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Antidiabetic and Hypolipidemic activities of *momordica tuberosa* unripe fruit extract on diabetic induced rats

Palanivel. V¹*, Mohammed Shafi² Senthil Kumar K.L³.¹PRIST University Thanjavur, TamilNadu²Department of Pharmacology, Padmavathi College of Pharmacy & Research Institute, TamilNadu³Department of Pharmaceutics, Padmavathi College of Pharmacy & Research Institute, TamilNadu(Received: 10th October 2013;Accepted: 6th November 2013)**Abstract**

The aim of this research was to investigate antidiabetic and antilipidemic activities of *momordica tuberosa* unripe fruit extract on streptozotocin induced diabetic albino rats. Alcoholic extract of *momordica tuberosa* was prepared with dried unripe fruit powder & 80% ethanol and subjected to phytochemical screening tests. Preliminary phytochemical investigations showed the presence of glycosides, flavonoids, saponins in ethanolic extract which are proved to act as potent antioxidants indicating the possibility of the antidiabetic nature. Selection of dose was made on the basis of acute oral toxicity study as per OECD guidelines 423. A comparison was made between the action of *momordica tuberosa* extract and glibenclamide (6mg/kg body wt.). Albino rats were divided into groups for normal control, diabetic control, diabetic treated with GBC (6mg/kg BW) and diabetic received *momordica tuberosa* (150 & 300 mg/kg BW). Ethanolic extract of *momordica tuberosa* unripe fruit possess significant ($P < 0.05$) hypoglycemic potential in STZ induced hyperglycemic rats and showed significant improvement in the lipid profile comparable to glibenclamide treated group. However, improvement in lipid profile was less than that achieved with the standard drug glibenclamide.

Corresponding author

Tel +919894269874

¹Department of Pharmacology
PRIST University, Thanjavur,
TamilNadu, India
velmpfarm@gmail.com**Key Words**Antidiabetic activity, *momordica tuberosa*
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Hypolipidemic activity,
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INTRODUCTION

Diabetes mellitus is a group of metabolic diseases characterized by high blood sugar (glucose) levels that result from defects in insulin secretion, or its action, or both. Diabetes mellitus, commonly referred to as diabetes, these was first identified as a disease associated with "sweet urine," and excessive muscle loss in the ancient world. Elevated levels of blood glucose (hyperglycemia) lead to spillage of glucose into the urine, hence the term sweet urine. Normally, blood glucose levels are tightly controlled by insulin, a hormone produced by the pancreas. Insulin lowers the blood glucose level.^{1, 2, 3.} Currently in India about 30 to 33 million people are suffering from diabetes mellitus and estimated to be 70 million in 2025. Undesirable side effects of currently available of antidiabetic drugs demand for alternative therapy. Herbs play a major role in the treatment of such disease and are well known to mankind since time immemorial to treat a number of ailments by virtue of their contents. One of such plants is *Momordica tuberosa* Cogn. (cucurbitaceous) originates in the tropical regions of India and South East Asia as a climber. The plant is a perennial herbaceous climber, either allowed to trail on the ground or climbing on supports with the aid of tendrils. It is found in the Indian states of Andhra Pradesh, Karnataka, Madhya Pradesh, Maharashtra and Tamil Nadu as a weed. It is commonly known by the name Athalkkai and Karchikai in regional languages in India^{4.} The tubers of the plant are used traditionally as Abortifacient^{5.}

Fruits of the plant contain vitamin C, a known antioxidant^{6,} and possess antihyperglycemic activity⁷. The present study is designed to compare the hypoglycemic activity of *momordica tuberosa* extract with standard oral hypoglycemic drug glibenclamide.

MATERIALS AND METHODS

Drug and chemicals

Glibenclamide drug was obtained from Micro lab Hosur, STZ received from Himedia laboratory Mumbai; 80% Ethanol were purchased from SD Fine Chem Ltd, Mumbai; all other chemicals used for the study were of analytical grade.

Plant Material

The plant material (unripe fruits) of *momordica tuberosa* used for the investigation was obtained from Madurai vegetable market and authenticated by Dr. A.K. Pradeep, Herbarium Curator, Dept. of Botany, University of Calicut, Kerala, India.

Alcoholic Extraction

The unripe fruits were collected and shadow dried. The shade-dried unripe fruits were subjected to pulverization to get coarse powder. The coarsely powder of unripe fruits *momordica tuberosa* was used for extraction with 80% ethanol in soxhlet apparatus. The extract was evaporated to dryness with the help of rotator vacuum evaporator.

Phytochemical screening

A preliminary phytochemical analysis was carried out in the ethanolic

extract of *momordica tuberosa* by employing the standard phytochemical procedures to reveal the presence of various phytoconstituents.

Animals

Albino rats of wister strain of either sex weighing 150-200 gms breed in the central animal house, Padmavathi college of pharmacy and Research Institute were used for these studies. The experimental protocol has been approved by institutional animal ethics committee Ref: No. CPCSEA / PCP / IAEC / MPHARM / 127 / 2013. Before and during the experiment, rats were fed with standard diet. After randomization into various groups and before initiation of experiment, the rats were acclimatized for a period of 7 days under standard environmental conditions of temperature, relative humidity, and dark/light cycle. Animals described as fasting were deprived of food and water for 16 hours *ad libitum*

Acute oral toxicity study

Acute oral toxicity study was carried out by using Wistar rats by "fixed dose" method of OECD guideline NO. 420 and a starting dose of 1500 mg/kg bodyweight was adopted. There were no toxic effects or mortality observed up to 14th days with the extract.

Experimental Design

Five groups of rats, six in each received the following treatment schedule.

Group I: Normal control (saline).

Group II: Streptozotocin (50mg/kg body wt.ip).

Group III: Streptozotocin +GBC (6mg /kg body wt.p.o).

Group IV: Streptozotocin +MTE (150 mg/kg body wt.p.o).

Group V: Streptozotocin +MTE (300 mg/kg body wt.p.o).

Induction of Diabetes in Experimental Animals

Rats were induced diabetic by a single intraperitoneal injection of STZ (50 mg/kg) STZ was first weighed individually for each animals according to the body weight then solubilised in ice cold 0.1M citrate buffer pH 4.5 kept in ice and administer within five min at a dose of 50mg/kg body weight. After 48 hours of streptozotocin administration the rat with moderate diabetes having glycosuria & hyperglycemia was observed.

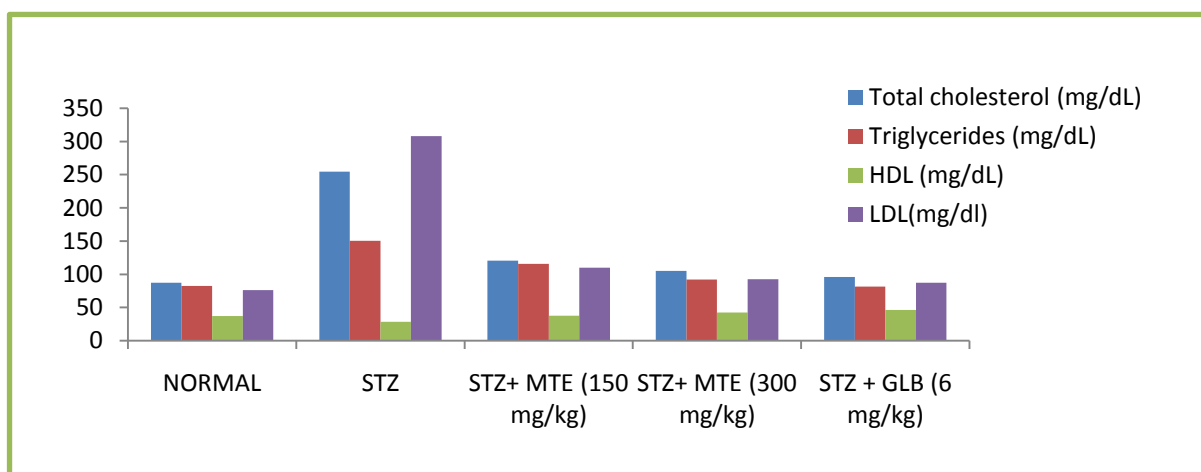
Evaluation of hypoglycemic activity

MT unripe fruit extract was screened to find out hypoglycemic effect by estimation of BSL in STZ induced hyperglycemic rats. Blood samples were drawn at the end of study (21st day). Fasting blood glucose estimation (GOD-POD) and body weight measurement were done on day 1 and 21 of the study. At the end of the experimental period on the 21 days, the rats were deprived of food overnight and blood was collected in a tube containing heparin for the estimation of cholesterol (CHOD-POD), triglycerides (GPO-POD), HDL, and LDL method by puncturing the retro orbital under mild ether anesthesia.

Tab 1. Antidiabetic effect of MTE in STZ-induced diabetic rats (Mean \pm SEM)

Group	Treatment	Blood glucose level (mg/dL)	
		Day 1	Day 21
I	Normal	115.27 \pm 4.50	113.82 \pm 2.40
II	STZ	268.81 \pm 2.30	402.00 \pm 3.40
III	STZ + GBC (6 mg/kg)	278.27 \pm 3.20	118.53 \pm 3.50***
IV	STZ + MTE (150 mg/kg)	280.45 \pm 2.37	142.48 \pm 2.70*
V	STZ +MTE (300 mg/kg)	299.29 \pm 3.80	130.43 \pm 3.50**

*P<0.05, **P <0.001, When groups III, IV and V compared with diabetic control, i.e. group II. (Among the treatment groups IV group shown more significant effect)

Fig 1. Mean (\pm SD) values of lipids level in different groupsTab 2. Effect of MTE on body weights in diabetic rats (Mean \pm SEM)

Groups	Treatment	Body weight	
		Day 1	Day 21
I	Normal	219.20 \pm 2.30	222.47 \pm 3.20
II	STZ	235.23 \pm 3.40	188.25 \pm 4.30
III	STZ + GBC (6mg/kg)	235.34 \pm 2.70	233.25 \pm 1.80***
IV	STZ+ MTE (150 mg/kg)	238.24 \pm 2.70	236.14 \pm 2.80*
V	STZ+ MTE (300 mg/kg)	243.43 \pm 3.40	240.73 \pm 2.50**

P<0.05, **P<0.001, When groups III, IV and V compared with diabetic control i.e. group II. (Among the treatment groups IV group shown more significant effect)

Tab 3. Effect of MTE on lipid profiles in diabetic rats (Mean \pm SEM)

Groups	Treatment	Total cholesterol (mg/dL)	Triglycerides (mg/dL)	HDL (mg/dL)	LDL (mg/dl)
I	Normal	87.28 \pm 3.80	82.42 \pm 5.16	37.32 \pm 2.9	76.4 \pm 3.11
II	STZ	254.73 \pm 7.60	150.52 \pm 4.71	28.23 \pm 2.2	308 \pm 11.29
III	STZ + GBC (6 mg/kg)	95.72 \pm 5.30***	81.47 \pm 4.5***	46.28 \pm 4.8***	87.45 \pm 2.89***
IV	STZ+ MTE (150 mg/kg)	120.54 \pm 3.40*	115.55 \pm 4.62*	37.47 \pm 5.7*	110.10 \pm 18*
V	STZ+ MTE (300 mg/kg)	105.27 \pm 3.40**	92.29 \pm 4.23**	42.23 \pm 4.9**	92.5 \pm 2.23**

*P<0.05, **P<0.001, When groups III, IV and V compared with diabetic control i.e. group II. it shown significant effect. (Among the treatment groups IV group shown more significant effect)

Histopathology study on pancreas

The animals were sacrificed immediately after experimental period under mild ether anesthesia. The pancreas of each was isolated, they were fixed in 10% formalin buffer and carried out histopathology studies.^{8,9}

Statistical analysis

The data were analyzed by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison tests to determine level of significance. A value of P<0.01 was considered significant results are expressed as mean SEM.

RESULTS AND DISCUSSION

Preliminary investigations

Preliminary phytochemical investigations showed the presence of glycosides, flavanoid, saponins in ethanolic extract which are proved to

act as potent antioxidants indicating the possibility of the antidiabetic nature. In acute oral toxicity study, ethanolic extract at a dose of 1500 mg/kg body wt. showed no toxic effects or mortality upto 14 days, based on this, assessment of hypoglycemic activity, two doses were selected i.e. first dose 1/10th of the LD50 cut off value and second dose doubled that of one tenth dose i.e. (150 and 300mg/kg respectively). After 48 hours streptozotocin injected, the rats were showed diabetes symptoms such as glycosuria & hyperglycemia (i.e. blood glucose in ranges of 268-300mg/dl).

Effect on blood glucose level

The antidiabetic effect of MTE on the blood glucose levels in diabetic rats is presented in Tab 1, shows variation in blood glucose levels from day 1 to day 21 in each group. Mean BGL in non

diabetic control and diabetic induced varied between 115 to 268 mg/dl throughout the study period. In standard control group (GBC) there was significant reduction of BGL from Day 1 (278 mg/dl) to Day 21 (118 mg/dl). In test groups, which received 150 mg/kg body weight of unripe fruit extract of *Momordica tuberosa*, shows significant reduction in BGL on day 1, from 280mg/dl to 142.5 mg/dl on day 21. However, animals treated with dose of 300mg/kg body showed increased in decreasing BSL, when the groups (MTE two doses and diabetic control) were compared between day 1 and 21 findings, the difference was found statistically significant $P < 0.05$ and $P < 0.001$ at the doses of 150 and 300 mg/kg of MTE respectively.

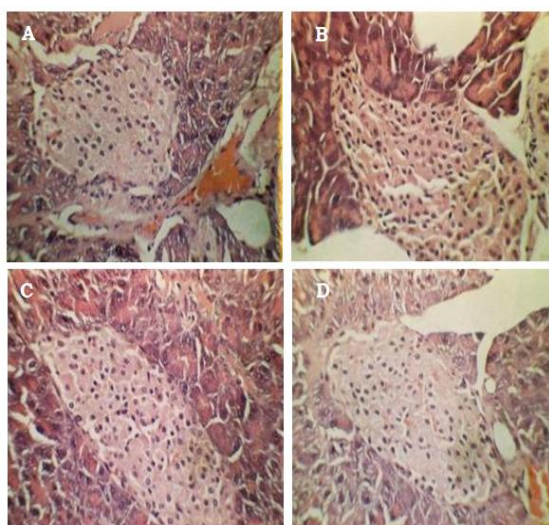


Fig 2. Histopathological studies of pancreas of A) diabetic control , B) GBC treated (6 mg/kg), C) (STZ + MTE(150 mg/kg)treated and D) STZ + MTE (500 mg/kg) treated.

Effect on body weight

The body weight significantly ($p < 0.01$) decreased in STZ-treated group compared to control group. The MTE at the dose level of 150 and 300 mg

/kg b.w/p.o showed a significant improvement in the body weight on ($p < 0.05$ and $p < 0.01$) 21th day respectively compared with diabetic control, which depicts in Tab 2.

Effect on lipid profile

The marked increased in lipid level is observed (21 days) in STZ-induced diabetic animals shown in Tab 3. Treatments with MTE extract remarkably decreased in the total cholesterol and triglyceride levels. The treatment with MTE (150 mg/kg b.w/p.o and 300mg/kg b.w/p.o) showed significant ($p < 0.01$) decrease in serum cholesterol, triglyceride when compared to STZ induced diabetic rats. As well as the treatment with MTE (150 mg/kg b.w/p.o and 300mg/kg b.w/p.o) showed significant ($p < 0.01$) increase in serum HDL-cholesterol when compared to STZ-induced diabetic rats. However, glibenclamide (0.6mg/kg b.w/p.o) treatment showed significant ($p < 0.01$) increase of HDL-cholesterol and glycogen level in liver when compared to STZ-induced diabetic rats.

Histopathology

Histopathology studies in the control group showed reduction in the number of pancreatic islets as well as in the number of beta cells. The islets were irregularly shaped, relatively small and atrophic. Most of the beta cells were destroyed and even if present, they were destroyed partially (Fig 2A). Most cells of the islets were small and degranulated with scanty cytoplasm. Insulin producing beta

cells were drastically decreased, whereas glucagon producing alpha cells were predominantly present. Severe vacuolation and degranulation were present in the beta cells of a maximum number of islets. The treatment group (MT) showed an increase in the number of pancreatic islets and in the number of beta cells in the pancreas. Beta cells were seen in clusters (Fig 2C&D). This indicated that MT was regenerating beta cells. The regeneration of the beta cells of the STZ destructed islets is probably due to the fact that the pancreas contains stable (Quiescent) cells which have the capacity of regeneration. Therefore, the surviving cells can proliferate to replace the lost cells. Restore the secretion of insulin, and thus regulates hyperglycemia.

CONCLUSION

From this preminarily study, concluded that *Momordica tuberosa* unripe fruit extract have shown significant antidiabetic & hypolipidemic effects.

The exact mechanism of action of hypoglycaemia seen with the MT unripe fruit extract cannot be explained on the present results. However it could be proposed that the various phytoconstituents of MT unripe fruit extract and the regenerating property on pancreas be responsible for the hypoglycemic and hypolipidemic activities. However, further studies are required to establish the exact mechanism of action of the same to have beneficial effects in diabetes mellitus that holds the hope of new generation of antidiabetic drugs.

Abbreviations used: MT= *Momordica tuberosa* (unripe fruit); MTE= Ethanolic extract of *Momordica tuberosa*; OECD= Organization of Economic Co-Operation and Development; HDL= high density lipids; LDL= low density lipids; STZ= streptozotocin; GBC=Glibenclamide; GPO-POD= Glycerokinase Peroxidase-Peroxidase, CHOD-POD= Cholesterol oxidase- peroxidase enzyme.

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