



## BENEFICIAL EFFECTS OF DIFFERENT EXTRACTS OF MOMORDICA DIOICA SEED ON LIPID PROFILE STATUS IN STREPTOZOTOCIN INDUCED DIABETIC RATS

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### ABSTRACT

Diabetes mellitus is one of the widespread and severe metabolic disorders in human all over the world. The present study was designed to evaluate the potential anti-hyperlipidemic efficacy of chloroform and ethylacetate extracts of *Momordica dioica* seeds in diabetic rats. Diabetes was induced by giving Streptozotocin intraperitoneally, rats which showed blood glucose levels of >250 mg/dl were selected for the study. Different extracts were administered at a dose of 200 mg/kg orally and blood glucose levels were estimated by glucose-oxidase method. Metformin (50 mg/kg) was administered as standard oral hypoglycaemic agent. The plasma levels of low density lipoproteins (LDL), very low density lipoproteins (VLDL), cholesterol (CH) and triglycerides (TG) were estimated and found to be significantly ( $p < 0.0001$ ) lowered in diabetic rats. The results showed that the present study provided a rationale for the use of *Momordica dioica* seed extracts as an anti-diabetic agent and anti-hyperlipidemic agent.

**KEYWORDS:** Diabetes mellitus, *Momordica dioica*, Streptozotocin, cardiovascular complications, anti-hyperlipidemic agent.



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## INTRODUCTION

Diabetes mellitus is one of the most major metabolic diseases and cause of death in modern society. Diabetes is a group of chronic disorders characterised by disarrangement in carbohydrates, proteins and fat metabolism caused by hyperglycemia (or) reduced insulin secretion (or) both. There are various severe diabetic complications such as retinopathy, neuropathy, nephropathy, cardiovascular complications and ulceration. Apart from the above complications, cardiovascular risk is most important with altered lipid profile. It is characterised by increased levels of Cholesterol (CH), triglycerides (TG), low density lipoproteins (LDL) and very low density lipoproteins (VLDL)<sup>1</sup>. An unusual deposition of fat in the liver and muscle is observed which elicits the insulin resistance that terminates in  $\beta$ -cell reduction in type 2 diabetes. In Diabetes, biochemical alterations of glucose and lipid metabolism occur which leads to an elevated production of Reactive oxygen species (ROS), a decline in anti-oxidative defence mechanism which promote the development of late complications. To reduce the late complications and negative outcomes of the disease, it is necessary to control the blood glucose levels and lipid levels<sup>2</sup>. Therefore, successful management depends upon diminished glucose levels in the blood and lipid homeostasis, which combats with the cardiovascular obstacles. Many side effects have been reported with oral synthetic hypoglycemic agents and they were not successful in maintaining euglycemia and controlling long-term microvascular and macrovascular complications. According to W.H.O 300 million people will have diabetes by the year 2025<sup>3</sup>. The use of herbal medicines for the treatment of diabetes has gained importance throughout the world. Hence, there is an increased demand to use natural products with anti-diabetic activity due to the side effects associated with the use of insulin and oral hypoglycemic agents. Hypercholesterolemia and hypertriglyceridemia are common complications of diabetes in addition to hyperglycemia. Hyperlipidemia contributes significantly in the manifestation and development of atherosclerosis and coronary

heart disease<sup>4</sup>. India is a country with rich natural resources and wide variety of medicinal plants. The plants which show significant pharmacological activity and low toxicity need extensive screening. *Momordica dioica* Roxb. Ex.Wild. (Cucurbitaceae) is a perennial, dioecious climber with tuberous roots found throughout India from Himalayas to Ceylon. The whole plant has many medicinal properties and used for the treatment of eye diseases<sup>5</sup>, poisoning, and fever. Fruits are used as vegetables and also used in the treatment of inflammation, mental and digestive disorders. Leaves of the plant are antihelminthic, aphrodisiac. It is used to cure jaundice, asthma, bronchitis, hepatic damages and urinary retention<sup>6</sup>. Roots were found to possess full of medicinal values. Juice of root is used as stimulant, astringent, antiseptic whereas powder of root is applied to skin to make it soft and to reduce perspiration<sup>7</sup>.

### **Phytochemical Screening of Organic extract**

Freshly prepared organic extracts were tested for the presence of alkaloids, glycosides, tannins, saponins, carbohydrates and cardiac glycosides using standard procedure.

The aim of the present study was to evaluate the effects of chloroform and ethylacetate extracts of *Momordica dioica* (ME) seed on circulatory lipids in diabetic rats induced with Streptozotocin. Oral hypoglycaemic agent Metformin was used as a standard drug.

## MATERIALS & METHODS

### **Collection of Plant and preparation of Extract**

Fresh fruits of *Momordica dioica* (5 kg) were collected locally, during July-August, 2011 and seeds were removed mechanically and dried under shade. They were identified and authenticated by S. V. University, Botany department, Tirupati. The seeds were powdered in electric grinder. The powder was subjected to chloroform and ethylacetate extraction, in Soxhlet apparatus. After filtration through Whatman filter paper, the filtrates were evaporated to dryness in desiccator.

**Test animals**

Animal Protocol was approved by IAEC (Institutional Animal Ethical Committee) of CPCSEA (Committee for Purpose of Control and Supervision of Experimentation on Animals) through its reference no: IAEC/SVCP/2011/006, dated: 26/7/11. Male Wistar rats, weighing (180-250 gms) were obtained from NIN (National Institute of Nutrition), Hyderabad. The animals were housed with free access to food and water for at least one week in an air conditioned room (25°C) under a 12 hr light:dark cycle prior to the experiment. They were fed with standard diet (Hindustan Lever) and water *ad libitum*.

**ANTIDIABETIC ACTIVITY****Induction of Experimental Diabetes**

Diabetes was induced by a single intraperitoneal injection of a freshly prepared Streptozotocin (STZ) solution (Sisco Research laboratories pvt ltd. Mumbai-93, India. Batch No: T-835796) (Dose: 30-50mg/kg) in citrate buffer 0.1 M, pH 4.5 to overnight fasted rats. Diabetes was identified by polydipsia, polyuria and by measuring blood glucose levels 48 hr after injection of STZ. Animals which did not develop blood glucose levels more than 250 mg/dl were rejected<sup>8</sup>.

Experimental groups: The animals were divided into seven groups, six rats in each group.

Group I: Normal untreated rats (Control)

Group II: Normal rats administered with Chloroform extract of *Momordica dioica* seeds (200mg/kg) (po)

Group III: Normal rats administered with Ethylacetate extract of *Momordica dioica* seeds (200mg/kg) (po)

Group IV: Diabetic rats

Group V: Diabetic rats administered with Metformin (50 mg/kg) (po)

Group VI: Diabetic rats administered with Chloroform extract of *Momordica dioica* seeds (200mg/kg) (po)

Group VII: Diabetic rats administered with Ethylacetate extract of *Momordica dioica* seeds (200mg/kg) (po)

Animals of Group I were given with 0.9% saline and served as control, and group II was administered with Chloroform Extract of *Momordica dioica* seeds (CEMDS 200mg/kg dissolved in 0.25% Carboxy Methyl Cellulose)

orally. Group III was administered with Ethylacetate Extract of *Momordica dioica* seeds (EEMDS 200mg/kg dissolved in 0.25% Carboxy Methyl Cellulose) orally. Group IV were Diabetic control rats, Group V was given with Metformin (50 mg/kg), a standard oral Hypoglycemic agent. Group VI was diabetes induced rats; administered with Chloroform Extract of *Momordica dioica* seeds (CEMDS 200mg/kg dissolved in 0.25% Carboxy Methyl Cellulose) orally. Group VII was also diabetes induced rats; administered with Ethylacetate Extract of *Momordica dioica* seeds (EEMDS 200mg/kg dissolved in 0.25% Carboxy Methyl Cellulose) orally. All experimental animals were administered with the two extracts of *Momordica dioica* for a period of 15 days, and on 16<sup>th</sup> day blood was collected by retro-orbital sinus puncture. Blood withdrawn was centrifuged and serum was separated for biochemical study. Serum lipid profiles (total cholesterol, triglycerides, HDL-cholesterol, LDL cholesterol and VLDL-cholesterol), was measured by using ERBA reagents and ERBA kit in Semi-Auto Analyser. The Fasting blood glucose (FBS) and Post-Prandial glucose (PLBS) levels were estimated by Glucose-oxidase method<sup>9</sup>.

**Statistical Analysis**

The results of the estimation were reported as Mean  $\pm$  SEM. Student's t-test was applied when two groups amongst were compared. The values were considered significant when  $p < 0.05$ ,  $p < 0.001$ ,  $p < 0.0001$ . Statistical calculations were done using Graph Pad Prism.

**RESULTS & DISCUSSION**

In the present study the hypoglycemic and anti-hyperlipidemic activities of chloroform and ethylacetate seed extracts of *Momordica dioica* seeds were evaluated in Streptozotocin-induced diabetic rats. A continuous treatment of different extracts (chloroform and ethylacetate) of *Momordica dioica* seeds for a period of 15 days caused a significant reduction in blood glucose level in diabetic rats indicating that the chloroform and ethylacetate extracts of *Momordica dioica* seed may be useful to control hyperglycaemia

in diabetes. This finding supports the previous reports of the effectiveness of the plant in the treatment of diabetes. Cholesterol is transported in the bloodstream by lipoproteins. Low-density lipoproteins (LDL) tend to deposit cholesterol-laden "plaques" in artery walls, thus narrowing the opening through which blood flows and increasing the risk of heart disease<sup>10</sup>. 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. Although this study is limited; 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. The effect of different extracts of *Momordica dioica* seed on fasting blood glucose and post-prandial blood glucose levels in normal and diabetic rats was evaluated. Diabetic rats showed significant increase ( $p < 0.0001$ ) in blood glucose levels compared to corresponding normal rats. In normal rats, following the oral administration of seed extracts of chloroform and ethylacetate, the post-prandial glucose levels were decreased significantly ( $p < 0.0001$ ) and showed the values  $89.92 \pm 2.83$  and  $81.83 \pm 1.74$  in extract treated normal rats. In

diabetic rats, the chloroform and ethylacetate seed extracts of *Momordica dioica* exhibited a significant reduction ( $p < 0.0001$ ) in blood glucose levels, showed the values as  $173.33 \pm 3.57$  and  $182.50 \pm 2.14$  as compared to diabetic rats. Anti-hyperlipidemic activity of *Momordica dioica* seed extracts was evaluated. When chloroform extract of *Momordica dioica* seed was given to diabetic rats, there was a significant decrease in CH, TG, LDL and VLDL showed the values as  $123.7 \pm 2.56$ ,  $91.67 \pm 3.77$ ,  $89.33 \pm 1.56$  and  $27 \pm 0.58$  as compared to diabetic rats. Similarly when ethylacetate extract of *M. dioica* seed was given to diabetic group, there was a decrease in CH, TG, LDL and VLDL; showed the values as  $132.17 \pm 0.94$ ,  $109.08 \pm 3.32$ ,  $88.33 \pm 1.58$  and  $26.67 \pm 0.67$  as compared to diabetic rats. The levels of HDL were less in diabetic rats which showed the values as  $20 \pm 0.58$  when compared to normal rats, and following the treatment with both the seed extracts in diabetic rats, showed a significant increase ( $p < 0.0001$ ) in HDL levels. In the present study, metformin was used as a standard oral hypoglycaemic agent which showed a significant reduction in PLBS as compared to diabetic rats.

**Table I**  
**Effect of different extracts of *Momordica dioica* seed on blood glucose levels in Normal and diabetic rats**

Groups	Treatment	FBS (Fasting blood sugar, mg/dl)	PLBS (Post-prandial blood sugar, mg/dl)
I	Normal (Control)	$83.83 \pm 4.61$	$132.5 \pm 2.5$
II	Normal + CEMDS	$81.17 \pm 3.22$	$89.92 \pm 2.83^a$
III	Normal + EEMDS	$81 \pm 2.45$	$81.83 \pm 1.74^a$
IV	Diabetic control	$300 \pm 13.27$	$294.166 \pm 14.16^a$
V	Diabetic+ Metformin	$280.07 \pm 15.36$	$153.344 \pm 2.47^a$
VI	Diabetic + CEMDS	$278.55 \pm 5.93$	$173.33 \pm 3.57^{a,b}$
VII	Diabetic + EEMDS	$283.42 \pm 3.11$	$182.50 \pm 2.14^{a,b}$

Values were reported as MEAN $\pm$ SEM, Diabetic control compared with normal, <sup>a</sup> $p < 0.0001$ ; Normal+CEMDS compared with normal, <sup>a</sup> $p < 0.0001$ ; Normal+EEMDS compared with normal, <sup>a</sup> $p < 0.0001$ ; Diabetic+CEMDS compared with diabetic control, <sup>a</sup> $p < 0.0001$ ; Diabetic+EEMDS compared with diabetic control, <sup>a</sup> $p < 0.0001$ ; Diabetic+Metformin compared to diabetic control, <sup>a</sup> $p < 0.0001$ ; Diabetic+CEMDS compared with diabetic+Metformin, <sup>b</sup> $p < 0.001$ ; Diabetic+EEMDS compared with diabetic+Metformin, <sup>a</sup> $p < 0.001$ .

**Table II**  
**Effect of different extracts of *Momordica dioica* seed on lipid profile status in normal and diabetic rats**

Groups	Treatment	CH (mg/dl)	TG(mg/dl)	HDL(mg/dl)	LDL(mg/dl)	VLDL(mg/dl)
I	Normal (Control)	81.34±0.84	62.83±1.22	54.17±1.25	93.5±0.85	23.5±0.43
II	Normal+CEMDS	92.5±2.14 <sup>a</sup>	132±2.08 <sup>a</sup>	41.5±0.85 <sup>a</sup>	95.67±2.67 <sup>NS</sup>	27.67±0.49 <sup>NS</sup>
III	Normal+EEMDS	120±2.89 <sup>a</sup>	132.17±2.24 <sup>a</sup>	40.83±1.01 <sup>a</sup>	105±1.82 <sup>a</sup>	25.67±0.80 <sup>NS</sup>
IV	Diabetic control	216.34±1.56 <sup>a</sup>	155±1.83 <sup>a</sup>	20±0.58 <sup>a</sup>	138.83±0.98 <sup>a</sup>	43.67±0.88 <sup>a</sup>
V	Diabetic+Metformin	192.5±0.88 <sup>a</sup>	143.84±1.30 <sup>a</sup>	31±1.03 <sup>a</sup>	100±2.82 <sup>a</sup>	26±0.63 <sup>a</sup>
VI	Diabetic+CEMDS	123.7±2.56 <sup>a</sup>	91.67±3.77 <sup>a</sup>	40.5±0.43 <sup>a</sup>	89.33±1.56 <sup>a</sup>	27±0.58 <sup>a</sup>
VII	Diabetic+EEMDS	132.17±0.94 <sup>a</sup>	109.08±3.32 <sup>a</sup>	41.2±0.33 <sup>a</sup>	88.33±1.58 <sup>a</sup>	26.67±0.67 <sup>a</sup>

Values were reported as MEAN±SEM, Diabetic control compared with normal, <sup>a</sup>p < 0.0001; Normal+CEMDS compared with normal, <sup>a</sup> p < 0.0001, NS-Not-significant; Normal+EEMDS compared with normal, <sup>a</sup> p < 0.0001, NS-Not-significant; Diabetic+CEMDS compared with diabetic control, <sup>a</sup> p < 0.0001; Diabetic+EEMDS compared with diabetic control, <sup>a</sup>p<0.0001; Diabetic+Metformin compared to diabetic control, <sup>a</sup> p < 0.0001.

## CONCLUSION

Our study had shown that the chloroform and ethylacetate extracts of *Momordica dioica* seeds possesses anti-hyperlipidemic activity in diabetes induced rats. So, from the evident of results it can be concluded that chloroform and ethylacetate extracts may be used for control and management of diabetes.

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