Bitter Gourd (Momordica charantia): A Dietary Approach to Hyperglycemia

Michael B. Krawinkel, MD, and Gudrun B. Keding, MSc agr

Bitter gourd (Momordica charantia) is a vegetable with pantropical distribution. It contains substances with antidiabetic properties such as charantin, vicine, and polypeptide-p, as well as other unspecific bioactive components such as antioxidants. Metabolic and hypoglycemic effects of bitter gourd extracts have been demonstrated in cell culture, animal, and human studies. The mechanism of action, whether it is via regulation of insulin release or altered glucose metabolism and its insulin-like effect, is still under debate. Adverse effects are also known. Nevertheless, bitter gourd has the potential to become a component of the diet or a dietary supplement for diabetic and prediabetic patients. Well-designed interdisciplinary research by nutritionists, medical doctors, and agronomists is needed before a dietary recommendation can be given and a product brought to the market.

Key words: bitter gourd, diabetes mellitus, dietary supplement, hypoglycemia, insulin, Momordica charantia

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INTRODUCTION

Diet is the primary therapy for non-insulin-dependent diabetes mellitus (NIDDM) and is an important adjunctive treatment in insulin-dependent diabetes mellitus (IDDM). Fortunately, traditional diets in many parts of the world are well adapted to the current concepts of NIDDM management: a diet low in fat and high in complex carbohydrates.1 Simple dietary advice for diabetic patients1 only includes the avoidance of sugar and sugary foods, regular meals, small snacks between meals (for patients on insulin), and half of the usual portions of the local staple carbohydrate food for overweight patients not on insulin. However, no general suggestions have been made for the consumption of specific foods with hypoglycemic properties.2 Bitter gourd (Momordica charantia) is one of the vegetables known to have antidiabetic effects. Knowledge on bitter gourd is increasing rapidly; this review presents the current status of the research.

MAIN CHARACTERISTICS OF M. charantia

Vernacular English names of M. charantia include bitter gourd, bitter melon, balsam pear, bitter apple, and bitter, African, or wild cucumber. Several different names in Asia and Africa exist. The most popular is “karela,” which is used both in India and in east Africa. Synonyms of M. charantia are M. indica L., M. elegans Salisb., M. chinensis Sprengel, and M. thollonii Cogn. M. charantia is an important market vegetable in southern and eastern Asia. In tropical America, local varieties originate from Asia and are cultivated on a small scale only.3 M. charantia is a common cucurbit and is widely spread throughout most of tropical Africa. The local species of bitter gourd are close to extinction because they are being replaced by commercially cultivated plants.3 However, they are occasionally collected from the environment as a vegetable or medicinal plant.3

In India and southeast Asia, cultivated M. charantia is divided into two groups: fruits with a diameter less than 5 cm (var. minima Williams & Ng) and fruits larger than 5 cm in diameter (var. maxima Williams & Ng).4 Other wild African species include M. balsamina L., M. foetida Schum., and M. rostrata A. Zimm. Fruits and leaves of most wild Momordica species are consumed as vegetables, and have a similar bitter taste and almost identical medicinal uses.4

CONSTITUENTS OF M. charantia AND CONSUMPTION EFFECTS

M. charantia has a higher nutritional value than other cucurbits due to its higher content of minerals (e.g.,
iron) and vitamins (e.g., ascorbic acid). Bitterness is attributed to the non-toxic alkaloid momordicine. Table 1 gives an overview of the constituents of the different parts of *M. charantia*.

The immature fruits of *M. charantia* can be prepared in many ways. In addition to frying or cooking (e.g., for curries), the fruits can be dehydrated, pickled, or canned. They are usually blanched or soaked in salt water before cooking to reduce the bitter taste. Fruits, flowers, and young shoots are also used as a flavoring. The young shoots and leaves are sometimes cooked and eaten as leafy vegetables.

Several proteins that show a variety of pharmacological effects (e.g., antitumor, antiviral, and immunotoxic) have been isolated from *M. charantia*. Charantin, vicine, and polypeptide-p are thought to be the main hypoglycemic components in bitter gourd. Polypeptide-p is an unidentified insulin-like protein similar to bovine insulin that was characterized from *M. charantia* fruit, seed, and tissue culture by Khanna et al. and Sofowora.

Various studies over the last 20 years have found endocrine and biochemical mechanisms behind the hypoglycemic activity of bitter gourd extracts. A number of studies have shown an insulin-like activity. Older studies were focused on effects on hepatic glucose metabolism, while more recent studies associate the insulin-like effects with antioxidative activity and glucose uptake in skeletal muscle cells by GLUT4. Investigations of the antidiabetic activity of bitter gourd have used liquid or dry plant extracts without specification or quantification of the bioactive compounds. This partially explains why different investigations of the pharmacological mechanism(s) of the hypoglycemic activity of bitter gourd have not led to conclusive results. It is also unclear whether one single mechanism or even different bioactive components are involved and responsible for some of the observed effects.

**CELL CULTURE STUDIES**

In one study, it was discovered that streptozotocin-induced apoptosis in rat insulinoma (RIN) cells was reduced, which indicates a mode of protection, after adding bitter gourd juice to RIN cells, islets, and pancreatic β-cells. Another study found that bitter gourd may play a role in the regeneration of or facilitate the recovery of partially destroyed β-cells.

**ANIMAL STUDIES**

Most studies have shown a blood-glucose-lowering effect of the fruit of bitter gourd when fed orally as a single dose. In earlier research, it was recognized that viable β-cells (i.e., those capable of producing insulin) appeared to be essential for bitter gourd’s hypoglycemic activity. The juice formulations of bitter gourd have proven to be more effective in lowering blood sugar and HbA1c levels than its dried fruit products. Further glucose-lowering effects were found in ethanolic plant extracts, fresh fruit extracts, and acetone extracts of whole fruit powder. In comparison, the effect of fried bitter gourd was not so obvious. *Momordica* seeds and seed extracts contain hypoglycemic ingredients. Very different results were found after feeding either methanol extract or saponin-free methanol extract of bitter gourd fruit pulp juice, seed, or whole plant to healthy, IDDM, or NIDDM rats. In this study, only the saponin-free methanolic

### Table 1. Constituents of *Momordica charantia* According to Sofowora

<table>
<thead>
<tr>
<th>Plant Part</th>
<th>Constituents</th>
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</thead>
<tbody>
<tr>
<td>Leaf</td>
<td>Two acidic resins and momordicine (bitter substance), vitamin C, carotene (depending on the sample), γ-aminobutyric acid</td>
</tr>
<tr>
<td>Root</td>
<td>About 13% ash (major elements: silicon, calcium, phosphorus, strontium, copper, lead, zinc, sodium, and iron)</td>
</tr>
<tr>
<td>Fruit</td>
<td>About 7% ash (major elements: see root), no free pectic acid but soluble pectins, saponins, 5-hydroxytryptamine, alkaloid momordicine, 0.3% total alkaloid, steroidal glucosides</td>
</tr>
<tr>
<td>Fresh immature fruit</td>
<td>0.035% charantin isolated in pure state as a neutral non-nitrogenous principle presenting the characters of phytosterolines</td>
</tr>
<tr>
<td>Seed</td>
<td>32%–35% of a purgative fixed oil (stearic acid, oleic acid, linoleic, and α-eleostearic acid); albumin; globulin; glutelin; niacin, pantothenic acid, and other B-vitamins; β-carotene; α-amino butyric acid</td>
</tr>
<tr>
<td>Dry plant</td>
<td>0.038% alkaloid (unnamed), 8.35 μg/g total carotenoid pigments</td>
</tr>
<tr>
<td>Entire plant</td>
<td>Trace amounts of alkaloids and saponins, no flavonoids, tannins, quinines, steroids, and terpenes (Congo), orthophthalic acid (Brazil)</td>
</tr>
</tbody>
</table>
Table 2. Summary of 17 Studies of the Hypoglycemic Effects of *Momordica charantia*

<table>
<thead>
<tr>
<th>Animal (number)</th>
<th>Component Fed</th>
<th>Duration of Feeding</th>
<th>Results</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Wistar rats (28 STZ-induced diabetic + 12 normal rats)</td>
<td>Fruit devoid of seeds, air-dried and powdered</td>
<td>45 d</td>
<td>Diabetes-related increase in intestinal disaccharidases: amelioration in the activities of maltase and lactase ($P &lt; 0.05$); no significant change of sucrase activity; diabetes-related decrease in renal disaccharidases: alleviation of reduction in maltase ($P &lt; 0.05$); no significant change in activities of sucrase and lactase</td>
<td>Shetty et al., 2005</td>
</tr>
<tr>
<td>Male albino Wistar rats (24 STZ-induced diabetic + 6 normal rats)</td>
<td>Aqueous seed extract of two varieties (country MCSEt1 and hybrid MCSEt2)</td>
<td>30 d</td>
<td>Normalizing of the impaired antioxidant status in STZ-induced diabetes (similar to glibenclamide) ($P &lt; 0.05$); rapid protective effects against lipid peroxidation ($P &lt; 0.05$); effect was slightly more distinctive in MCSEt1 compared to MCSEt2 (not significant)</td>
<td>Sathishsekar et al., 2005</td>
</tr>
<tr>
<td>Male albino Wistar rats (24 STZ-induced diabetic + 6 normal rats)</td>
<td>Aqueous seed extract of two varieties (country MCSEt1 and hybrid MCSEt2)</td>
<td>30 d</td>
<td>Significant reduction in blood glucose, HbA$_{1c}$, glucose-6-phosphatase, lactate dehydrogenase, fructose-1,6-bisphosphatase, and glycogen phosphorylase (all $P &lt; 0.05$); increase in glycosgen and activities of hexokinase and glycogen synthase ($P &lt; 0.05$); hypoglycemic effects of MCSEt1 more pronounced compared with MCSEt2 and glibenclamide (no statistical test provided)</td>
<td>Sekar et al., 2005</td>
</tr>
<tr>
<td>Male albino Horts Men rats (10 diabetic + 5 normal rats)</td>
<td>Methanol extract from dried fruits</td>
<td>30 d</td>
<td>Significant decrease in triglyceride and low-density lipoprotein; significant increase in high-density lipoprotein ($P &lt; 0.001$); improvement in oral glucose tolerance curve (not significant)</td>
<td>Chaturvedi et al., 2004</td>
</tr>
<tr>
<td>Male Wistar rats (20 STZ-induced diabetic + 10 normal rats)</td>
<td>Juice of fresh fruit</td>
<td>70 d</td>
<td>Regulation of glucose uptake into jejunum membrane brush border vesicles ($P &lt; 0.05$) and stimulation of glucose uptake into skeletal muscle cells ($P &lt; 0.05$)</td>
<td>Ahmed et al., 2004</td>
</tr>
<tr>
<td>KKAy mice (15–18 diabetic + 5–6 normal mice)</td>
<td>Water extract, lyophilized</td>
<td>35 d</td>
<td>Blood glucose tolerance improved with and without exercise ($P &lt; 0.05$); insulin levels lower than control ($P &lt; 0.01$) and lower than exercise alone ($P &lt; 0.05$)</td>
<td>Miura et al., 2004</td>
</tr>
<tr>
<td>Male Charles Foster albino rats (5 alloxan diabetic rats + 5 normal rats)</td>
<td>Ethanolic extract of dried plants</td>
<td>14 d</td>
<td>Blood glucose lowering effect within 2 weeks ($P &lt; 0.05$); blood glucose level brought down near to normal fasting level at a dose 250 mg/kg once, twice, or three times daily</td>
<td>Kar et al., 2003</td>
</tr>
<tr>
<td>Albino mice of both sexes (16 STZ-induced diabetic mice + 8 normal mice)</td>
<td>Lyophilized extract of fresh green fruit (without cuticle)</td>
<td>60 d</td>
<td>Reduction of plasma glucose concentration after 40 days of treatment ($P &lt; 0.001$); higher tail flick latency and gastric transit time in diabetic animals modified favorably ($P &lt; 0.05$)</td>
<td>Grover et al., 2002</td>
</tr>
</tbody>
</table>
Table 2. (Cont’d) Summary of 17 Studies of the Hypoglycemic Effects of *Momordica charantia*

<table>
<thead>
<tr>
<th>Animal (number)</th>
<th>Component Fed</th>
<th>Duration of Feeding</th>
<th>Results</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albino rats of both sexes (40 alloxan diabetic + 8 normal rats)</td>
<td>Lyophilized aqueous extract of fruit (without cuticle)</td>
<td>120</td>
<td>Improved diabetic control ($P &lt; 0.001$); results superior to <em>Eugenia jambolana</em>, <em>Tinospora cordifolia</em>, and <em>Mucuna pruriens</em> (no statistical test provided)</td>
<td>Rathi et al., 2002(^{41})</td>
</tr>
<tr>
<td>Male and female albino Wistar rats and albino mice (pilot study: 56 alloxan diabetic + 8 normal rats; chronic study: 16 alloxan diabetic + 8 normal rats; 16 STZ-induced diabetic + 8 normal mice)</td>
<td>Aqueous (lyophilized, without cuticle) and alcohol extracts of fruit</td>
<td>21 d for pilot study; 120 d (rats) and 50 d (mice) for chronic study</td>
<td>64% decrease in serum glucose level after 1 month ($P &lt; 0.01$) and 67% after 2 months ($P &lt; 0.001$); increase in glucose-6-phosphorylase and phosphofructokinase activity compared with untreated diabetic animals ($P &lt; 0.001$)</td>
<td>Rathi et al., 2002(^{42})</td>
</tr>
<tr>
<td>Adult male ddY and KKAy mice (40–48 diabetic + 40–48 normal mice)</td>
<td>Lyophilized aqueous extract of fruit</td>
<td>21 d</td>
<td>Reduction of blood glucose ($P &lt; 0.01$) and lowering of serum insulin in diabetic mice ($P &lt; 0.01$); increased muscle GLUT4 content ($P &lt; 0.01$)</td>
<td>Miura et al., 2001(^{30})</td>
</tr>
<tr>
<td>Male and female albino mice (12 STZ-induced diabetic mice + 6 normal mice)</td>
<td>Lyophilized aqueous extract of fruit (without cuticle)</td>
<td>40 d</td>
<td>Reduction of plasma glucose concentration by 24.4% ($P &lt; 0.005$); prevention of polyuria ($P &lt; 0.001$), increase in urinary albumin level ($P &lt; 0.0001$), and renal hypertrophy ($P &lt; 0.05$); more effective than extracts from <em>Eugenia jambolana</em>, <em>Mucuna pruriens</em>, and <em>Tinospora sordifolia</em> (no statistical test provided)</td>
<td>Grover et al., 2001(^{43})</td>
</tr>
<tr>
<td>Male Wistar rats (12 STZ-induced diabetic rats + 12 normal rats)</td>
<td>Fruit extract</td>
<td>70 d</td>
<td>Lipid profile improved, i.e., LDL-cholesterol lowered, HDL-cholesterol increased ($P &lt; 0.05$)</td>
<td>Ahmed et al., 2001(^{44})</td>
</tr>
<tr>
<td>Male Wistar rats (12 STZ-induced type 1 diabetic + 12 normal rats)</td>
<td>Fruit extract (juice)</td>
<td>98 d</td>
<td>Reversal of diabetic alterations of P450-dependent monooxygenase activities in kidney ($P &lt; 0.05$) and GSH-dependent oxidative stress in brain ($P &lt; 0.05$)</td>
<td>Raza et al., 2000(^{45})</td>
</tr>
<tr>
<td>Male Wistar rats (8–10 STZ-induced diabetic rats + 4–5 normal rats)</td>
<td>Juice from fresh fruit without seeds</td>
<td>70 d</td>
<td>Number of β-cells increased in treated animals ($P &lt; 0.004$); number of α- and δ-cells did not change significantly</td>
<td>Ahmed et al., 1998(^{13})</td>
</tr>
<tr>
<td>Male Wistar rats (10 STZ-induced diabetic + 10 normal rats)</td>
<td>Freshly prepared fruit pulp juice</td>
<td>70 d</td>
<td>Reversal of diabetes-induced increase in aniline hydroxylase and 7-ethoxycoumarin-O-deethylase (ECOD) ($P &lt; 0.05$)</td>
<td>Raza et al., 1996(^{46})</td>
</tr>
<tr>
<td>Female Wistar rats (36 STZ-induced diabetic + 24 normal rats)</td>
<td>Lyophilized alcoholic extract of unripe fruit without seeds</td>
<td>4 h (diabetic rats) and 7 d (normal rats)</td>
<td>Decreased plasma glucose levels in normoglycaemic rats by 10%–15% ($P &lt; 0.001$) 1 hour after load; insulin secretion not changed; in diabetic rats reduction of plasma glucose by 26% after 3.5 h ($P &lt; 0.02$)</td>
<td>Sarkar et al., 1996(^{21})</td>
</tr>
</tbody>
</table>

MCSEt: *Momordica charantia* seed extract; STZ, streptozocin.
extract of the fruit had a significant hypoglycemic effect both in the fasting and the postprandial states of NIDDM rats.

During the last 10 years, a great many trials have focused on the glucose-lowering effects of bitter gourd components; 17 of these are summarized in Table 2. In these studies, hypoglycemic activity could not be demonstrated in normoglycemic animals.20,21

Other studies have suggested that the mechanism of action of bitter gourd may include tissue glucose uptake, liver muscle glycogen synthesis, glucose oxidation, and decreased hepatic gluconeogenesis.7,21,22 Different investigators have proposed that the antidiabetic effect of bitter gourd derived from an increase of glucose transporter 4 (GLUT4) in the membrane of the muscle cell.20

HUMAN STUDIES

In folk medicine, bitter gourd is not only used to treat diabetes,3,4 but also for a number of other illnesses. In diabetic patients, fresh bitter gourd juice was shown to significantly reduce plasma glucose concentrations and improve the response to an oral glucose load.3 While in one trial the effect of an aqueous extract of bitter gourd was described to have a cumulative and gradual blood sugar-lowering effect in diabetic patients at the end of 3 weeks, different research suggested that this effect is more acute and transient than cumulative.3 Another study showed that extract of bitter gourd has synergistic effects with oral hypoglycemics and that it may aggravate hypoglycemia in NIDDM patients.23

Bitter gourd is used medicinally mainly for the treatment of type 2 diabetes mellitus.16 An earlier study on the development of diabetic cataracts demonstrated that blood sugar level-dependent cataract formation was slowed down by the consumption of bitter gourd fruit extract in association with better glucose homeostasis.24 Today, processed bitter gourd in the form of capsules or tablets is commonly advertised and sold. The products are marketed under the brand names Gourdin, Karela, and Glucobetic in Canada, India, the United Kingdom, the United States, and many Asian countries. Products can also be ordered online. However, Diabetes UK has released a warning with regard to the use of Karela capsules, because it is not yet known what dose is safe when taken with other antidiabetic agents, and there is a lack of information on other potential bioactive components of the capsules.25

OBSERVED ADVERSE EFFECTS

A number of adverse effects have been described for M. charantia. In animal studies, the fertility rate of mice dropped26 and spermatogenesis in dogs was inhibited27 when fed daily with 1.75 g of dry M. charantia fruit extract for 60 days.

Children have been reported to become ill from eating bitter gourd and, in fact, one death has been attributed to its consumption.28 After drinking bitter gourd tea, hypoglycemic coma and convulsions have been observed in children, and headache has been reported after the ingestion of bitter gourd seeds.29 Toxic lectins in seeds and in the outer rind were described as inhibiting protein synthesis in human intestinal mucosa cells, but these findings could not be linked to clinical signs or symptoms.30 Finally, the glycosidic compound vicine may cause hemolysis in patients with glucose-6-phosphat-dehydrogenase (G6PD) deficiency.31

SCOPE FOR FUTURE RESEARCH ON THE ANTIDIABETIC POTENCY OF BITTER GOURD

Although M. charantia has been studied in non-randomized, controlled trials only, it is considered to be one of the most promising supplements with blood sugar-lowering properties.7 Up to now, the mechanism of hypoglycemic activity of bitter gourd was not fully understood.3 A review by Basch et al.16 found four human studies indicating some hypoglycemic effect of bitter gourd, but these studies were either weakly designed or lacked statistical analysis. Since some results are still contradictory, it was concluded that more research needs to be done on the hypoglycemic activity of bitter gourd. Some analytical studies are in progress to isolate the active components in M. charantia seeds and their role in controlling glucose homeostasis and metabolism.32 Moreover, a better understanding of the toxic components of bitter gourd is necessary: separation of toxic substances from the insulin-potentiating components is an essential step in gaining a useful botanico-medicinal (nutriceutical) product from bitter gourd.

Proposed goals of future research into bitter gourd are:

- To better understand the mechanism of action.
- To test various M. charantia types from different environments and different growing sites for differences in their hypoglycemic activity.
- To perform long-term and better randomized, controlled trials to assess the clinical efficacy and safety and the optimum dosage.
- To improve acceptance (e.g., by modification of the bitter taste).

In conclusion, bitter gourd is a vegetable containing bioactive components with blood glucose-lowering properties. However, well-designed interdisciplinary research by nutritionists, medical doctors, and agronomists is needed before a dietary recommendation can be given and an effective product introduced into the market.
REFERENCES

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