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Review Article

Anti-diabetic Activity of *Momordica Charantia* or Bitter Melon: A Review

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Abstract

Momordica charantia or Bitter Melon belong to family Cucurbitaceae. The bitter melon plant is a vine with green leaves and yellow flowers; the fruit itself is oblong and green, resembling a cucumber, grows in topical areas of the Amazon, Asia, South America, India, East Africa and Caribbean, and is used traditionally as both food and medicine. Bitter melon has a long history of use as a hypoglycemic agent in Asia, Africa, and Latin America, where the plant extract has been referred to as vegetable insulin. A part of vegetable insulin bitter melon fruit is also used as tonic, stomachic, stimulant, emetic, antibilous, laxative and alterative. The fruit has various useful effect on treatment of gout, rheumatism and even in cuing diseases of spleen and liver. It is also used to purify blood and dissipate melancholia and gross humours. In this review article we have narrated about anti-diabetic activity of fruits of *Momordica charantia* or Bitter Melon.

Keywords: Bitter Melon (*Momordica charantia*); Anti-Diabetic Activity

Introduction

Momordica Charantia or Bitter Melon a vegetable consumed in india and also considered to have traditional medicinal use, even in Ayurveda, the fruit is considered as tonic, stomachic, stimulant, emetic, antibilous, laxative and alterative. Bitter melon has been used in various Asian traditional medicine systems for a long time [1]. *Momordica charantia* contains an collection of biologically active plant chemicals including triterpens, proteins, steroids, alkaloids, saponins, flavonoids and acids due to which plant possesses anti-fungal, anti-bacterial, anti-parasitic, anti-viral, anti-fertility, anti-tumorous, hypoglycemic and anti-carcinogenic properties. Fruits are used as traditional medication to cure various diseases like: rheumatism, gout, worms, colic, illness of liver and spleen.It is also found useful in the treatment of cancer and diabetes [2-16].

The wild bitter gourd (*Momordica charantia* L. var. *abbreviata* Seringe, MCA), normally smaller than domesticated bitter gourd (*Momordica charantia* L., MC), belongs to the family Cucurbitaceae. The fresh fruits of MC and MCA are frequently used as vegetables in Taiwan, and even their traditional medicinal use is listed in Chinese pharmacopia [17]. *Momordica charanti*a L., MC extract partitions reportedly show many pharmacological activities [6], including hypoglycemic [18-20], anti-bacterial [21], anti-viral [22], cytotoxic [23], triglyceride-lowering [24] and antiinflammatory activities [25].

Momordica charantia L. var. *abbreviata* Seringe, MCA extracts activated peroxisome proliferator-activated receptor α [26], and had anti-inflammatory [27], and antioxidant activities [28].

Momordica charantia plants rich in term of minerals such as Cu, Fe, Mg, Zn, and Ca. Some fatty acids such as lauric, myriaatic, palmitic, stearic, and linolaic acids are also present [29].

Momordica charantia Linn. (Karela) has many synonyms like *M. chinensis*, *M. elegans*, *M. indica*, *M. operculata*, *M. sinensis*, *Sicyos fauriei*. It is known with different common names in different languages i.e. Hindi – Karela; English – Bitter gourd; Sanskrit – Karavelli; Marathi – Karli; Gujarati – Karelo; Bangali – Baramasiya; Kannada – Karali; Malayalam – Kaypa; Tamil – Pakar; Telugu – Kakara [30].

Botanical Description

Momordica charantia Linn. (Karela) (Figure 1) is a flowering climber of family cucurbitaceae. The herbaceous, tendrilbearing plant grows up to six meter or more. Leaves are 4-12 cm across, with 3-7 deeply separated lobes (Figure 1).

Figure 1: Plant of *Momordica Charantia* bearing fruits.

The lobes are mostly blunt but have small marginal points. Stipules are absent. Flowers are actinomorphic and always unisexual. Perianth has a short to prolonged epigynous zone; yellow on short (female) or long (male) peduncles that are short-lived. Fruit has ovoid, ellipsoid or spindle shaped usually distinct warty looking exterior and an oblong shape (Figure 2).

Figure 2: Fruits of *Momordica Charantia.*

It is hollow in cross-section with a relatively thin layer of flesh surrounding a central seed cavity filled with large flat seed and pith [31]. Seeds in size 8-13mm, long compressed, corrugate on the margin, sculptured on both faces [32].

Parts used

The fruits of bitter melon are utilized as vegetable where as the whole plant parts like, fruits, leaves, roots and seeds of bitter melon as medicine.

Biological activities of bitter melon

The different parts of plant show the following biological activities;

- Root: Acrid, astringent.
- Leaf: Antipyretic, bitter, emetic, purgative.
- Fruits: Acrid, anthelmintic, anti-diabetic, anti-inflammatory, appetizer, bitter, depurative, digestive, purgative, stimulant, stomachic, thermogenic [33].

Chemical constituents

The main constituents of bitter melon are triterpene, protein, steroid, alkaloid, inorganic, lipid, and phenolic compounds.

Momordica charantia (Karela) consists the following chemical constituents those are alkaloids, momordicin and charantin (Figure 3), charine, cryptoxanthin, cucurbitins, cucurbitacins, cucurbitanes, cycloartenols, diosgenin, elaeostearic acids, erythrodiol, galacturonic acids, gentisic acid, goyaglycosides, goyasaponins, guanylate cyclase inhibitors, gypsogenin, hydroxytryptamines, karounidiols, lanosterol, lauric acid, linoleic acid, linolenic acid, momorcharasides, momorcharins, momordenol, momordicillin, momordicinin, momordicosides, momordin, momordolo, multiflorenol, myristic acid, nerolidol, oleanolic acid, oleic acid, oxalic acid, pentadecans, peptides, petroselinic acid, polypeptides, proteins, ribosome-inactivating proteins, rosmarinic acid, rubixanthin, spinasterol, steroidal glycosides, stigmastadiols, stigmasterol, taraxerol, trehalose, trypsin inhibitors, uracil, vacine, v-insuline, verbascoside, vicine, zeatin, zeatinriboside, zeaxanthin, zeinoxanthin Amino acidsaspartic acid, serine, glutamic acid, thscinne, alanine, gamino butyric acid and pipecolic acid, ascorbigen, bsistosterol-d-glucicide, citruline, elasterol, flavochrome, lutein, lycopene, pipecolic acid [34,35].

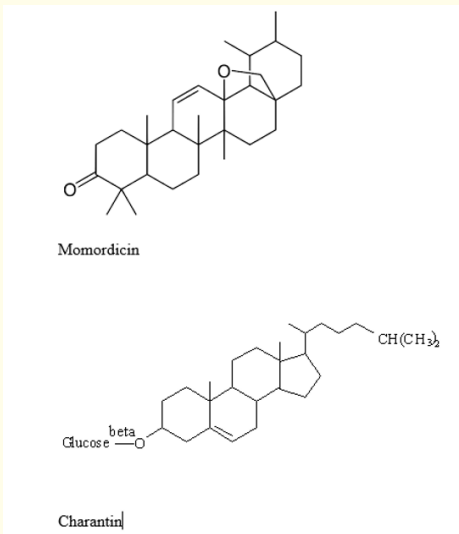

Figure 3: Chemical structure of momordicin and charantin.

Main pharmacologically active chemical constituents of *Momordica charantia* (Karela) are present in fruits and leaves.

Fruits consists glycosides, saponins, alkaloids, reducing sugars, resins, phenolic constituents, fixed oil and free acids [31] and leaves are rich in minerals like calcium, magnesium, potassium, phosphorus, and iron; fruits and leaves are great source of B vitamins (Thiamine, Riboflavin, Niacin. vit. B6, Folate) [30,34].

Traditional Use of *Momordica charantia*

Bitter melon is used in various Asian traditional medicine systems for a long time, as useful for preventing and treating various diseases.

Fruits of bitter melon used in asthma, burns, constipation, cough, diabetes, fever, gout, helminthiases, inflammation, leprosy, skin diseases, ulcer and wound. It shows hypoglycemic properties in animal as well as human studies. Juice of the leaves used to treat piles, purify blood and even used in liver damages, dyspepsia, jaundice, cholera [36-38].

Regular use of bitter melon to control diabetics

Bitter melon juice

Bitter melon leaves are cleaned and washed then chopped. Six tablespoon of the chopped leaves are added in two glass of water. This mixture must be boiled for approximately 15 minutes in an uncovered pot. Then it is allowed to cool. Dose is 1/3 cup of it thrice a day. This recipe is very effective in the treatment of diabetes type 2 [38].

Anti-Diabetic Benefits of *Momordica Charantia*

J. Virdi., et al. explained that oral administration of fresh fruit juice (dose, 6 c.c./kg. body wt.) lowered the blood sugar level in normal and alloxan-diabetic rabbits [39].

P. B. Aswar., *et al*. proved that *Momardica charantia* fruit juice is claimed to be useful in diabetes. Results of anti-diabetic activity of *Momardica charantia* fruit extracts established the scientific basis for the utility of this plant in the treatment of diabetes [40]. Alcoholic extracts of the fruit found to possess antidiabetic, hepatoprotetive activities when tested in rats [41,42]. Bioactive compounds present in bitter gourd activate a protein called AMPK (AMP-activated protein kinase α), which regulates fuel metabolism and enabling glucose uptake processes which are impaired in patients with diabetes [39,43].

Lectin of *Momardica charantia* has insulin-like activity and which is due to its linking together of 2 insulin receptors. This lectin lowers blood glucose concentrations by acting on peripheral tissues and, similar to insulin's effects in the brain, suppressing appetite. Lectin is likely a major contributor to the hypoglycemic effect that develops after eating bitter gourd and it may be a way of managing adult-onset diabetes. Lectin binding is non-protein specific, and this is likely why bitter gourd has been credited with immunostimulatory activity - by linking receptors that modulate the immune system, thereby stimulating said receptors [44].

Vijayalakshmi., *et al*. studied the changes in glycolconjugate metabolism during the development of diabetic complications and their modulation by feeding bitter gourd and spent turmeric as a fiber-rich source [45].

Effect of bitter gourd on streptozotocin-induced diabetic rats with particular emphasis on kidney heparin sulfate (HS) was studied by Sureshkumar., *et al*. This Study showed a partial reversal of all the diabetes induced effects by bitter gourd. Increase in the components of glycol-conjugates during diabetes was significantly decreased by the feeding of bitter gourd. Diabetes associated elevation in the activities of enzymes involved in the synthesis and degradation of glycosaminoglycans (GAGs) were significantly lowered by bitter gourd supplementation. GAGs composition revealed decrease in amino sugar, and uronic acid contents during diabetes and bitter gourd feeding was effective in countering this reduction. Decrease in sulfate content in the GAGs during diabetes was also ameliorated by the intake of bitter gourd which indicated the beneficial role of bitter gourd in controlling glyco-conjugate and heparin sulfate related kidney complications during diabetes thus prolonging late complications of diabetes [46].

Charantin is one of the hypoglycemic compounds consisting of a mixture of (1:1) sitosteryl glucoside (C35H60O6) and stigmasteryl glucoside (C35H58O6), belongs to steroidal saponins. Lolitkar and Rao have shown that charantin when taken either orally or intravenously in rabbits, it produces hypoglycemic effects [47]. Protein P-insulin is an another hypoglycemic agent of polypeptide in nature with the molecular weight of about 11,000 Da and consists of 166 amino acids. Clinical study revealed that the polypeptide-pZnCl2 produced blood sugar lowering effect. Khanna and Mohan reported that besides the fruits, p- insulin was also found in seeds and tissue cultures of *Momordica charantia* [48]. According to Dutta., et al. and Barron., et al. the seeds of bitter gourd contain pyrimidine nucleoside, vicine which has been found to induce hypoglycemia in rats, when administered intraperitonially. Charantin-rich extract is a potential agent for increasing insulin-sensitivity in type 2 diabetic (T2D) patients [49-51]. Recently, 8 new cucurbitanetype glycosides were isolated by bioactivity-guided fractionation that also exhibited a hypoglycemic effect in vitro [52].

Karela contains bitter chemicals like, charantin, vicine, glycosides and karavilosides along with polypeptide-p a plant insulin, which are hypoglycemic in action and improve blood sugar levels by increasing glucose uptake and glycogen synthesis in the liver, muscles and fat cells [30]. Reports indicate that they also improve insulin release from pancreatic beta cells, and repair or promote new growth of insulin-secreting beta cells. P-Insulin, a polypeptide from the fruits and seeds rapidly decreased and normalized the blood sugar level in rats. Bitter melon contains another bioactive compound i.e. lectin that has insulin like activity. The insulin-like bioactivity of lectin is due to its linking together 2 insulin receptors. This lectin lowers blood glucose concentrations by acting on peripheral tissues and, similar to insulin's effects in the brain, suppressing appetite. This lectin is a major contributor to the hypoglycemic effect that develops after eating Karela. Charantin extracted by alcohol, is a potent hypoglycemic agent composed of mixed steroids which is sometimes used in the treatment of diabetes to lower the blood sugar levels [31,53,54]. Nkambo W., et al. confirmed by their experimental study that the methanolic fruit extract of *Momardica charantia* exhibits dose dependent hypoglycaemic activity in vivo [55]. Eman A. Moussa and Maliha A. Almarzooq explained that *Momordica charantia* extract caused a significant decrease of creatinine, and cholesterol levels in the blood. *Momordica charantia* juice lowered cholesterol levels in alloxan diabetic mice. The juice may exert rapid protective effects against lipid peroxidation by scavenging of free radicals there by reducing the risk of diabetic complications [56]. Kaushal Parmar., et al. clearly demonstrated that bittergourd fruit juice can have marked beneficial effects in the treatment of diabetes mellitus, bittergourd fruit juice administration may be useful as an adjunct therapy with oral hypoglycaemic agents in the management of diabetes mellitus [57]. Sonal Desai and Pratima Tatke confirmed by their experiment that charantin, a natural steroidal glycoside present in the fruits of this medicinal plant, has been reported to possess potential hypoglycemic activity [58].

Baldwa., *et al*. studied the effects of bitter melon on blood sugar levels in patients with diabetes. Nineteen subjects were enrolled, including 14 patients with type 1 or type 2 diabetes mellitus. An extraction method was performed to isolate vegetable insulin, which was suspended in sterile water and made available in a subcutaneous form with a concentration of 1.8 mg of vegetable insulin per 40-unit dose. Nine of the diabetic patients were placed on a sliding scale to receive 10 units of this suspension if the fasting blood glucose concentration was <180 mg/dL, 20 units for 180–250 mg/dL, and 30 units for >250 mg/dL. Five diabetic patients and five healthy volunteers received placebo. The primary endpoint was a decrease in fasting blood glucose, which was measured at multiple time points over 12 hours.

The authors reported a mean decrease in serum glucose levels for the diabetic patients receiving bitter melon, with effects noted as early as 30 minutes (a 21.5% decrease from a mean baseline glucose concentration of 295 mg/dL), a maximum reduction at 4 hours (a 49.2% drop), and persistent effects after 12 hours (a 28% drop). In contrast, a mean decrease in serum glucose of about 5% was seen during the study period in both the diabetic patients and the healthy controls. Although these results appear promising, no statistical analysis was performed, and the study was not blinded or randomized. The diabetic patients who received bitter melon had a substantially different mean baseline serum glucose concentration from the placebo group (295 versus 210 mg/dL, respectively). Furthermore, both type 1 and type 2 diabetes mellitus were represented in the study; these diseases have different etiologies and mechanisms. As a result of these weaknesses, the results can be considered only preliminary [59].

Leatherdale., *et al*. conducted a case-series study of nine patients with type 2 diabetes mellitus, of whom eight were taking concomitant sulfonylureas. The subjects underwent a baseline glucose tolerance test (GTT), a GTT after ingestion of 50 mL of bitter melon juice (obtained from approximately 200 g of fresh fruit), and then another GTT after 8–11 weeks of daily ingestion of 0.23 g of fried bitter melon fruit. The GTT performed after the period of fried fruit ingestion revealed a mean decrease in glucose levels of approximately 6% after one hour. This result does not appear to have been statistically significant. The GTT after juice consumption showed a significant decline in glucose of approximately 12% after one hour. In addition, consuming fried bitter melon for 8–11 weeks reduced glycosylated hemoglobin (HbA1c) levels 8% from baseline. Because of methodological weaknesses, including a lack of controls, failure to describe patients' baseline characteristics, and inadequate explanation of statistical methods, firm conclusions cannot be drawn [60].

Welihinda., *et al*. reported a case series study involving 18 patients with newly diagnosed type 2 diabetes mellitus. The subjects were each given 100 mL of bitter melon fruit juice 30 minutes before glucose loading for a GTT. The results were compared with the subjects' own responses to a GTT on a previous day, when water was administered as a control. Thirteen (73%) of the patients showed moderate, significant improvements in GTT results after taking bitter melon. It is not clear what baseline differences might have existed in the five nonresponders. Although suggestive, these results cannot be considered conclusive. Even with patients serv-

ing as their own controls, the lack of true controls or randomization increases the possibility of confounding. Again, the study was not blinded, and patients' baseline characteristics were poorly defined [61].

Srivastava conducted a case series study involving 12 patients with type 2 diabetes mellitus over 21 days.

The patients were not using other treatments, aside from diabetic diets. Each subject received one of two bitter melon preparations: (1) an aqueous extract, prepared by boiling 100 g of chopped bitter melon in 200 mL of water until the volume was reduced to 100 mL, given daily as a single morning dose, and (2) 5 g of dried fruit powder given three times daily. After three weeks of therapy, patients in the powder group (n = 5) showed a nonsignificant 25% reduction in the mean blood glucose level. In the aqueous extract group (n = 7), a significant 54% reduction in the mean blood glucose level was observed, and the mean Hb A1c level fell from 8.37% to 6.95% ($p< 0.01$). Once again, this study was poorly designed and written. The statistical analysis was not properly described, and controls, a description of the patients' baseline characteristics, and a measurement of fasting glucose levels were absent [62].

Conclusion

In this review article we have studied about anti-diabetic activity of *Momordica charantia* or Bitter Melon. Here different author used extraction of fruit and leaf of *Momordica charantia*. Ethanol, methanol and water were used as extraction media. *Momordica charantia* or Bitter Melon or Karela contains charantin, pyrimidine nucleoside, vicine, p- insulin, glycosides and karavilosides along with polypeptide-p a plant insulin. Charantin-rich extract is a potential agent for increasing insulin-sensitivity in type 2 diabetic (T2D) patients. A part of anti-diabetic property those extracted media also decreased the serum cholesterol level in diabetic rats.

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