracts obtained from various parts of the tree are cooling, alterative and demulcents. The power of astringency, resulting from the presence of tannins, varies from part to part. The latex is said to have an aphrodisiac action.

MATERIAL AND METHODS

Animal

Male albino rats (Wister strain, weighing 150-200g) were purchased from Tamil Nadu Veterinary and Animal Sciences University, Madhavaram, Chennai and Housed under standard husbandry conditions (30ºC, 60-70 % relative humidity and 12h: 12h day-night cycle) and allowed standard pelleted rat feed and water adlibitum.The experiment was designed and conducted in accordance with the guidelines of Institutional Animal Ethical Committee (IAEC).

Herbal Drug

Ficus bengalensis Linn. leaves were collected in the month of May 2011, from Jayankondam Ariyalur District, Tamil Nadu. The plants were authenticated and voucher specimen was submitted to S.T.E.T.Women's College, Mannargudi, Tamil Nadu. *Ficus bengalensis* Linn. leaves were washed with distilled water, shade dried, powdered and extracted with ethanol using soxhlete apparatus. The concentrated ethanolic extract was used as a herbal medicine.

Chemicals

Alloxan was purchased from Sigma Chemical Co. All the other chemicals were of analytical grade & of highest purity,purchased from local chemical company .

Allaxon Induced Diabetes mellitus

Male albino rats (150-200g) were made diabetic by intravenous injection of alloxan (150 mg/g) in citrate buffer pH 4.0. Fasting blood glucose (FBG) was performed every week for 15 days. Then the animals were arbitrarily divided into four groups for convenience (II, III, IV & V) as indicated below based on their FBG pattern. Six rats were used in each group.

Group I: This group animal was kept as control without diabetic induction and Herbal treatment.

Group II: This group animal was alloxanised and kept as diabetic control.

Group III: This group animal was alloxanised and they received low dose of Herbal treatment (0.5ml (250mg)/kg of body weight).

Group IV: This group animal was alloxanised and they received high dose of Herbal treatment (1ml (500mg)/kg of body weight).

Group V: This group animal was orally administered glibenclamide (0.3 mg/kg b.wt/day) dissolved in 0.5ml distilled water.

Herbal Drug Administration

Herbal Drug was administered through oral route. Before drug administrations, Group III, IV and V animals were allowed to starve for 2 hours to enhance the intestinal absorption of drug. Group III and IV rats were administered with low dose and high dose of herbal drug (i.e., 0.5 ml / kg and 1.0 ml/kg of body weight) respectively, and the experiments was carried out for 15 days. After 15 days, the biochemical parameters were assayed by using serum.

RESULT&DISCUSSION

In the present work, we investigated the hypoglycemic effect of ethanolic extract of *Ficus bengalensis* Linn. in the alloxan diabetic model. Alloxan cause diabetes through its ability to destroy the insulin producing beta cells of the pancreas [6]. In vitro studies have shown that alloxan is selectively toxic to pancreatic beta

cells causing cell necrosis [7]. The cytotoxic action of alloxan is mediated by reactive oxygen species, with a simultaneous massive increase in cytosolic calcium concentration, leading to a rapid destruction of beta cells [8].

Intraperitoneal administration of alloxan to overnight fasted normal animals caused marked elevations in serum glucose and hemoglobulin(Hb) levels [9]. These levels were observed to be increase until day 15(day of sacrificing animal) . Regular drug administration (0.5ml/kg b.w. for 15 days) to diabetic rats antagonized the remarkable alteration in serum glucose and Hb levels.

The total haemoglobulin level is decreased and glycosylated heamoglobulin is increased in alloxaon diabetic rats [10]. The ethanolic extract and its fraction significantly prevented elevation in glycosylated haemoglobulin thereby increasing the level of total haemoglobulin in diabetic rats. This could be due to the result of improved glycemic control produced by plant extract. 1ml/kg.b.wt extract possess high anti diabetic property.

The present study clearly reveals that the 1ml/kg.b.wt ethanolic extract of leaves produces the maximum reduction in blood glucose level as compared to the 0.5ml/kg.b.wt extract of *Ficus bengalensis* Linn.. It seems that the extract either protected the cells from the toxic effect of alloxan or the cells recovered after the initial injury [11].

The results in Table1 shows significant increase in the level of urea, uric acid and creatinine which are markers of renal dysfunction [12] in the diabetic group compared to group I level. After treatment of alloxan diabetic rats with ethanolic extract the levels of urea, uric acid and creatinine significantly decreased (group III, IV) compared to those in untreated diabetic group (group II). This further confirms the utility of this plant in diabetes associated renal complications and also authenticate the folk medicinal usage of this plant for kidney disorders Table 2 shows that increased level of cholesterol in the diabetic rat could arise from a rise in cholesterol biosynthesis. Increased activities of hydroxyl methyl glutaryl reductase, a rate-limiting enzyme in cholesterol biosynthesis have been reported in diabetic rats. The higher level of fatty acids may be attributed to the extraction of fatty acids from plasma, which in turn leads to the accumulation of toxic fatty acid metabolites [13]. A rise in fatty acids from plasma, which in turn leads to the accumulation of toxic fatty acid metabolites contributes to elevation of cholesterol in diabetic rats.

This abnormal increase in the level of serum lipids is mainly due to decrease in the action of lipolytic hormones on the fat depots mainly due to the action of insulin. Under normal circumstances, insulin activates the enzyme lipoprotein lipase, which hydrolysis triglycerides. However, in diabetic state lipoprotein lipase is not activated due to insulin deficiency resulting in hypertriglyceridemia and insulin deficiency is also associated with hypercholesterolemia due to metabolic abnormalities [14].

The metabolism of proteins is abnormal in diabetes (Table 3) due to insulin secretion defect, leading to various metabolic disorders [15]. Serum total protein and albumin levels were reduced in diabetic rats as reported by Prakasam [16] from their herbal antidiabetic drug study. Total protein and albumin level reduction (group II) may be due to increased protein catabolism caused by alloxan [17]. Drug administration (group III, IV) causes normalization of serum protein and albumin levels, possibly through the increase in insulin mediated amino acid uptake, enhancement in protein synthesis and inhibition in protein degradation [18].

An increased activity of serum ALP and ACP was observed in diabetic rats. It is able to nurture the alloxan damaged cell membrane for getting ACP and ALP leakage into the bloodstream [19]. Further studies are necessary to find out the mechanism of function of

ethanolic extract of *Ficus bengalensis* Linn. against diabetes.

Glibenclamide activate receptors on the beta islet cells of the pancreas to release more stored insulin in response to glucose. They do not increase insulin formation. They are ineffective in totally insulin deficient patients and for successful therapy probably requires about 30% of normal beta cells function subjects as well as diabetes [20].

From the above results, it was concluded that the ethanolic extract of leaves of *Ficus bengalensis* Linn. at the dose level of 1ml/kg has more potent antihyperglycemic activity in allaxon induced diabetic animals. Further studies are warranted to isolate and characterise the antidiabetic principles from the leaves of *Ficus bangalensis* Linn.

Table 1
Effect of Fiscus bengalensis Linn. on Biochemical parameters.

Parameters	Group I	Group II	Group III	Group IV	Group V
Glucose	115±0.004	290±0.004	180±0.005	172±0.006	125±0.004
Glycosylated Hb	12.1±0.005	13.1±0.003	12.9± 0.006	12.8±0.004	12.0±0.001
Urea	40±116.3	65±134.7*	61±74.08NS	57±117.19 NS	43±75.04
Uric acid	9±116.3	20±134.7*	17±15.3 *	13±12.9 NS	11±36.8
Creatinine	1.5±0.08	2.9±0.1**	2.4±0.08**	2.1±0.07**	2.0±0.04

Values are expressed as mean ± SD for 6 animals
Statistical significance, *p<0.005, **p<0.001, ***p<0.001,NS –Not significant Vs Normal

Table 2
Effect of Fiscus bengalensis Linn. on Biochemical parameters

Parameters	Group I	Group II	Group III	Group IV	Group V
Cholesterol	188±0.11	210±0.47 NS	200 ±0.11**	195±0.10***	192±0.09
TGL	176±0.16*	235±0.27*	220±0.15**	202±0.34**	186±0.37
HDL	48±79.80	39±68.29***	39±120.76 NS	46 ±137.25	47±96.31
LDL	97±79.83	112±68.32***	42±120.79 NS	00±137.28***	101±84.01
VLDL	35±0.27	47±0.59 NS	47 ±0.60**	40 ±0.50**	36±0.11

Values are expressed as mean ± SD for 6 animals.
Statistical significance, *p<0.005,**p<0.001,p<0.001,NS –Not significant Vs Normal***

Table 3
Effect of Ficus bengalensis Linn.on biochemical parameters

Parameters	Group I	Group II	Group III	Group IV	Group V
Protein	7.5±0.24	6.8±0.56 ^{NS}	7.0±0.57	7.4±0.47**	7.3±0.12
Albumin	3.9±0.27	3.4±0.59 ^{NS}	3.6±0.60***	4.0±0.50**	4.1±0.34
Globulin	2.1±79.83	2.6±68.32**	2.3±120.79 ^{NS}	3.4± 137.28***	2.4±75.24
ALP	8.9±6.07	25.1±20.4***	16.8±8.03*	15.5±9.27 ^{NS}	9.1±4.54
ACP	5.4 ±6.10	11.6±20.7**	7.2±8.06*	6.6±9.30 ^{NS}	6.0±5.65

Values are expressed as mean ± SD for 6 animals
Statistical significance, *p<0.005, **p<0.001, ***p<0.001,^{NS} –Not significant Vs Normal

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