Original Research Article

Effect of *Momordica Charantia* juice on blood glucose levels in healthy and diabetic rats

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Abstract

Background and Objectives: Pharmacotherapeutic interventions in diabetes are expensive and also associated with adverse effects therefore the need for alternate treatment modalities. *Momordica Charantia*(MC) is commonly used as food and medicine by both diabetic and healthy people. MC is widely being used in healthy people, in whom its glycaemic effects are unknown. The present study therefore aimed to investigate the blood glucose lowering effect of MC in both healthy and diabetic subjects using laboratory animal model and its potency was compared with a standard antidiabetic drug like pioglitazone. **Methodology:** Albino rats were divided into 5 groups; Group 1(normal controls), Group 2(normal controls fed with bitter melon juice) Group 3(diabetic controls), Group 4(diabetic rats treated with pioglitazone) and Group 5(diabetic rats treated with bitter melon juice (BMJ). Type 1 Diabetes was induced by intraperitoneal injection of streptozotocin to group 3, 4 and 5. Blood glucose levels were estimated on day 0, 7, 14 21 and 28 days. Fasting blood glucose was estimated by glucose oxidase assay. Results were analyzed by repeated measure ANOVA test. **Result:** There was significant reduction in blood glucose levels in group 2 rats when compared to normal controls. BMJ significantly reduced blood glucose levels in group 5 as compared to pioglitazone group (p=0.05).**Conclusion:** Blood glucose level in both group 1 and 2 remained within the normal range thus emphasising the role of BMJ in modulating the blood glucose. BMJ consumed over a period of time may prove useful in prevention and treatment of diabetes.

Key Words: *Momordica Charantia*, diabetic rats, blood glucose

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INTRODUCTION

Diabetes mellitus is a metabolic disorder and a major cause of morbidity in developed countries. It is a group of metabolic disorders characterized by hyperglycemia resulting from defect in insulin secretion, insulin action or both. Worldwide, 3.2 million diabetes-related deaths are reported annually[1]. India has 69.2 million people living with diabetes as per the 2015 data[2]. DM in the younger age group has been on the rise, they are more prone for long term complications like nephropathy, neuropathy, retinopathy. The dreaded microvascular complications of DM are related to the degree of metabolic decomposition and also in high risk individuals which can be prevented or postponed by achieving persistant control and also by sensitising the individuals for prophylactic treatment in prediabetics or high risk individuals[3]. A number of medicinal herbs/vegetables/green leaves are being used to treat DM in recent years due to its hypoglycemic and antioxidant properties which may protect the organs involved in long term complications of DM. *Momordica Charantia* (MC) has been used traditionally as an antidiabetic agent, the fruit of which is called as karela[1]. Bitter melon is used in various forms such as extracts, in our study fresh bitter melon juice was used which are the most common form consumed. The present study therefore aimed to investigate the effect of MC on blood glucose levels in healthy and diabetic subjects using an animal model.

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MATERIALS AND METHODS

The study was conducted at Department of Biochemistry, JSS Medical College, Mysore after the approval from Institutional Animal Ethics Committee with registration number of 261/PO/ReBi/2000/CPCSEA renewed on 14-8-2015 from Government of India. Animals used were healthy adult albino rats of wistar strain, weighing between 170- 250gm. The rats were inbred in the central animal house of JSS Medical College, Mysore. Animals were housed in polypropylene cages at 22 ± 2^{oC} with relative humidity of 30-70% under 12 hour's light and dark cycle. They were feed with standard laboratory animal feed and water *ad libitum*. Following an overnight fast, 18 rats were injected intraperitonally, with freshly prepared streptozotocin (dissolved in sodium citrate buffer) under aseptic precaution in a dose of 55 mg/kg body weight[4] 3 days before the experiment. Blood glucose levels were recorded daily morning at around 9.00 am for 3 days. All animals developed stable hyperglycemia after 3 days. Only those animals with blood glucose level more than 250mg/dl were selected for the study[4.] Animals were divided into five groups each group having six rats-

Group 1: NORMAL CONTROL (NC): rats of this group served as control group which were given 0.5 ml Gum acacia.

Group 2: NORMAL RATS FED WITH BITTER MELON JUICE GROUP (NBM): this group includes normal rats fed with bitter melon juice at a dose of 6ml/kg BW

Group 3: DIABETIC CONTROL (DC): The diabetic rats [STZ 55mg/kg BW, i,p] were treated with 0.5 ml Gum acacia.

Group 4: DIABETIC RATS TREATED WITH PIOGLITAZONE (DPIO):The diabetic rats [STZ 55mg/kg BW, i,p] were treated with pioglitazone suspended in 0.5 ml of gum acacia, in a dose of 45 mg/kg body weight.

Group 5: DIABETIC RATS TREATED WITH BITTER MELON JUICE (DBM): The diabetic rats [STZ 55mg/kg BW, i,p] were treated with fresh BMJ in a dose of 6 ml/kg body weight.(DBM). The fruit of *Momordica Charantia* was purchased from a local market. The fruit was washed, weighed and juice was prepared from the whole fruit in a regular household juicer. Dose of BMJ was 6ml/kg body weight[5]. Body weights (BW) of the individual rats were measured on the respective days before blood sugar estimation. Blood was collected from overnight fasted rats after the last dose administration by tail bleeding and blood glucose was estimated by glucose oxidase method on 0, 7, 14, 21 and 28^{th} day.

Statistical Analysis: Collected data was expressed as mean ± SD. 't' test for difference between two means and repeated measures ANOVA for serial measurement of variables over different time intervals were applied. All the grouped data was analysed using SPSS version for windows. p values of less than 0.05 was considered to be statistically significant

RESULTS

In the present study the effect of fresh bitter melon juice on blood glucose has been evaluated and its efficacy has been compared with that of a standard oral hypoglycemic drug pioglitazone in streptozotocin induced diabetic rats and healthy rats. The control group of rats did not show significant change in blood glucose levels. Group 2 rats showed a significant decrease in blood glucose levels but remained within the normal range. The diabetic control rats showed consistent hyperglycemia while group 4 rats did not show appreciable decrease in blood glucose level (BGL) from 1^{st} to 7^{th} day but thereafter produced persistent decrease in BGL up to 28^{th} day and group 5 rats showed persistent decrease in BGL from 1^{st} to 28^{th} day. In control group mean values of blood glucose levels range between 81 on day 0 to 79.5 mg/dl on day 28 without much of variation during the study. In group 2 mean values of blood glucose levels range between 80 mg/dl on day 0 to 75.3 mg/dl on day 28. In untreated diabetic control rats the blood glucose levels gradually increased from 341.2 mg/dl on day 0 to 430.5 mg/dl on day 28^{th} showing an increase in blood glucose value. In pioglitazone treated rats the mean blood glucose levels was 370.5 mg/dl on day 0, which showed decrease only after the 7^{th} day, and then steadily decreased to 115.5 mg/dl on 28^{th} day, here there is persistent reduction of blood glucose level from D1 to D28. In *Momordica Charantia* treated group the blood glucose level on day 0 was 363.3 mg/dl, which reduced to 318.5 on day 7 and later there as persistent decrease from 265.7 on day 14 to 147mg/dl on day 28 which was statistically significant compared to diabetic controls.(table 1) There was significant reduction in blood glucose levels in group 2 rats when compared to normal controls ($P<0.04$). BMJ significantly reduced blood glucose levels in group 5 as compared to diabetic controls ($p<0.001$) as on day 28. Similiar findings were found in pioglitazone treated group when compared to diabetic controls ($p<0.001$). Furthermore there was also a significant change in blood glucose levels between the BMJ and pioglitazone treated groups as on day 28 ($p<0.005$). The above data shows that there is significant blood glucose lowering effect of BMJ in healthy subjects as compared to normal group. Further *Momordica Charantia* (6 ml/kg body weight) also shows a good hypoglycemic effect in diabetic rats treated with BMJ and is comparable to that of the standard drug Pioglitazone (45 mg/kg body weight) There was no much

change in body weight in control group of rats throughout the study and there was slight reduction in BW of control group treated with BMJ. In diabetic control group, there was reduction of 20% body weight from day1 to day 28 while in the standard group there was an increase in body weight of upto 10% and in the test group there was slight reduction in body weight (table-2)

Table 1: MEAN+SD values of Blood Glucose levels in different groups:

GROUPS	D0 (mg/dl)	D7 (mg/dl)	D14 (mg/dl)	D21 (mg/dl)	D28 (mg/dl)
1.Normal Control	81+5.762	81+4.733	79.83+6.145	80.83+5.529	79.5+4.183
2.Normal rats treated with BMJ	80+3.56	78.3+3.82	77.5+3.62	76+2.42	75.3+1.55
3.Diabetic control	341.2+ 24.64	368+36.57	394.5+ 44.94	410.3+49.43	430.5+58.45
4.Diabetic rats treated with Pioglitazone	370.5+11.76	374+22.77	304.7+14.4	215.3+11.71	115.5+12.8
5.Diabetic rats treated with BMJ	363.3+10.67	318.5+15.03	265.7+14.75	220.2+14.08	147+17.33

Table 2: MEAN body weight of rats in grams in different groups on different days

GROUPS	D0 (gms)	D7 (gms)	D14 (gms)	D21 (gms)	D28 (gms)
1.Normal Control	185±02	185±03	182±03	187±02	189±02
2.Normal rats treated with BMJ	187 ±02	185±03	183±03	180±02	178±02
3.Diabetic control	200±02	183±04	176±02	170±02	164±03
4.Diabetic rats treated with Pioglitazone	190±03	182±03	191±02	195±02	200±02
5.Diabetic rats treated with BMJ	188±02	184±03	190±04	189±02	180±02

DISCUSSION

Diabetes results as a consequence of environmental factors acting on genetically predisposed individuals. Environmental factors can be modified in order to prevent or postpone the condition[6]. The long asymptomatic phase of type II DM gives a false impression that it is a mild disease but leads to a situation where 15-20% of patients present with micro or macrovascular complications at the time of diagnosis[3]. There is an urgent need for effective prevention or postponing of manifestations of DM and to delay or prevent the onset of complications. There are many drugs for treatment of diabetes and to prevent its complications, but drugs for postponement of development of manifestations of diabetes in high risk individuals is not available[3]. The present study undertaken with this scenario in mind, shows that there is good blood glucose lowering effect of the herbal drug-*Momordica Charantia* (6 ml/kg body weight) in both healthy and diabetic rats and is comparable to that of the standard drug Pioglitazone (45 mg/kg body weight). The body weight of diabetic control rats were decreased whereas the body weight gradually increased in pioglitazone treated rats and slight reduction in bitter melon treated group. Since, *Momordica Charantia* has shown a significant reduction in blood glucose in healthy rats and the levels are well maintained within the normal range so it can be safely used by healthy subjects who are at an increased risk of developing diabetes. The study also shows a significant reduction in blood glucose in diabetic rats treated with BMJ when compared to the standard drug pioglitazone therefore MC can be used as an adjuvant to standard hypoglycemic agents for better glycemic control. *Momordica Charantia* acts in both healthy and diabetic animals by converting glucose to glycogen for storage in the liver as well as to increase its peripheral utilisation, both of which results in glucose-lowering effect[6]. Hypoglycemic activity of fresh BMJ is due to the bioactive components, Charantin (a steroid glycoside), Vicine and polypeptide"p"or plant insulin (a 166 residue insulinmimetic peptide). Mechanisms of action include increased insulin-like effects, stimulation of pancreatic secretion, leading to decreased hepatic gluconeogenesis, increased hepatic glycogen synthesis and increased peripheral glucose oxidation[7]. Study done by Matheka D M *et al*.(2011) have shown that oral administration of *Momordica Charantia juice* extract to rats showed significant reduction in blood glucose levels as compared to normal controls[6]. Study done by Fernandes N *et al*.(2007) have shown that oral administration of *Momordica Charantia* extract showed significant reduction in blood glucose levels as compared to untreated diabetic rats[8]. Studies using oral administration of aqueous extract of MC by Bano F *et.al*., over a period of 5 weeks showed significant decrease in blood glucose (17%, $p<0.01$) and decrease in body weight of rats[9]. Dietary interventions play an important role in

controlling blood glucose, hence MC may be cost effective and used as an adjuvant in prevention and treatment of diabetes mellitus.

CONCLUSION

The results indicate that the test compound *Momordica Charantia* at a dose of 6ml/kg BW has significant blood glucose lowering effect in healthy and diabetic rats. Blood glucose level in both group 1 and 2 remained within the normal range thus emphasising the role of BMJ in modulating the blood glucose.BMJ consumed over a period of time may prove useful in prevention and treatment of diabetes. The test drug however showed an immediate onset of action which was long acting and needs to be further evaluated before the compound could be used as an adjuvant to standard hypoglycemic agents for better glycemic control. Fresh BMJ mimics action of pioglitazone belonging to TZD group thus showing a potential for further research in identifying the active molecules responsible for glucose lowering action. Further studies in this respect along with long term safety studies and clinical trials are necessary to add this novel drug to the existing ones for overall management of type 2 DM.

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