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ANTIDIABETIC ACTIVITY OF *MANGIFERA INDICA* ROOT IN ALLOXAN INDUCED DIABETES IN RATS

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ABSTRACT

Present investigation was undertaken to evaluate antihyperglycemic, activity of ethanolic extract of *Mangifera indica* roots in alloxan induced diabetic rats. Alloxan produced a significant increase in serum glucose, creatinine, urea, uric acid, ALT, AST levels. Treatment with *Mangifera indica* extract produced decrease in alloxan induced glucose, urea, uric acid, and creatinine levels. There was a significant decrease in total protein, haemoglobin, body weight, albumin and globulin. Administration of *Mangifera indica* to diabetic rats reduced the effect of alloxan and increased the levels of above parameters. The results suggest *Mangifera indica* to be beneficial for the treatment of diabetes mellitus.

Key words: Ethanolic extract, Alloxan, Diabetes mellitus, Hypoglycemic effect, *Mangifera indica*.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disease caused by an absolute or relative lack of insulin and or reduced insulin activity, which results in hyperglycemia and abnormalities in carbohydrate, protein and fat metabolism [1]. The presence of diabetes mellitus confers increased risk of many divesting complications such as cardiovascular diseases, peripheral vascular diseases [2], coronary artery diseases, stroke, neuropathy, renal failure, retinopathy amputations and blindness [3]. The main disadvantage of current drugs (biguanides, sulfonylureas) that they have to give throughout the life and produce side effects [5].

India having a rich heritage of traditional medicine constituting with its different components like ayurveda, siddha and unani. Botanicals constitute of major part of these traditional medicines..The Root of *Mangifera indica* has been used in the indigenous systems of medicine in India for the treatment of

several diseases. *Mangifera indica* (Mango) tree which is believed to be a native of Asia, is a member of the Anacardiaceae family. It is grown widely in different parts of Africa, especially in the southern part of Nigeria. *Mangifera indica* is used medicinally to treat ailments such as asthma, cough, diarrhea, dysentery, leucorrhoea, jaundice, pains and malaria [6, 7, 16]. The ethanolic extract contains the plant part is plant root of *Mangifera indica*. The present study is an attempt to investigate the effect of EEMI on alloxan induced diabetes in Wister rats.

Alloxan is a toxic glucose analogue, which selectively destroys insulin producing β cells in the pancreas [8, 9]. administered to rodents and many other animal species, it causes insulin dependent diabetes mellitus [10] (called "Alloxan diabetes") in these animals, with characteristics similar to type 1 diabetes in humans. Alloxan is selectively toxic to insulin producing pancreatic beta cells because it preferentially accumulates in beta cells through uptake via the

GLUT2 glucose transporter. Alloxan, in the presence of intracellular thiols, generates reactive oxygen species (ROS) in a cyclic reaction with its reduction product, dialuric acid [11, 12]. The beta cell toxic action of alloxan is initiated by free radicals in this redox reaction [13].

MATERIALS AND METHODS

Plants Collection:

For the present investigation, the root of the plant *MANGIFERA INDICA* was collected from different regions of Nugivedu, vijayawada, after proper identification by an expert taxonomist Dr. A. Srinivas Rao, Department of botany, VRS &YNR Degree college, Chirala. After that the roots are shade dried and powdered.

Extraction Procedure:

Equal amount of MI root coarse powder were mixed and blended. The coarse powder was used for the extraction by successive solvent extraction by Soxhlet apparatus using ethanol solvent.

Ethanol extract

Marc obtained from the above extract was dried and extracted with 2.5litre of ethanol. Then it was filtered and stored in desiccator.

Animals:

Male albino Wistar rats, aged 4 months (body weight: 180 ± 10 g) were used for the present study, procured from Sainath enterprises, Hyderabad, India. The animals were housed in poly acrylic cages (38 cm × 23 cm × 10 cm) with not more than six animals per cage, at an ambient temperature of $18 \pm 2^{\circ}\text{C}$ with 12-h-light/12-h-dark cycle. Rats have free access to standard chow diet and water ad libitum. The maintenance and the handling of animals were performed according to the rules and regulations of Institutional animal Ethical Committee (IAEC) of GSN PHARMACEUTICAL LABORATORY, kukatpally, secenderabad (NO.769/2010/CPCSEA)

Other Chemicals and reagent:

Alloxan, and Glibenclamide were procured from SISCO laboratories (Mumbai, India). Glucose, Total cholesterol, Triglyceride, HDL, LDL and VLDL kit were procured from Coral laboratories. All the solvents and other chemicals were procured from SS Pharma,Hyderabad they were of analytical grade quality. Albino rats and mice were procured from Mahaveer Enterprises, Hyderabad.

1) Preliminary phytochemical screening:

Semi purified Plant extracts were evaluated for Phyto-constituents, components in each extract is identified with the help of simple chromatographic techniques like paper chromatography and Thin layer chromatography.

2) Acute toxicity studies:

Rats were divided into six groups of six animals each. The control group received normal saline (2ml/kg, p.o.) The other groups received 50, 200, 400, 800, 2000 and 4000mg/kg of the extracts, respectively. Immediately after dosing the animals were observed for their behavior continuously for the first four hours. They were kept under observation up to 5 hrs after extract administration to find out the mortality and body weight [13, 3].

Procedure:

Preparation of dose:

1. Dose of the drug prepared in Distilled water, and administered 1 ml/100gm body weight of the animal. Starting dose is 4000Mg/kg for group 1.
2. If there is no mortality then we can select a dose range up to 2000mg/kg and the drug should be considered as a safe drug. But if > 2 animals die.
3. 800mg/kg dose has to be administered in group II. If no mortality maximum dose range would be less up to 800mg/kg. If > 2animals die.
4. Group III can be treated with 400mg/kg dose. If no mortality then dose range can be selected up to 50mg/kg. If > 2 animals die.
5. Group IV can be treated with 200mg/kg dose. If no mortality then dose range can be selected up to 200mg/kg. If > 2 animals die.
6. Group V would be treated with 50mg/kg. If > 2animals die, the drug will be categorized as highly toxic drug.

3) Experimental design:

The Wistar rats weighing 180-250 gm of either sex were used for the experimental study. The animals were divided into five groups of 6 animals in each.

EEMI was administered for 21 days at a two different dose levels 200,400mg/kg of EEMI made in aqueous and given orally. The blood was collected by sinus orbital under light diethyl ether anesthesia. The blood was centrifuged at 3000 rpm for 10 minutes.

Body weight, glucose was analyzed every week and lipid and lipoprotein profile from serum (TC, TG, HDL, LDL, VLDL) were analyzed after 21 days.

4) Induction and assessment of diabetes

A) Induction of diabetes

A single dose of 150mg/kg alloxan prepared in normal saline water was injected intraperitoneally to overnight fasted animals to induce diabetes. The control rats received an equal volume of normal saline water and used along with diabetic animals [14, 4].

B) Assessment of diabetes

Diabetes was confirmed after 48 hr of alloxan injection, the blood samples were collected through retro-orbital puncture and plasma glucose levels were

2) Acute toxicity studies

Acute toxicity studies on rats showed no mortality at a dose of 4000mg/kg, during a time period of 14 days. During the study, no noticeable responses were seen in the rats. This help to predict that it does not contain any type of toxicity and is safe. So 200 mg/kg b.w (1/5th) and 400 mg/kg b.w (1/10th) were selected of that dose for further study.

3) Effect of EEMI on serum glucose levels

Alloxan treatment produced significant increase in serum glucose level ($P < 0.001$) with respect to normal control group. The administration of ethanolic extract 200mg/kg, 400mg/kg and glibenclamide 5mg/kg ($P < 0.001$) significantly reversed the increase in serum glucose concentration in alloxan induced rats [19].

4) Effect of EEMI on serum lipid and lipoprotein profile

Alloxan diabetic rats group were found to have significantly increased VLDL, LDL, TG, TC, levels and markedly decreased HDL levels as compared to normal control group ($P < 0.001$). Treatment with ethanolic extract 200 mg/kg and 400mg/kg reduced significantly VLDL, LDL, TG, TC, levels and markedly increased HDL levels as compared to diabetic control group ($P < 0.001$). Positive control was significantly preventing the increasing the serum TC, TG, LDL, VLDL and decreasing the HDL level as compared to diabetic group. Thus the ethanolic extract treatment restored all these changes near to normal value.

Ethanolic extract *per sec* did not show significant change in serum lipid and lipoprotein profile [18, 20]. The change in serum lipid and lipoprotein profile were tabulated in table: 3

In our study, there was a significant elevation in blood glucose level in diabetic control group as compared with normal animals. The EEMI root extract treated group exhibited significant reduction of fasting plasma glucose levels as compared to the diabetic control

estimated by enzymatic GOD-POD diagnostic kit method. The rats having fasting plasma glucose levels more than 250 mg/dL were selected and used for the present study [15].

RESULTS AND DISCUSSION

1) Preliminary phytochemical screening

The EEMI was subjected to chemical tests as per the standard methods for the identification of the various constituents. The results of phytochemical analysis were given in table: 1

group. Over production of glucose by means of excessive hepatic glycogenolysis and gluconeogenesis is one of the fundamental basis of hyperglycemia in diabetes mellitus.

The most commonly observed lipid abnormalities in diabetes are hypertriglyceridemia and hypercholesterolemia [14, 15].

A marked increase in total cholesterol and decrease in HDL cholesterol have been observed in diabetic control rats. Insulin deficiency results in failure to activate lipoprotein lipase thereby causing hypertriglyceridemia. There was a significant control of the levels of serum lipids in Poly herbal extract treated diabetic rats [17].

In diabetes, LDL carries cholesterol to the peripheral tissues where it is deposited, whereas HDL transports cholesterol from peripheral tissues to the liver and thus aids its excretion. Hence increase in LDL is atherogenic. In our present study, there was a significant decrease in TG, LDL, and total cholesterol levels, whereas there was a significant increase in the HDL level.

CONCLUSION

The present study is an attempt to investigate the effect of EEMI root on alloxan induced diabetes in Wister albino rats. The Phytochemical screening showed the presence of tannins, carbohydrates, flavonoids, alkaloids, phenols, reducing sugar and amino acids which are responsible for the antidiabetic activity.

The animals were induced with alloxan at a dose of 150 mg/kg intraperitoneally and the diabetic animals were treated with EEMI extract (200mg/kg, 400mg/kg) for 21 days orally. The serum glucose, body weight and lipid profile parameters from pancreas homogenate were measured which showed significant activity.

The findings of the present investigation suggest that EEMI root extract has potential for its evaluation as a protective agent against toxicity induced by alloxan.

Table 1: Experimental Design

GROUPS	TREATMENT	Purpose
Group 1	Normal control	To serve as normal
Group 2	Diabetic control	To serve as disease control
Group 3	Diabetic + Glibenclamide (5mg/kg)	To serve as standard
Group 4	Diabetic + EEMI Extract (200mg/kg)	To study the effect of low dose of GP
Group 5	Diabetic +EEMI Extract (400mg/kg)	To study the effect of high dose of GP

Table: 2 Qualitative phytochemical screening of extract

Plant constituent	Ethanol extract
Alkaloids	+
Carbohydrates	+
Glycosides	+
Saponins	-
Protein and amino acids	+
Phytosterol	+
Phenols and tannins	+
Flavonoids	+

Table: 2 Effect of EEMI on serum glucose levels in normal control and alloxan induced diabetic rats on 0th day, 7, 14 & 21st day.

S.no	Groups	Mean ± SD			
		0 th day	7 th day	14 th day	21 th day
1.	Vehicle control	90.05±0.096	90.3±0.20	90.23±0.24	89.81±0.63
2.	Diabetic control	262.53±0.821	261.35±0.95	260.35±0.39	256.87±0.44
3.	Glibenclamide 5mg/kg	259.83±1.32	120.5±1.87	119.05±0.28	108.82±0.37
4.	200mg/kg EEMI	260.33±1.366	186.88±0.47	173.16±3.32	169.97±1.09
5.	400mg/kg EEMI	261±2.6430	130.66±1.21	121.9±0.60	105.54±0.6

Table: 3 lipid and lipoprotein profile

S.no	Groups	Mean ± SD				
		cholesterol	triglycerides	VLDL levels	LDL levels	HDL levels
1.	Vehicle control	81.48±0.37	73.22±0.31	14.15±0.25	39.72±0.81	23.73±0.36
2.	Diabetic control	222.53±0.94	114.46±0.60 ^a	22.52±0.52 ^c	132.58±0.93 ^a	20.91±0.33 ^a
3.	Glibenclamide 5mg/kg	84.85±0.90	81.52±0.55	17.00±0.06 ^a	34.55±0.56 ^a	32.40±0.37 ^a
4.	200mg/kg EEMI	132.9±0.48	95.02±0.05 ^c	20.04±0.03 ^a	68.48±0.51 ^a	40.22±0.37 ^a
5.	400mg/kg EEMI	108.8±0.41	78.03±0.05	17.98±0.06 ^a	45.89±0.41 ^a	34.02±0.02 ^a

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