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Hypoglycemic and Hypolipidemic Activities of *Momordica dioica* Roxb Fruit Pulp Extracts on Alloxan-Induced Diabetic Rats

Received: 01-Mar-09

Revised: 26-May-09

Accepted: 06-Jun-09

Abstract

Purpose: To investigate the effect of *Momordica dioica* fruit pulp extract on blood glucose and other biochemical parameters on alloxan-induced diabetic rats.

Methods: Diabetes was induced in adult albino Wistar rats by intra peritoneal (ip) injection of alloxan (150 mg/kg). Hexane extract (HE) and ethyl acetate soluble fraction of methanolic extract (EASFME) of *M. dioica* fruit pulp (400 mg/kg) were administered as a single dose per day to the diabetes rats for 15 days. The control group received distilled water for the same duration. Blood glucose levels and serum lipid profiles were measured in the diabetic and non-diabetic rats.

Results: In the diabetic rats, the elevated blood glucose levels, total cholesterol and triglycerides were reduced to the normal values by both HE and EASFME of *M. dioica*.

Conclusion: *M. dioica* fruit pulp possesses anti-hyperglycemic and anti-lipidemic effects. The present investigation of this plant established pharmacological evidence to support the folklore claim that it is an anti-diabetic agent.

Keywords: Alloxan; Hypoglycemia; Hypolipidemic; *Momordica dioica*.

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Introduction

Momordica dioica Roxb belongs to the family, Cucurbitaceae. Other members from the same genus, *M. charantia*, *M. balsamina*, *M. cochinchinensis* and *M. cymbalaria*, are well known for their hypoglycemic activity [1-7]. *M. dioica* is a perennial dioeciously climber with tuberous roots found throughout India [8]. The fruits have been used in the treatment of inflammation caused by lizard excretion [9] as well as mental and digestive disorders [10]. The whole plant is known for its use in the treatment of eye disease, poisoning and fever. Local people routinely use this fruit as vegetables and also for the treatment of diabetes mellitus. The hypoglycemic activity of *M. dioica* was reported earlier [11], but no scientific investigation was conducted on this plant. This study was therefore taken to evaluate the antidiabetic activity and other related metabolic effects of the fruit pulp of *M. dioica* in alloxan-induced diabetic rats.

Materials and Methods

Plant material

The plant was collected from Kolli hills, in the month of September 2002 and identified by a Taxonomist, Dr P Jayaraman with voucher specimen (No. MD/111) was preserved in our college museum for future reference. The plant material was shade dried at room temperature for 10 days, coarsely powdered with the help of a hand-grinding mill and the powder was passed through sieve No. 60 and used for extraction.

Animals

Wistar albino rats of either sex weighing 180-200 g were obtained from the Tamil Nadu Veterinary and Animal Science University, Madhavaram, Chennai, India. They were placed in polypropylene cages with wire-net floors in a controlled room environment ($25\pm 2^\circ\text{C}$) and were provided with standard laboratory food and boiled water *ad libitum*

under natural day-night cycle. Before each experiment, the animals were fasted for at least 18 hr.

Preparation of extracts

The fruit pulp was air-dried, coarsely powdered and extracted by maceration successively with hexane and methanol for 48 hr. Then the extract was vacuum dried using rotary vacuum flash evaporator to yield a solid residue of the respective hexane extract (HE, yield = 0.5% w/w) and methanol extract. The methanolic extract was further fractionated with ethyl acetate to get ethyl acetate soluble fraction of methanolic extract. The soluble fraction was separated and concentrated under vacuum to get dried residue ((EASFME, yield = 2.6% w/w).

Toxicity studies

Minimum lethal dose (MLD) in Wistar albino mice in group of 10 each for each dose was calculated for both HE and EASFME by the method of Litchfield and Wilcoxon [12]. The animals were administered oral graded doses of HE and EASFME. MLD for both HE and EASFME was >3.2 g/kg.

Hypoglycemic activity

The following five groups of six animals each were used in the experiment:

- Group I – normal untreated rats
- Group II – diabetic rats
- Group III – diabetic rats given glibenclamide 10 mg/kg
- Group IV – diabetic rats given HE 400 mg/kg
- Group V – diabetic rats given EASFME 400 mg/kg body weight, orally for 15 days, respectively

Diabetes was induced in the appropriate animals by an intraperitoneal (ip) injection of freshly prepared alloxan (120 mg/kg). The glucose levels of the rats were evaluated and the rats with blood glucose levels more than 350 mg/dl were considered diabetic and used for the experiment.

Oral glucose tolerance test

After an overnight fasting, blood sample (0.2 ml) was collected from each of the rats in the different groups by the orbital sinus puncture. The rats of all the groups were administered glucose solution (3 g/kg) by gavage without delay. Blood was collected at 30, 60, 90 and 120 min time intervals after glucose administration and the serum glucose levels were then measured using standard procedures.

The change in body weight before and after the treatment and also urine sugar of all the rats were determined on 16th day.

Statistical analysis

The glucose levels were determined in triplicates and expressed as mean ± SEM (standard error of mean). The statistical analysis was performed using one-way analysis of variance (ANOVA) followed by

Dunnett's test. At 95% confidence interval, p values <0.05 were considered statistically significant.

Results

Table 1 shows the changes in the levels of blood glucose in normal, diabetic control and rats treated with the extracts after oral administration of glucose (3 g/kg). The diabetic rats showed significant increase in the blood glucose at 30 and 120 min. In extracts and glibenclamide treated animals, blood glucose concentrations significantly decreased after 60 min. A significant reduction in blood glucose levels in both HE and EASFME treated animals was observed (p < 0.001).

The cholesterol and triglyceride levels were significantly higher in the diabetic group when compared to normal rats. The HE treated diabetic rats has significantly reduced

Table 1: Glucose tolerance test in normal and experimental group

Groups	Blood glucose levels (mg/dl)				
	0 min	30 min	60 min	90 min	120 min
Normal	81.1 ± 4.1	180.6 ± 6.4	155.4 ± 4.6	110.5 ± 5.1	92.7 ± 4.2
Diabetic control	172.3 ± 7.1	255.4 ± 7.9	298.6 ± 8.7	312.4 ± 8.2	304.5 ± 8.1
Glibenclamide 10 mg/kg	96.7 ± 4.3	195.8 ± 5.1**	172.1 ± 6.4**	122.9 ± 5.2*	106.2 ± 5.5*
Diabetic + HE 400 mg/kg	93.5 ± 3.4	210.1 ± 6.4*	187.6 ± 4.9*	143.2 ± 3.3**	111.3 ± 3.6
Diabetic + EASFME 400 mg/kg	94.9 ± 3.7	222.3 ± 6.6	202.4 ± 5.6	174.5 ± 4.1*	136.7 ± 4.6**

Values are given as mean ± S.E.M for six rats in each group. * P < 0.05, ** P < 0.001 as compared with control

Table 2: Effect of *M. dioica* fruit pulp extract on serum glucose, cholesterol and triglycerides in diabetic rats

Groups	Glucose (mg/dl)	Cholesterol (mg/dl)	Triglycerides (mg/dl)
Normal	82.2 ± 8.8	76.3 ± 3.9	76.0 ± 7.8
Diabetic control	500.0 ± 42.8	194.7 ± 3.7	104.2 ± 5.1
Glibenclamide 10 mg/kg	198.3 ± 18.9** (73.1)	82.2 ± 3.4** (95.1)	43.2 ± 2.1** (216.4)
HE 400 mg/kg	219.0 ± 26.1* (67.3)	58.2 ± 6.4** (115.4)	81.2 ± 3.7 (81.7)
EASFME 400 mg/kg	205.0 ± 18.5* (70.6)	88.2 ± 6.4** (89.9)	71.3 ± 3.6* (116.5)

Values are given as mean ± SEM for six rats in each group. Figures in the parenthesis indicate the percent protection in individual parameters from their elevated values. The % of protection is calculated as 100 x (values of diabetic control - values of samples) / (values of diabetic control - values of control). *P < 0.05, ** P < 0.001 as compared with diabetic control

levels of both cholesterol and triglycerides (58.2 ± 6.4 and 81.2 ± 3.7 mg/dl, respectively) when compared to diabetic control (194.7 ± 3.7 and 104.2 ± 5.1 mg/dl, respectively). EASFME treated diabetic rat also reduced the levels of cholesterol and triglycerides (Table 2).

The body weights of diabetic control group animals decreased when compared with the normal group. However, after the administration of the extract, the weight of the animals became nearly normal.

Discussion

In the present study the hypoglycemic and hypolipidemic activities of the fruit pulp extract of *M. dioica* was evaluated in alloxan-induced diabetic rats. The continuous treatment of *M. dioica* extract for a period of 15 days caused a significant reduction in blood glucose level in diabetic rats indicating that the plant extracts may be useful in the management of diabetes. This finding supports the previous reports of the effectiveness of the plant in the treatment of diabetes. Thus, *M. dioica* share the hypoglycemic property with other species of this genus namely *M. charantia* and *M. foetida* known to have hypoglycemic effects [15]. Aqueous extract of *M. charantia* fruits reduced the fasting glucose levels of both hyperglycemic and normoglycemic mice and foetidin, isolated from *M. foetida*, has been shown to lower the blood glucose level of normal rats, but not in diabetic animals.

For several years, it has been known that high levels of cholesterol and triglycerides in the blood can increase the risk of developing heart disease. Cholesterol is transported in the bloodstream by lipoproteins. Low-density lipoproteins (LDL's) tend to deposit cholesterol-laden "plaques" in artery walls, thus narrowing the opening through which blood flows and increasing the risk of heart disease.

People with Type 2 diabetes are at especially high risk for hyperlipidemia, most

commonly in the form of elevated triglyceride levels and decreased high density lipoprotein (HDL) levels. In recognition of the link between blood cholesterol levels and heart disease, a total blood cholesterol level of less than 200 mg/dl is desirable, a level of 200 mg/dl to 239 mg/dl is considered borderline, and a level of 240 mg/dl or above is regarded as high. Similarly, an LDL cholesterol level of less than 100 is optimal, a level of 100 to 129 mg/dl is near optimal, a level of 130 to 159 is borderline, and a level of more than 160 mg/dl is considered high. An HDL cholesterol level below 40 mg/dl is also thought to place people at increased risk for heart disease.

Although this study is limited by the absence of the data on LDL and HDL, it is assumed that the extracts possibly have the ability to reduce LDL and triglycerides thereby having the ability to reduce the risk of cardiovascular diseases.

Conclusion

Our study has shown that the extracts of *M. dioica* possess blood glucose, cholesterol and triglycerides lowering effect in alloxan induced hyperglycemic rats. The work confirms the folklore use of *M. dioica* for the control of diabetes.

Acknowledgements

Authors are grateful to Dr R Shivakumar, Pro-Vice Chancellor, SRM University and Dr KS Lakshmi, Dean, College of Pharmacy, SRM University, for providing necessary facilities to carry out this work.

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