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Comparative Evaluation of Hypoglycaemic Activity of Two Medicinal Plants in Alloxan Diabetic Rats

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Abstract: Aqueous extracts of the seeds of fenugreek (*Trigonella foenum graecum*) and fruits of bitter gourd (*Momordica charantia*) were tested for their hypoglycemic activity. The aqueous extracts or just the solvent alone (control) were orally administered daily for 7 days (short term) or 15 days (long term) to alloxan-induced diabetic rats. Blood glucose and plasma insulin levels and the subsequent effect on Oral Glucose Tolerance Test (OGTT) were monitored at 3, 6 and 9 h after the last administration. Daily administration of *T. foenum graecum* for 7 days failed to induce any significant change in the blood glucose levels. However, an extended 15-day treatment regimen was found to significantly reduce the blood glucose levels. The blood glucose levels were found to decrease at 6 and 9 h after the final administration of the extract. In contrast, both 7 and 15 days daily administration of *M. charantia* reduced the blood glucose levels drastically ($p < 0.05$ and $p < 0.01$, respectively). Significant reduction in blood glucose levels was observed at 6 and 9 h after the short-term treatment and at 3, 6 and 9 h after the long-term treatment. Long term administration of both *T. foenum graecum* and *M. charantia* was found to decrease blood glucose levels during OGTT at 30, 60 and 90 min when compared to OGTT of diabetic animals. There was no change in plasma insulin levels subsequent to administration of either *T. foenum graecum* or *M. charantia*. The observed results indicate that *T. foenum graecum* and *M. charantia* have hypoglycemic effect. The fact that the plasma insulin levels were unaltered suggests that the probable mechanism does not involve β -cell and may be attributable to decrease in intestinal absorption of glucose.

Key words: *Trigonella foenum graecum*, *Momordica charantia*, fenugreek, bitter gourd, antidiabetic, hypoglycemic plants

INTRODUCTION

Treatment of diabetes aims at maintaining blood glucose homeostasis, prevention of ketosis and secondary complications. The major mode of control over diabetes can be achieved by diet and exercise, insulin replacement therapy and by the use of oral hypoglycemic agents^[1]. Diet therapy along with insulin or oral hypoglycemic agents, thus, forms an important feature in diabetes^[2].

The major drawback of insulin therapy is the side effects which include insulin allergy, lipodystrophy and lipoatrophy, insulin antibodies, altered metabolic control, placental transfer of insulin antibodies, autoimmunity and other late complications like morphological changes in kidneys and severe vascular complications^[3-5]. Similarly, the oral hypoglycemic drugs

have many side effects such as nausea and vomiting, cholestatic jaundice, agranulocytosis, aplastic and hemolytic anemias, generalized hypersensitivity reactions, dermatological reactions and lactic acidosis^[6].

Since time immemorial various plant extracts have been used as hypoglycemic drugs, though the exact mechanisms involved have not been scientifically addressed^[7-9] and several hypotheses can be proposed. These extracts can act directly on pancreatic cells and stimulate insulin secretion by β -cells and/or inhibit α -cells and the release of hyperglycemic factor. They can also enhance the effect of insulin and adrenalin and, assist in inhibiting the synthesis of glucose-6-phosphate phosphatase, fructose diphosphatase, pyruvate carboxylase or phosphoenol pyruvate carboxykinase and stimulate the synthesis of glucokinase^[7].

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A large variety of compounds obtained from several plant families were found to have hypoglycemic effect. The glycosides, glycans, certain triterpenes, various types of sulfide molecules, polysaccharides, oils, vitamins, alkaloids, saponins, glycoproteins, peptides, amino acids and proteins isolated from various plant families showed beneficial effects in reducing the blood sugar^[7].

In the present study, the fenugreek seeds (*Trigonella foenum graecum* L. Leguminosae) and the bitter gourd (*Momordica charantia* L. Cucurbitaceae) which are commonly available and used by many people of India as food, have been selected to study their hypoglycemic activity.

Hypoglycemic activity of *T. foenum graecum* seed, commonly called as fenugreek has been reported long back^[10,11]. It has been demonstrated that the antidiabetic action of *Trigonella* can be associated with the defatted seed material which contains fibers, saponins and proteins^[12,13] and more specifically with subfraction-a^[14]. Amin-Riyad *et al.*^[15] demonstrated that treatment of streptozotocin-diabetic rats with diets containing 20% fenugreek seeds showed a general improvement in their clinical status where hyperglycemia, free fatty acids, cholesterol and triglyceride levels were reduced. Recent studies have shown that disrupted free radical metabolism in diabetic animals may be normalized by fenugreek seed supplementation in the diet^[16]. Similarly, there are reports about the hypoglycemic activity of *M. charantia* in various forms^[17]. There are contradictory reports on the effect of *M. charantia* not associated with an increase in circulating insulin^[18,19], but Welihinda *et al.*^[20] demonstrated that an aqueous extract from the fruit of *M. charantia* was a potent stimulator of insulin release from β -cell-rich pancreatic islets isolated from obese-hyperglycemic mice^[21]. Ahmed *et al.*^[22] has reported hypotriglyceridemic and hypocholesterolemic effects of *M. charantia* fruit extract in streptozotocin-induced diabetic rats.

In the present study, an attempt has been made to evaluate the mechanism involved in the hypoglycemic effect of two indigenous plants, (*T. foenum graecum* and *M. charantia*) which are easily available, cost-effective and is consumed in one form or the other by majority of the population^[23]. Crude aqueous extracts of the edible parts of these plants (viz., fenugreek seeds and bitter gourd fruit) without causing any major alterations in their natural form has been administered by oral intubation to alloxan-diabetic rats proportional to their body weight. The improvement in their diabetic

state was followed by monitoring blood glucose and insulin levels at various duration of the administration. Oral Glucose Tolerance Test (OGTT) was also performed in order to assess the specific effect of the extracts on glucose challenge. The present study is additional information on the mechanisms involved in the hypoglycemic effect of these two plants and this may pave way for future investigations useful in the treatment of diabetes.

MATERIALS AND METHODS

Animals: Healthy adult male albino rats of Wistar strain (*Rattus norvegicus*), weighing 190-210 g 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 a constant 12 h light/dark schedule. The animals were fed with standard rat pelleted diet (Hindustan Lever Ltd., Bombay, India) and clean drinking water was made available *ad libitum*.

Experimental design

Induction of diabetes: Rats were fasted overnight before inducing diabetes with alloxan (Loba Chemie, India). The rats were given an intraperitoneal (i.p.) injection of alloxan, freshly dissolved in saline (100 mg mL⁻¹), at a dose of 120 mg kg⁻¹ body weight so as to induce diabetic state with blood glucose levels >250 mg dL⁻¹.

At this dose of alloxan (120 mg kg⁻¹ b. wt.), diabetic induction was 90% with a mortality rate of 10-20%. Blood glucose was monitored after alloxan treatment to confirm the diabetic state and the diabetic rats were included in the experiment ten days after alloxan treatment.

Control and diabetic rats were weighed, matched for body weight and divided into the following groups:

- Group I: Control rats treated with single i. p. injection of vehicle (saline alone).
- Group II: Alloxan-diabetic rats administered orally with equal volumes of vehicle (distilled H₂O) alone.
- Group III: Alloxan-diabetic rats administered with decoction of *T. foenum graecum* (fenugreek) seeds at a dose of 2 mL/100 g b. wt./day by oral intubation. Fenugreek seeds, were added (100 g) to 750 mL of boiling water and macerated well and boiled for 10 min. The 400 mL final filtrate was then cooled, filtered, stored as the aqueous extract at 4°C and used for oral administration.

Group IV: Alloxan-diabetic rats administered with aqueous extract of *M. charantia* fruits at a dose of 2 mL/100 g b.wt./day by oral intubation. For the preparation of aqueous extract, *M. charantia* (Bitter gourd) fruits (450 g) were cut into small pieces and macerated in a blender mixer. To this, 120 mL of distilled water was added and the fruit concentration obtained i. e., 450 g in 360 mL was used as the aqueous extract for the administration.

After 7 days of aqueous extract administration, 5 animals were used to assess the short-term effect on the pattern of change in blood glucose up to 9 h after the administration. Other animals were continued with the administration for 15 days. On 16 th day, 5 animals were used to monitor the pattern of change in blood glucose up to 9 h after the administration, while another five animals were subjected to Oral Glucose Tolerance Test (OGTT) after overnight fasting. Equal numbers of control and diabetic rats were also included.

Oral Glucose Tolerance Test (OGTT): The OGTT is the only form of glucose tolerance testing recommended for the diagnosis of diabetes. The changes in blood glucose concentration, which result from an oral carbohydrate load is theoretically dependent on the rate at which carbohydrate enters the small intestine, the rate of digestion and intestinal absorption of glucose and the rate of insulin-driven metabolism. The relationship between plasma levels of glucose and insulin after an external load of glucose can be studied using OGTT.

Procedure: At the end of 15 days of administration of the extracts, the animals were fasted overnight and water was provided *ad libitum* for the performance of OGTT. At the day of OGTT, the animals were given an oral dose of glucose (10 mL kg⁻¹ b. wt., 50% w/v) along with the decoction/aqueous extract after collecting blood for fasting blood glucose estimation. Blood samples were collected subsequently at 30, 60, 90 and 180 min and plasma glucose and insulin were estimated. Decoction of *T. foenum graecum* and aqueous extract of *M. charantia* were given along with the glucose load to two separate groups of rats.

Collection of blood samples: Blood samples for plasma glucose and insulin determinations were collected in heparinized microfuge tubes by puncturing the orbital sinus with the help of heparinized microhematocrit

capillary tubes^[24]. Then, they were centrifuged for 10 min at 800 x g within 30 min after collecting the sample to prevent autoglycolysis by leukocytes.

Estimation of blood glucose: Blood glucose level was estimated using a glucose kit (Menarini Diagnostics, Italy) in which glucose oxidase and peroxidase enzymes are used along with chromogen 4-aminophenazone and phenol^[25].

Radioimmunoassay of insulin: Plasma insulin was measured by radioimmunoassay (RIA). RIA was performed using ¹²⁵I-insulin RIA kit supplied by Incstar Corporation, USA and the rat insulin standard was a gift from Novo Nordisk, Copenhagen, Denmark.

The calculation was done by % B/B₀ versus log concentration. The average CPM was calculated for each standard, quality control and unknown samples. The average CPM of the NSB tubes was subtracted from all counts. The corrected CPM of each standard, quality control or unknown sample was divided by the corrected CPM of the zero standard and multiplied by 100 and expressed as % B/B₀ using the formula as given below:

$$B/B_0(\%) = \frac{\text{CPM of standard or sample} - \text{CPM of NSB}}{\text{CPM of zero standard} - \text{CPM of NSB}} \times 100$$

Using 2 cycle semi-log or log-logit graph paper, percent B/B₀ for the insulin standards (vertical axis) versus the concentration (horizontal axis) was plotted. A best-fit line is drawn through the points. The levels of insulin in the unknown samples were interpolated from the plot. Maximum binding was calculated by dividing CPM of zero standard by the average total counts obtained in the total count tubes. The sensitivity was 2.0 μU mL⁻¹ and the % cross reactivity with C-peptide of insulin is <0.01. The insulin values are expressed as μU mL⁻¹.

The data on blood glucose and insulin levels were subjected to statistical analysis and expressed as mean±SEM (Standard Error of Mean). Student's 't' test^[26] was used to calculate the degree of significance at levels of p<0.001, p<0.01 and p<0.05.

RESULTS

In the present study, the significant reduction (p<0.05) in the blood glucose after long term administration of *T. foenum graecum* seed decoction (Fig. 1) suggest that the extract exert some kind of

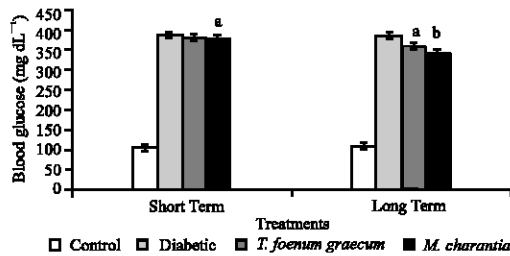


Fig. 1: Effect of short and long term treatment of *Trigonella foenum graecum* seed decoction and *Momordica charantia* fruit extract on blood glucose (mg/dl) levels of male albino rats. Each histogram is mean of 5 animals and vertical line on top of the histogram represents SE. a = $p < 0.05$; b = $p < 0.01$ compared with diabetic

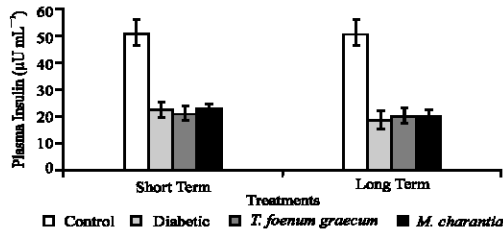


Fig. 2: Effect of short and long term treatment of *Trigonella foenum graecum* seed decoction and *Momordica charantia* fruit extract on plasma insulin ($\mu\text{U mL}^{-1}$) levels of male albino rats. Each histogram is mean of 5 animals and vertical line on top of the histogram represents SE

hypoglycemic effect. The short-term administration of *T. foenum graecum* seed decoction had no significant effect on blood glucose levels (Fig. 1).

Long term administration of *T. foenum graecum* seed decoction markedly reduced ($p < 0.05$) the blood glucose levels at 6 and 9 h only, whereas short term administration had no effect (Fig. 3). However, there is no change in the plasma insulin levels during short term and long term administration (Fig. 4).

During oral glucose tolerance test (OGTT), long term administration of *T. foenum graecum* seed decoction was able to decrease the blood glucose levels at 30 min ($p < 0.05$), 60 min ($p < 0.01$) and 90 min ($p < 0.05$) when compared to the OGTT pattern of diabetic rats (Fig. 5). However, it had no significant effect on plasma insulin levels (Fig. 6).

There is a two fold increase in blood glucose after 30 min of oral glucose load in control animals and at 60 and 90 min there is a fall and at 180 min the blood glucose level was back to normal levels. Whereas, in diabetic animals, the increase was about 3 fold at 30 min and it was

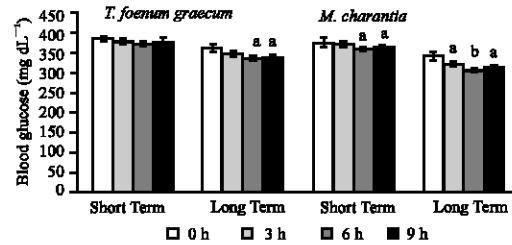


Fig. 3: Effects of short and long term treatment of *Trigonella foenum graecum* seed decoction and *Momordica charantia* fruit extract on blood glucose (mg/dl) pattern (up to 9 h) of male albino rats. Each histogram is mean of 5 animals and vertical line on top of the histogram represents SE. a = $p < 0.05$; b = $p < 0.01$ compared with 0 h

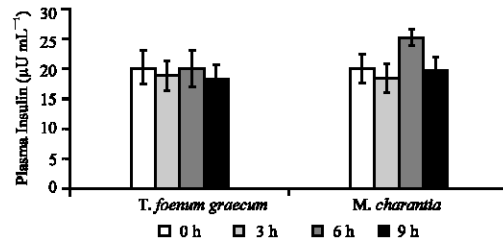


Fig. 4: Effects of long term treatment of *Trigonella foenum graecum* seed decoction and *Momordica charantia* fruit extract on plasma insulin ($\mu\text{U mL}^{-1}$) (up to 9 h) of male albino rats. Each histogram is mean of 5 animals and vertical line on top of the histogram represents SE

sustained until 60 min and the reduction was observed at 90 and at 180 min the hyperglycemic state still persisted. The diabetic animals administered with the extract behaved as that of control, the blood glucose levels at 30, 60 and 90 min were much lower than the corresponding diabetic animals without the extract administered.

Unlike fenugreek seed decoction, a significant reduction in the blood glucose levels were observed after short term ($p < 0.05$) and long term ($p < 0.01$) administration of aqueous extract of *M. charantia* fruits (Fig. 1) to alloxan-diabetic rats. The aqueous extract of *M. charantia* fruits had no significant effect on plasma insulin levels (Fig. 2).

A significant reduction ($p < 0.05$) in the plasma glucose levels were observed at 6 and 9 h after short term administration of aqueous extract of *M. charantia* fruits, whereas, long term administration resulted in a significant decrease in blood glucose at 3 h ($p < 0.05$), 6 h ($p < 0.01$) and 9 h ($p < 0.05$), irrespective of the unaltered insulin levels (Fig. 3 and 4).

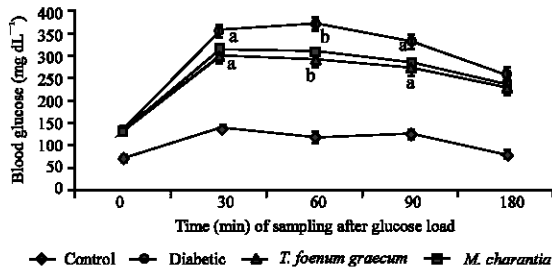


Fig. 5: Effects of long term treatment of *Trigonella foenum graecum* seed decoction and *Momordica charantia* fruit extract on oral glucose tolerance test of male albino rats. Each histogram is mean of 5 animals and vertical line on top of the histogram represents SE. a = p<0.05; b = p<0.01 compared with 0 min

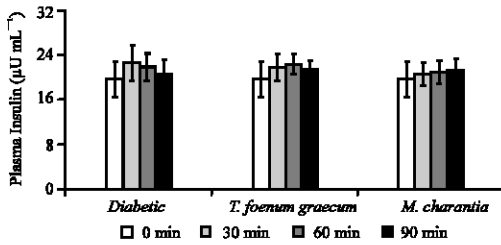


Fig. 6: Effects of long term treatment of *Trigonella foenum graecum* seed decoction and *Momordica charantia* fruit extract on plasma insulin levels ($\mu\text{U mL}^{-1}$) during oral glucose tolerance test of male albino rats. Each histogram is mean of 5 animals and vertical line on top of the histogram represents SE

During oral glucose tolerance test, long term administration of *M. charantia* fruit extract was able to decrease the blood glucose levels at 30 min (p<0.05) and 60 min (p<0.01) when compared to the OGTT pattern of diabetic rats with the unaltered levels of insulin (Fig. 5 and 6).

DISCUSSION

Diabetes mellitus is a metabolic disease as old as mankind and its incidence is considered to be high (4-5%)^[1]. Treatment of this disorder takes three main forms (i) diet and exercise, (ii) insulin replacement therapy and (iii) the use of oral hypoglycemic agents. However, since time immemorial patients with non-insulin and insulin requiring diabetes have been treated orally in folk medicine with a variety of plant extracts^[1,7,8]. The evaluation of these plants and especially of their relative

natural principles is a logical way of searching for new drug to treat this disorder.

Several studies have found that adding fiber to the diet of diabetics improves plasma glucose^[27-35]. Anderson *et al.*^[36] demonstrated the possibility of either complete withdrawal or reduction in the insulin therapy in diabetic subjects provided with high carbohydrate-high fiber diets.

The possible physiological/biochemical interactions of *T. foenum graecum* seed decoction and aqueous extract of *M. charantia* fruits on hyperglycemic status of the diabetes mellitus have already been initiated^[12,14,17,22,37-55]. The current investigation is a step further in this direction, designed primarily with an objective to understand the possible mode of action of these plant extracts, to bring down the hyperglycemia associated with diabetes mellitus.

It has been reported that *Trigonella* seeds contain trigonelline, a major alkaloid component exerted a hypoglycemic effect lasting for 24 h in alloxan-diabetic rats^[10]. Ribes *et al.*^[12] have reported that administration of defatted fenugreek seeds at a dose of 1.86 g kg⁻¹ b. wt. for 8 days induces delayed hypoglycemic effects, which appear only after 8 days of administration in alloxan-diabetic dogs. In the present study, the short-term administration of *T. foenum graecum* seed decoction had no significant effect, but when administered for a longer term, there is a significant reduction (p<0.05) on blood glucose levels (Fig. 1). The differential response could be possibly due to differences in the animal model chosen, method of extract preparation and the dose administered.

Long term administration of *T. foenum graecum* seed decoction markedly reduced (p<0.05) the blood glucose levels at 6 and 9 h only, whereas short term administration had no effect (Fig. 3). However, there is no change in the plasma insulin levels during short term and long term administration (Fig. 4), clearly indicating that the hypoglycemic effect is not due to the increase in the circulating insulin levels.

During Oral Glucose Tolerance Test (OGTT), long term administration of *T. foenum graecum* seed decoction was able to decrease the blood glucose levels at 30 min (p<0.05), 60 min (p<0.01) and 90 min (p<0.05) when compared to the OGTT pattern of diabetic rats (Fig. 5). However, it had no significant effect on plasma insulin levels (Fig. 6).

There is a two fold increase in blood glucose after 30 min of oral glucose load in control animals and at 60 and 90 min there is a fall and at 180 min the blood glucose level was brought back to normal level. Whereas, in diabetic animals, the increase was about 3 fold at 30 min

and it was sustained till 60 min and the reduction was observed at 90 min and at 180 min the hyperglycemic state still persisted. The diabetic animals administered with the extract behaved as that of control, the blood glucose levels at 30, 60 and 90 min were much lower than the corresponding diabetic animals without the extract administered.

Anderson *et al.*^[24] have suggested that the fiber content may be involved, at least in part in the antidiabetic effect of fenugreek seed and more specifically the testa and endosperm of the seed which is rich in fibers^[12,13]. It is well demonstrated that an increased intake of dietary fiber (non-starch polysaccharides + lignin) and soluble dietary fiber in particular, has beneficial effects^[56-58]. A new dietary approach to the treatment of diabetic patients with a fiber-enriched diet has been recommended, which improves blood glucose and reduced serum cholesterol levels^[16,40,56,57,59]. Parillo *et al.*^[60] have shown that the high carbohydrate-high fiber diet is more advantageous because it improves blood glucose control and reduces serum cholesterol. This is of major importance because blood glucose control may influence the clinical course of diabetic nephropathy and possibly other associated long-standing diabetic complications^[61]. The mechanism by which diets high in complex carbohydrates including fiber can affect postprandial plasma glucose levels include prolonged gastric emptying and intestinal transit time, slowed starch hydrolysis and delayed glucose absorption^[62].

Jenkins *et al.*^[31] and O'Conner *et al.*^[63] have reported that the greatest reduction in the glycemic response to a meal is observed with soluble fibers, which are hydrated rapidly and develop significant viscosity in solution. The addition of soluble fiber to a meal increases the viscosity of the gastrointestinal contents^[64,65]. The increased viscosity of the meal retards the rate of carbohydrate digestion and absorption^[66-69] and that viscosity is the major key factor for the reduction in blood glucose^[65,70].

Further, Jenkins *et al.*^[71] have reported that a decrease in the absorption rate of starch from diets containing soluble dietary fibers by means of a shift or extension of the site of absorption towards the more distal part of the small intestine is the main factor in controlling the glycemic response. However, Johansen and Bach Knudsen^[72] have recently reported that delayed absorption leading to a lower glycemic response to cereal based diets naturally rich in soluble dietary fibers may not be induced by an impaired absorption in the proximal intestine where the capacity to absorb large quantities of digestible carbohydrate appear rate limiting and they reported that gastric emptying is a major factor controlling the glycemic response.

Probably, the observed decrease in the plasma glucose levels after long term administration of *T. foenum graecum* at 6 and 9 h and a decrease in the plasma glucose levels at 30, 60 and 90 min during OGTT when compared to the diabetic male rats may be due to the high fiber content of the fenugreek seed. Since the fenugreek seeds contain about 50% fiber^[12,13], it is suggested that the hypoglycemic effect may be attributed to the increased viscosity which ultimately leads to decreased absorption of glucose and/or the delayed gastric emptying resulting in hypoglycemic effect.

From the present study it is clear that the hypoglycemic effect of fenugreek seed decoction is not due to its action at the level of β -cells of the endocrine pancreas and may be brought about by the collective actions of the active principles present in the seeds and the gastro-intestinal actions of the fibers.

Unlike fenugreek seed decoction, a significant reduction in the blood glucose levels were observed after short term ($p < 0.05$) and long term ($p < 0.01$) administration of aqueous extract of *M. charantia* fruits (Fig. 1) to alloxan-diabetic rats. In accordance with the present study, aqueous extract of *M. charantia* fruits was reported to have hypoglycemic effects in normal rats and mice^[18,37] as well as in streptozotocin-diabetic mice^[19,50,52].

The aqueous extract of *M. charantia* fruits had no significant effect on plasma insulin levels (Fig. 2) when compared to diabetic rats suggesting that the extract may have an extrapancreatic effect similar to that of the fenugreek seeds. In this connection, it is reasonable to recall the earlier findings that the hypoglycemic effect of *M. charantia* in normal mice is not associated with an increase in circulating insulin^[18,19]. However, Khanna *et al.*^[73] have reported that a peptide, polypeptide-P, isolated from the fruits of *M. charantia* caused hypoglycemic effect when it was administered subcutaneously in patients with juvenile diabetes.

In the present investigation, the type of alteration seen in the blood glucose levels might have been contributed by the extrapancreatic effects and/or the existence of insulin-like compounds in the extract as reported by Ng *et al.*^[74].

A significant reduction ($p < 0.05$) in the plasma glucose levels were observed at 6 and 9 h after short term administration of aqueous extract of *M. charantia* fruits, whereas, long term administration resulted in a significant decrease in blood glucose at 3 h ($p < 0.05$), 6 h ($p < 0.01$) and 9 h ($p < 0.05$), irrespective of the unaltered insulin levels (Fig. 3).

During oral glucose tolerance test, long term administration of *M. charantia* fruit extract was able to decrease the blood glucose levels at 30 min ($p < 0.05$),

60 min ($p < 0.01$) when compared to the OGTT pattern of diabetic rats with the unaltered levels of insulin (Fig. 5 and 6).

The highly potent hypoglycemic activity associated with the aqueous extract of *M. charantia* fruits has been recorded by Karunanayake *et al.*^[37]. They have suggested that the extract may directly stimulate β -cells of the Islets of Langerhans to secrete more insulin and also facilitate peripheral utilization of glucose *via* the mediation of enhanced insulin secretion in normal rats. Contrary to this, it has been reported that the glucose lowering effect of orally administered extract of *M. charantia* does not appear to be associated with an increase in insulin concentration^[18,19].

In favor of the extra-pancreatic effect of extract to induce hypoglycemia, Meir and Yaniv^[75] have claimed the possible inhibition of intestinal glucose uptake while Welihinda and Karunanayake^[76] have reported the increase conversion of glucose to glycogen in liver and muscle. Day *et al.*^[39] have reported that the orally administered *M. charantia* extract lower glucose concentration independently of intestinal glucose absorption and an extrapancreatic effect is involved. Recently, Shibib *et al.*^[77] reported that the hypoglycemic effect of the extract may be mediated through (a) suppression of the key hepatic gluconeogenic enzymes, glucose-6-phosphatase and fructose 1,6-biphosphatase and (b) an accelerated rate of glucose metabolism through the pentose phosphate pathway. Similarly, the inhibition of gluconeogenesis and also a decrease in glucose absorption were shown to be responsible for the hypoglycemic effects of *M. charantia* extracts^[78].

In the present study, the insignificant change in the plasma insulin levels compared with that of diabetic rats suggests the absence of any appreciable stimulatory effect of the extract on the existing β -cells of endocrine pancreas in the diabetic rats. The alloxan treatment, a β -cell toxin, caused only partial destruction of β -cells as the plasma insulin level was brought down to 50% of the control value. It is, therefore, suggested that the hypoglycemic effect of the *M. charantia* fruit extract observed in the present study is primarily extrapancreatic caused in the absence of any significant increase in insulin levels.

The extrapancreatic effect of aqueous extract of *M. charantia* fruit was further confirmed by the reduction in the blood glucose levels without any significant change in plasma insulin observed after 3, 6 and 9 h of short and long term administration. The extrapancreatic effect may be attributed to the high fiber content of the extract^[79,80] which is likely to inhibit the intestinal absorption of glucose. The inhibitory effect of the extract on intestinal glucose absorption is also obvious in the

data on OGTT, where a significant reduction in blood glucose compared to blood glucose values of diabetic rats is seen at 30, 60 and 90 min after oral glucose load.

In conclusion, it may be stated that there occurs a selective decrease in the hyperglycemic state after the administration of these plant extracts. Knowing that mainly the water soluble fraction of dietary fiber content in fenugreek seeds and bitter gourd can be effectively utilized in the formulation of diabetic diet as they are commonly used by all in the regular diet and this may help to improve glycemic control in diabetics. In addition to this, the hypoglycemic effects may be mediated through a number of active principles/compounds present in the extracts. The present study suggests that these two plant extract can be successfully utilized for the management of diabetes due to their hypoglycemic action, further studies on the nature of active principles involved and their toxicity would enlighten the exact mechanism involved and thus help to rationalize their use in the treatment of diabetics more effectively.

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