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RESEARCH ARTICLE

Antihyperglycemic and Antihyperlipidemic Effect of Aqueous Fruit Extract of *Momordica charantia* against Alloxan Induced Diabetic Rats

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ABSTRACT

Momordica Charantia is used extensively in the indigenous system of medicine as an anti-diabetic agent. The current investigation focuses on the serum insulin augmentation, anti-hyperglycemic and anti-hyperlipidemic property of aqueous fruit extract *of Momordica Charantia* on alloxan induced diabetes in male *albino* rats. The diabetes induced animals were fed with the fruit extract at 250mg/kg body wt and 350mg/kg body wt. The aqueous fruit extract administrated animals revealed a significant ($P<0.001$) increment of serum insulin levels, higher reduction in hyperglycemia and hyperlipidemia when compared to the diabetic control rats ($P<0.001$). The histological studies of the endocrine region of pancreas of diabetic animals revealed shrinkage of ß-cells of islets of langerhans. The aqueous fruit extract treated animals revealed restoration of ß-cells.

KEYWORDS

Momordica Charantia, Alloxan, Hyperglycemia, Hyperlipidemia

INTRODUCTION

Diabetes mellitus is a group of metabolic disorders affecting many people in world wide. It is mainly characterized by chronic hyperglycemia, resulting from defects in insulin secretion or insulin action. Diabetes mellitus consists of a group of syndromes characterized by hyperglycemia; altered metabolism of lipids, carbohydrates, proteins, and also increased risk of complications from vascular disease[1].

The cardinal manifestation of diabetes mellitus is the result of two main factors. 1). Decreased entry of glucose into the cells and 2). Decreased utilization of glucose by the liver.

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Diabetes is characterized by symptoms such as weakness, polyurea, excessive thirst as well as ketonemia, ketonuria and ketosis due to altered metabolism of lipids, carbohydrate and proteins. In a diabetic condition, increased serum lipids are due to the increased lipolysis of adipose tissue and thereby abnormal lipoprotein concentration. The low HDL cholesterol and high VLDL lipoproteins cause atherosclerosis and renal damage[2].

According to World Health Organization (WHO) projections, the prevalence of diabetes is likely to increase by 35%. Currently there are over 150 million diabetic patients worldwide. Recent estimates project that the number of patients diagnosed with Type II diabetes will more than double to 300 million before 2025. India has more than 30 million people with

diabetes. It is estimated that by 2025, the number of diabetics will rise to 57 million in India, the highest number of diabetics in the World[3]. This is because none of the antidiabetic drugs is capable of giving long term glycemic control without causing any adverse side effects[4]. Meanwhile, medicinal plants that are effective in controlling plasma glucose level with minimal side effects are commonly used in under developed countries as alternative therapy[5].

There are several drugs in clinical practice for the treatment of diabetes mellitus. Many of these oral anti diabetic agents have been reported to show serious adverse effect such as liver problems, lactic acidosis and diarrhea[6]. In addition, they are not suitable for use during pregnancy.

It is apparent that due to the side effects of the currently used drugs, there is a need for a potent drug with minimal adverse effects, which can be taken for long durations. Plant materials which are being used as traditional medicine for the treatment of diabetes are considered one of the good sources for a new drug or a lead to make a new drug[7].

Throughout the world many traditional plant treatments for diabetes exist. However, few have received scientific or medical scrutiny and the WHO has recommended that traditional plant treatments for diabetes warrant further evaluation[8]. Many species of plants act as anti-diabetic agents but only a few of them have been investigated. *Momordica charantia* (Family: Cucurbitaceae) is a tropical household vegetable used as daily food and also as folk medicine especially for diabetes.

The present study was carried out in male albino rats to test the efficacy of aqueous fruit extract of *Momordica charantia* on serum insulin and serum lipid profile changes associated with alloxan induced diabetes.

MATERIALS AND METHODS

Plant Material

The unripe fruits of *Momordica charantia* were collected in and around Vellore District, Tamilnadu, India. The fruits were cleaned with distilled water and shade dried at room temperature and authenticated in the Department of Botany, C Abdul Hakeem College, Vellore District, Tamilnadu, India.

Preparation of Plant Extract

Fresh unripe fruits of *M. charantia* were collected, washed and cut into small pieces. The fruits were dried in shade and powdered. About 100gms of dried powdered fruits of *M. charantia* were taken and mixed with 500 ml of distilled water and magnetically stirred in a separate container overnight at room temperature. The residue was removed by filtration and the aqueous extracts were concentrated under vacuum to get solid yield of 7%. The plant extract was administered orally to animals in aqueous solution[9].

Animals

Male *albino* wistar rats weighing around 180-200gms were purchased from Tamilnadu Veterinary and Animal Science University, Chennai, India. The animals were kept in polypropylene cages and maintained in an animal room, under controlled temperature of 25±2ºC.Humidity and airflow conditions with a 12±1 hr light and dark schedule was maintained in the animal house till the animals were acclimatized to the laboratory conditions, and were fed with commercially available rat chow. They had free access to water. The experimental protocol was conducted in accordance with the institutional guideline[9].

Experimental Induction of Diabetes

Diabetes was induced in the rats by the administration of single intra-peritoneal injection of alloxan monohydrate (150mg/kg body wt) (SD Fine Chem. Limited, Mumbai) in normal saline[10]. After two days the alloxan induced rats were screened for diabetes. All animals were allowed free access to water and pellet diet and maintained at room temperature in polypropylene cages.

Experimental Design

Group I: Normal rats.

Group II: Diabetic induced control rats (Alloxan induced).

Group III: Diabetic induced animals fed with aqueous fruit extract of *M. charantia* (250 mg/kg body wt) for 30 days.

Group IV: Diabetic induced animals fed with aqueous fruit extract of *M. charantia* (350 mg/kg body wt) for 30 days.

In each group, six animals were maintained for 30 days, the body weight and blood glucose was measured daily. After the experimental period the normal, diabetic control and plant treated animals were anesthetized and sacrificed. The serum was separated for biochemical estimation and the pancreas stored in 10% formalin for histological analysis.

Biochemical Analysis

Blood glucose level: The blood was collected from the tip of the tail vein from the rats and the blood glucose was measured using Gluco Chek glucose estimation kit (Aspen diagnostic, India).

Estimation of Plasma Insulin Level

Plasma insulin was estimated using radio immuno assay (RIA) kit supplied by Linco research Inc, Stat diagnostic, Mumbai, India.

Estimation of Lipid Profile in Blood Samples

On completion of the treatment, blood samples were collected and lipid profiles for all groups of animals were measured using commercially available kits. Total cholesterol (TC), triglycerides (TG) and high density lipoprotein (HDL) cholesterol levels in serum were determined according to the instruction of the manufacturer (Transasia Bio Medical Limited, Mumbai, India). For the determination of very low density lipoprotein (VLDL) and low density lipoprotein (LDL) cholesterol Friedewald's formula which states: VLDL cholesterol = Triglycerides/5 and LDL cholesterol = Total cholesterol – (VLDL + HDL cholesterol) was used[13].

Histological Studies

The pancreatic tissues were dissected out and washed in ice cold saline immediately. A portion of pancreatic tissue was fixed in 10% neutral formalin fixative solution for histological studies. After fixation tissues were embedded in paraffin, solid sections were cut at 5µm and the sections were stained with haematoxylin and eosin.

Statistical Analysis

The results were expressed in mean ± standard deviation. Statistical analysis was carried out by using one way ANOVA as in standard statistical software package of social science (SPSS).

RESULT

The hypoglycemic effect of aqueous fruit extract of *M. charantia* was investigated in alloxan induced diabetic rats. The body weights of the control group decreased significantly by 18.42% when compared to the normal groups. In aqueous extract treated group, the body weight increased significantly by 6.45% in 250 mg/kg body wt and 15.48% in 350 mg/kg body wt. The insulin levels were tested in normal, control and plant treated groups. In group II animals, the level of insulin was significantly reduced by 83.52% when compared to the group I (normal rats). In extract treated rats, the levels of insulin were found to have increased significantly by 373.68% in 250mg/kg body wt and 475.37% in 350mg/kg body wt when compared to the level of control group (Table-1).

The glucose levels of group II animals were tested. The level of glucose was increased by 278.49% when compared to the normal group. The blood glucose level was reduced in extract treated rats (42.60% in 250mg/kg and 62.83% in 350 mg/kg body wt) when compared with the diabetic control rats. The highest reduction was recorded at 350 mg/kg body wt.

Lipid Profile

The lipid profile such as TC, TG, HDL, LDL and VLDL were tested in normal, control and plant extract treated groups. The level of TC, TG, LDL and VLDL is significantly increased in control group when compared to the normal group. In aqueous extract treated group there was significant reductions of TC (38.83%), LDL

Table 1: Effect of the aqueous fruit extract of *M. charantia* on body weight (gms), serum insulin (µu/ml), Blood glucose (mg/dl), and Lipid profile (mg/dl) in alloxan induced diabetic rats.

Parameters	**Normal rats (N)**	**Diabetic control rats (C)**	**% of changes N vs C**	**Plant extract treated groups**				*** P values**
				250mg/ kg body wt	**% of changes C vs 250mg/kg body wt**	**350mg/kg body wt**	**% of changes C vs 350mg/kg body wt**	
Body weight	190±4.87	155±2.81	-18.42	165±2.12	6.45	179±2.97	15.48	0.001
Serum insulin	57.66±1.36	9.50±0.76	-83.52	45.0±1.21	373.68	54.66±1.43	475.37	0.001
Blood glucose	99.50±1.57	376.6±4.40	278.49	216.16±5.26	-42.60	140.00±2.26	-62.83	0.001
Lipid profile								
TC	124.83±1.64	231.33±1.81	85.32	186.00±2.16	-19.60	141.50±1.87	-38.83	0.001
TG	100.83±1.81	285.6±3.22	183.25	175.66±3.01	-38.50	139.33±2.80	-51.22	0.001
HDL	54.66±1.25	19.00±1.52	-65.24	35.66±1.62	87.68	49.66±1.99	161.37	0.001
LDL	46.66±2.03	155.16±2.36	232.53	114.50±1.78	-26.21	63.66±1.99	-58.97	0.001
VLDL	25.33±1.23	57.66±1.3	127.64	33.16±1.91	-42.49	29.00±1.52	-49.71	0.001

Each value represents six individual observations. Mean ± SD, '+', '-' indicate percent increase or decrease over control. 'P' denotes the statistical significance and '*****P' denotes statistical significance of ANOVA, to test the difference between the experimental groups, TC- Total cholesterol, TG- Triglyceride, HDL -High density lipoprotein, LDL- Low density lipoprotein, VLDL- Very low density lipoprotein.

(58.97%), VLDL (49.71%), and TG (51.22%) when compared to the control group. In addition a significant increase in the level of HDL (161.37%) in the plant extract treated diabetic rats was seen. In the case of untreated diabetic rats, there was a fall in HDL level (65.24%). The effective reduction of TC, LDL, VLDL and TG was recorded at the doses of 350 mg/kg than 250 mg/kg body wt.

Histological sections of the endocrine regions of pancreas of alloxan induced diabetic rats revealed a significant reduction in the size of the islets of langerhans when compared to that of normal group (Fig-1). Further, the study revealed the presence of damaged ß-cell population. This damage to the ß-cell might be due to alloxan induction (Fig-2). Reduction in the size of islets of langerhans was recorded. On the other hand, studies on the supplementation of aqueous fruit extract of *M. charantia* to the diabetic rats revealed restoration of size of the islets along with ß-cells repair (Fig-3 and Fig-4).

Histological Observations

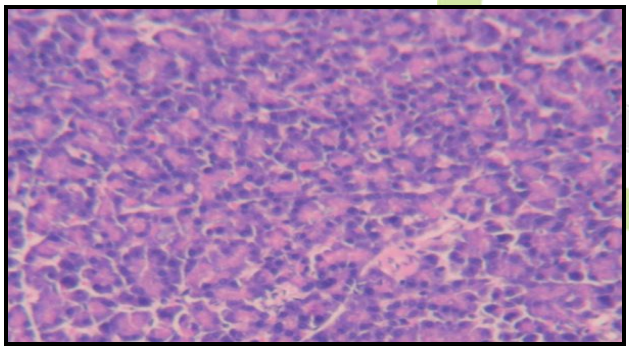

Figure 1: The Pancreatic islets of langerhans of normal rat showing alpha cells and beta cells.

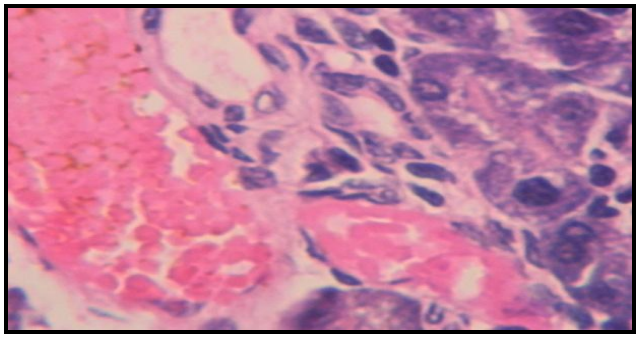

Figure 2: Alloxan induced diabetes damaged pancreatic islets showing reduced size and increased damage to beta cells

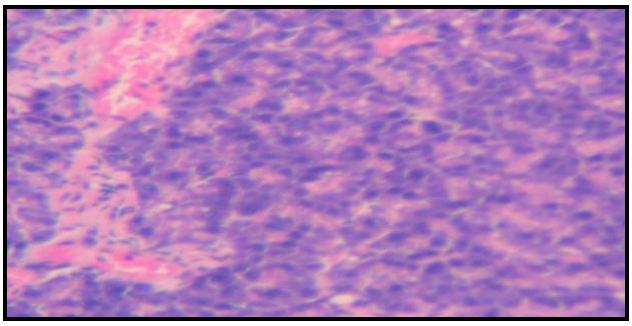

Figure 3: Plant extract (250mg/kg) treated pancreatic islets showing partial restoration, when compared to the alloxan induced diabetic control rats

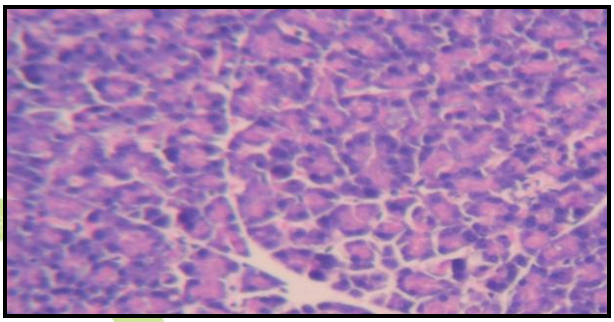

Figure 4: Plant extract (350mg/kg) treated pancreatic islets showing better restoration, when compared to the alloxan induced diabetic control rats and 250 mg/kg treated rats

DISCUSSION

Diabetes mellitus is a chronic and major endocrine disorder caused by inherited and/or acquired deficiency in the production of insulin by the pancreas, or by the ineffectiveness of the insulin produced. It is a growing health problem in most countries and its incidence is considered to be high all over the world. It is also associated with long-term complications, including retinopathy, nephropathy, neuropathy, angiopathy and several other complications[11]. Excessive oxidative stress has been implicated in the pathology and complications of diabetes mellitus[12].

The treatment of diabetes with medicines of plant origin that proved much safer than synthetic drugs is an integral part of many cultures throughout the world and has gained importance in recent years. India has a rich history of using various potent herbs and herbal components for treating various diseases

including diabetes. Many Indian plants have been investigated for their beneficial use in diabetes and its complications[6]. The present investigation reports the anti hyperglycemic and anti hyperlipidemic effects of aqueous fruit extract of *M. charantia* on alloxan induced diabetic rats.

In diabetes the increased blood sugar levels might be due to either insulin resistance of the body cells or decreased secretion of insulin from β- cells which manifests in the decreased serum insulin levels. The reduction in the serum insulin levels in the alloxan induced rats might be attributed to the reduced secretion of the hormone which might be due to the damage of the beta cells of the pancreas. The alloxan selectively destroys the pancreatic cells and induced hyperglycemia[14]. Aqueous fruit extract of *M. charantia* on alloxan induced diabetic rats at the dose of 350 mg/kg produced a significant fall in the blood glucose level in diabetic rats. It reveals that the β- cells in the pancreas were proliferating faster in aqueous extract treated rats, when compared to the control rats.

The blood glucose level of plant extract fed animal was significantly (P<.001) reduced. The highest depletion was recorded in the 350mg/kg body wt., dosage rats. The levels of serum TC, TG, LDL, and VLDL were found to be significantly reduced in the plant extracts treated diabetic animals. This might be due to the reduced hepatic triglyceride synthesis and or reduced lipolysis that might be due to the increase in serum insulin levels in the plant extract treated rats. The HDL increased significantly in the plant extract treated rats indicating a reversed atherogenic risk[14].

The histological studies of the endocrine region of the pancreas of the diabetic and plant extract treated animals revealed shrinkage of β-cells of islets of langerhans in the diabetic animals. The plant extracts treated animals' revealed restoration of β- cells. The restoration of the β-cells in extract fed diabetic animals corroborates with the increased serum insulin levels in treated animals.

The present study suggests that the aqueous plant extract had synergetic hypoglycemic effect as revealed by increased serum insulin levels and decreased serum lipid levels which can be attributed to the therapeutic value of the plant extracts of *M. charantia* to combat the diabetic condition in rats.

CONCLUSION

The present study suggests that the aqueous plant extract had synergetic hypoglycemic effect as revealed by increased serum insulin levels and decreased serum lipid levels which can be attributed to the therapeutic value of the plant extracts of *M. charantia* to combat the diabetic condition in rats.

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