

INTERACTION OF MOMORDICA CHARANTIA FRUIT JUICE WITH GLIBENCLAMIDE IN STREPTOZOTOCIN INDUCED DIABETIC RATS

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Summary

The present study was undertaken to determine the interaction of Glibenclamide, a sulphonylurea with unripe fruit juice of *Momordica charantia*, an herbal drug widely used as an antidiabetic agent. The pharmacodynamic interaction was evaluated in streptozotocin induced diabetic rats. Glibenclamide was given orally in two different doses of 0.25 mg/kg and 0.50 mg/kg. *M. charantia* fruit juice was administered at a dose of 20 ml/kg. The blood glucose estimation was carried out. Both glibenclamide and *Momordica charantia* fruit juice showed a hypoglycemic effect. The hypoglycemic effect observed with combination of glibenclamide and *Momordica charantia* fruit juice was significantly more than either of the drugs given alone. It was concluded that *Momordica charantia* fruit juice shows a synergistic effect with glibenclamide. This could be important in reducing the dose of glibenclamide to achieve an enhanced therapeutic effect with a minimum adverse effect.

Key Words- Diabetes, Pharmacodynamic interaction, *Momordica charantia*, Glibenclamide

Introduction

The interaction of herbs with drugs is well known. Herbal drug interaction can be characterized as either Pharmacodynamic (PD) or pharmacokinetic (PK) in nature. Pharmacodynamic interaction may occur when constituents of a herbal product have either synergistic or antagonistic activity in relation to a conventional drug. Pharmacokinetic interaction results from alteration of absorption, distribution, metabolism or elimination of a conventional drug by an herbal product or other.

Diabetes mellitus is in the top five of the most significant diseases in the developed countries and is gaining significance there and elsewhere. Present number of diabetics worldwide is 171 million and is likely to increase to 340 million or more by the year 2030. (1,2)

The major mode of control over diabetes can be achieved by diet, exercise, insulin replacement therapy and by use of oral hypoglycemic agents. (3) The major drawback of insulin therapy is the side effect which includes insulin allergy, lipid dystrophy and lipodystrophy, insulin antibodies, and other late complications like morphological changes in kidney and severe vascular complications. (4-6) Similarly oral hypoglycemic drugs have many side effects such as nausea and vomiting, agranulocytosis, aplastic anemia, generalized hypersensitivity reaction, dermatological reaction and lactic acidosis. (7) So there is a growing global interest in herbal and other forms of medicine. (8)

Various plant extracts have been found as hypoglycemic drugs, though the exact mechanism involved has not been scientifically addressed. (9-11) *Momordica charantia* is a widely used antidiabetic herb.

Momordica charantia also known as bitter melon, karela, balsum pear or bitter gourd is a popular plant used for the treating diabetes related condition among the indigenous population of Asia, South America, India and East Africa.(12-15)

Momordica charantia is a tendril belonging to the cucurbitaceae family. It is climbing perennial that usually grows up to 5 m and bears elongated fruit with a knobby surface. Momordica charantia fruit has a distinguishing bitter taste which more pronounced as it ripen. Juice of unripe fruit of Momordica charantia has been reported to produce fall in fasting blood glucose (FBG) and improve glucose tolerance in rabbits. (16-19) Dry powder of the unripe fruit was also shown to bring down FBG in rabbits. (20) Clinical Trial in diabetic patients also have shown that the juice of fresh unripe fruit could bring down FBG and bring about satisfactory improvement. (21)

Now a days many people use the antidiabetic herb and antidiabetic drug along with and hence there may be chance of interaction between them. Thus the present study was undertaken to evaluate any possible pharmacodynamic interaction between momordica fruit juice with oral hypoglycemic agent named glibenclamide.

Methodology

Plant Material- Momordica charantia were purchased from the local market and identified by the National Botanical Research Institute, Lucknow, India. A voucher specimen no is 97768.

Extraction of aqueous plant material- Momordica charantia fruit is cut and seed was separated then grinded into electronic grinder. The mixture was mixed with 5 ml distil water and filtered with muslin cloth. The prepared juice was collected and kept in refrigerator.(22)

Experimental Animal- Healthy adult rats of wistar strain weighing 110- 160 mg were used in the present study. The animals were housed in clean polypropylene cages and maintained in a well ventilated temperature controlled animal house with constant 12h light/dark schedule. The animals were fed with standard rat pellet diet and clean drinking water was made available ad libitum.

Experimental Design-

Induction of Diabetes- Rats were fasted overnight before inducing diabetes with streptozotocin. The rats were given an intraperitoneal injection of streptozotocin (50mg/kg) freshly prepared in 0.1M sodium citrate buffer. The diabetic state was confirmed 48 h after streptozotocin injection. Threshold value of fasting blood glucose was taken as > 200mg/dl.

Control and diabetic rats were weighed matched for body weight and divided into following group consisting five animals each.

Group I – Non diabetic control : treated with single ip injection vehicle

Group II – Diabetic Control : administrated orally with equal volume of vehicle alone

Group III – Diabetic rats administered with Momordica fruit juice at dose of 20ml/kg body weight

Group IV – Diabetic rats administered with Glibenclamide at low dose of 0.25 mg/kg

Group V – Diabetic rats administered with Glibenclamide at high dose of 0.5 mg/kg

Group VI – Diabetic rats administered with Fruit juice and low dose of Glibenclamide

Group VII – Diabetic rats administered with Fruit juice and high dose of Glibenclamide

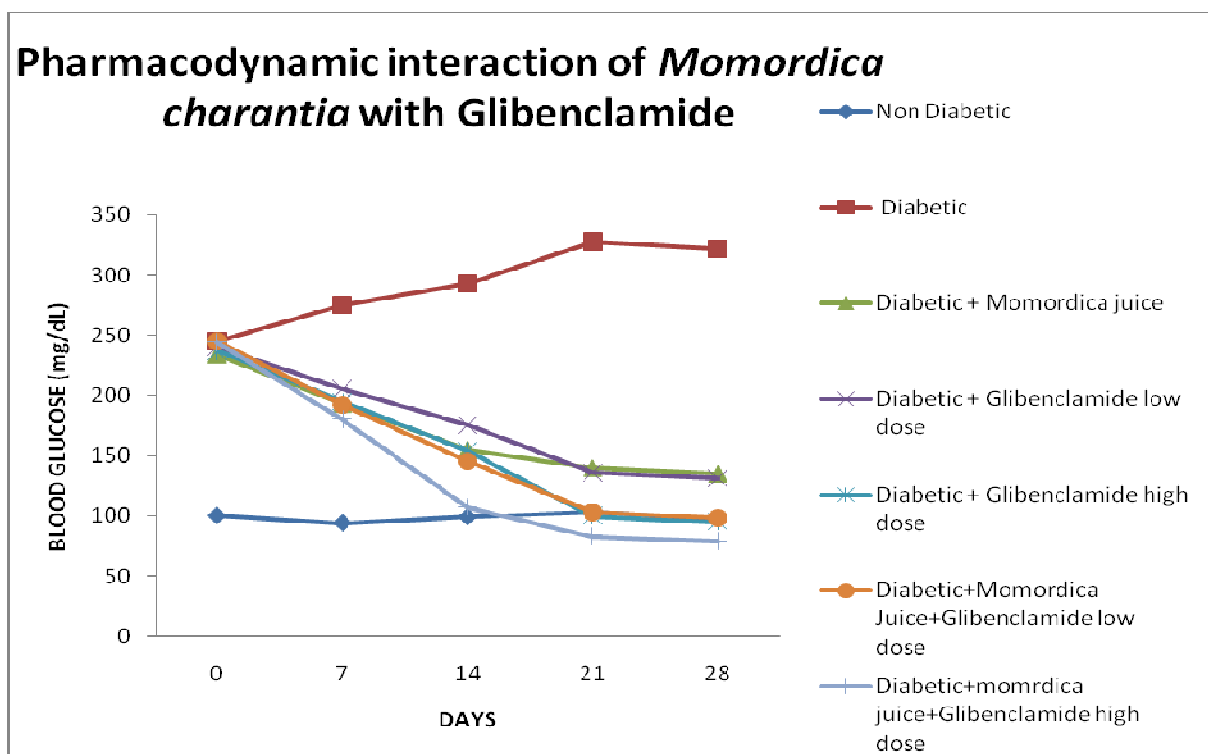
Blood Glucose Estimation- Blood sample was obtained through puncture tail vein and glucose was estimated on 0,7,14,21 and 28th day by Accu-Check Glucometer.

Statistical Analysis- Result were expressed as mean \pm SEM. Statistical analysis was carried out by using one way analysis of variance followed by Bonferroni multiple comparison test. A value of $P < 0.05$, $P < 0.01$ and $P < 0.001$ were considered significant.

Table 1: Effect of Momordica charantia fruit juice, Glibenclamide and Glibenclamide + Momordica charantia fruit juice on blood glucose

Groups	Blood Glucose				
	0 day	7 day	14 day	21 day	28 day
Non Diabetic control	100±2.5	94±3.9	99±5.2	103±2.6	98±3.9
Diabetic control	245±4.3	275±5.3	293±4.4	328±2.9	322±3.6
Diabetic + Momordica juice	234±3.6	193±2.8*	155±3.9*	140±2.8*	135±4.7*
Diabetic + Glibenclamide low dose	240±4.6	205±3.6*	175±2.8*	136±3.9*	131±5.3*
Diabetic + Glibenclamide high dose	237±3.8	195±4.2**	154±3.6**	100±3.8**	95±2.9**
Diabetic + Momordica juice + Glibenclamide low dose	245±1.3	192±2.4**	145±2.8**	103±4.9**	98±3.7**
Diabetic + Momordica juice + Glibenclamide high dose	244±3.4	180±3.7***	107±2.9***	83±2.8***	79±2.8***

All values are expressed as mean ± S.E.M (n=5). *P<0.05, **P<0.01, ***P<0.001 as compared to diabetic control. One-way ANOVA followed by Bonferroni multiple comparison test.



Results and Discussion

Table shows the effect of *M. charantia* fruit juice, Glibenclamide and their combinations in the fasting blood sugar of streptozotocin induced diabetic rats. *M. charantia* fruit juice showed significant decrease in blood sugar level in comparison to diabetic control group. Glibenclamide alone and the extract –glibenclamide combination

caused a steady and significant reduction in the glycemia throughout the duration of the monitoring period. Table 1 showed that *M. charantia* fruit juice significantly increase the hypoglycemic effect of half dose of glibenclamide and its nearby similar to the hypoglycemic effect obtained by glibenclamide high dose. The maximum hypoglycemic effect was seen by the high dose of glibenclamide with *M. charantia* fruit juice.

Many medicinal plants and pharmaceutical drugs are therapeutic at one dose and toxic at another. Interaction between herbs and drugs may increase or decrease the pharmacological or toxicological effects of either component. Synergistic therapeutic effects may complicate the dosing of long term medications e.g; herb traditionally used to decrease glucose concentrations in diabetes could theoretically precipitate hypoglycaemia if taken in combination with conventional drugs.

The present study was undertaken to evaluate the effect of *M. charantia* fruit juice on hypoglycemic activity on hypoglycemic action of glibenclamide. The result observed suggest that *M. charantia* fruit juice when combined with glibenclamide enhances the hypoglycemic activity of latter.

The combination of high dose of glibenclamide (0.5 mg/kg) with *M. charantia* fruit juice shows maximum hypoglycemic activity and the effect produced by the combination of glibenclamide (0.25 mg/kg) with *M. charantia* fruit juice was similar to hypoglycemic effect shown by glibenclamide alone (0.5 mg/kg).

The hypoglycemic potential of *Momordica charantia* in the present study could be explained by the mechanisms previously described by several authors in a diabetic animal model. As such, *Momordica charantia* increases the renewal of β cells in the pancreas or may permit the recovery of partially destroyed β cells and stimulates pancreatic insulin secretion. These could likely explain the significant increase in the plasma insulin level when streptozotocin-induced diabetic rats were treated with *Momordica charantia*. Furthermore, *Momordica charantia* displays insulin-like properties, remarkably stimulates glycogen storage by the liver and improves peripheral glucose uptake (22). Glibenclamide is used to treat DM. Sulphonylurea enhance cell insulin release by blocking the ATP-dependent K^+ channel and are widely used in the treatment of type 2 diabetes- mellitus. In chronic therapy the mechanism of action of Sulphonylurea is less clear. Studies have shown that the long-term use of these oral hypoglycaemic agents does not increase basal insulin release or enhance insulin secretion in response to metabolic stimuli in patients with type 2 diabetes, the drug has been described as a classical inhibitor of the K^+_{ATP} channels in pancreatic β cells whose target is the SUR receptor, a protein belonging to the ABC transporter family (23). Administration of an antidiabetic herb with a hypoglycemic drug for the treatment of diabetes may pose for potential drug-herb interaction that may have beneficial or adverse effects. It is generally believed that the use of herbs with medicine produces enhanced effect and reduces the adverse effect of drugs. The results of the present study indicate that combining *M. charantia* with glibenclamide could provide an opportunity to reduce the dose of glibenclamide, which may help in minimizing the adverse effect of glibenclamide as well as achieve enhanced therapeutic effect. At the same time proper precaution and care should be taken to avoid severe hypoglycemia that may occur due to combination of these agents.

Conclusion

From this study it is concluded that both *Momordica charantia* and glibenclamide can reduce the elevated blood glucose level. The hypoglycemic effect observed with combination of glibenclamide and *Momordica charantia* fruit juice was significantly more than either of drug given alone. It was concluded that *Momordica charantia* fruit juice shows synergistic effect with glibenclamide. This could be important in reducing the dose of glibenclamide to achieve enhanced therapeutic effect with minimum adverse effect.

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