IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

Anti-diabetic effects of bitter melon (Momordica charantia):A Review

Ms.Sneha bhimrao kokane, Ms.Siddhi Sartape, Mrs.Komal hole.MS.Nikita deokate.
Institute of pharmaceutical science and research (for girls)Babasaheb Ambedkar Technological University Lonere Maharashtra India.

Abstract:
Natural items have been used for millennia to prevent, treat, and cure a variety of diseases.
Some dietary substances are used as recommended remedies for chronic and difficult-to-treat disorders in a variety of medical systems. Momordica charantia, also known as bitter melon, is one such natural product. Bitter melon is grown in many places of the world, and many components of the plant, such as the fruit, leaves, seeds, and so on, have been shown in ancient literature to have medicinal properties. Several well-structured scientific research have been conducted over the last few decades to investigate the impact of bitter melon on various disorders.Bitter melon has been studied for its antioxidant, anticancer, anti-inflammatory, antibacterial, antifungal, antiviral, anti-HIV, anthelmintic, hypotensive, anti-obesity, immunomodulatory, antihyperlipidemic, hepatoprotective, and neuroprotective properties. This review seeks to outline the many results in the literature concerning the therapeutic properties of bitter melon. With such strong scientific backing for so many medical claims, bitter melon is on the verge of being deemed a panacea.

Keywords:
Bitter melon (MomordicacharantiaLinn)Anti-diabetic activity.

Introduction
Momordica Charantia, often known as Bitter Melon, is a vegetable used in India that is also said to have ancient medical uses. The fruit is regarded tonic, stomachic, stimulant, emetic, antibilous, laxative, and alterative in Ayurveda. Bitter melon has long been employed in different Asian traditional medicine systems (1). Momordica charantia contains a variety of biologically active plant chemicals such as triterpenes, proteins, steroids, alkaloids, saponins, flavonoids, and acids, which give the plant anti-fungal, anti-bacterial, anti-parasitic, anti-viral, anti-fertility, anti-tumorous, hypoglycemic, and anti-carcinogenic properties.Fruits are used in traditional medicine to treat a variety of ailments such as rheumatism, gout, worms, colic, and liver and spleen disorders.It has also been reported to be beneficial in the treatment of cancer and diabetes (2-16).
The bitter melon (Momordica charantia), which is smaller than the farmed bitter gourd (Momordica charantia L., MC), is a member of the Cucurbitaceae family.
Fresh MC and MCA fruits are commonly utilized as vegetables in Taiwan, and their traditional medical use is even noted in Chinese pharmacopia (17), MC extract partitions have been shown to have a variety of pharmacological effects (6),ncluding hypoglycemia (18-20), anti-bacterial (21)], anti-viral (22), cytotoxic (23), triglyceride-lowering (24), and antiinflammatory properties.var. abbreviata of Momordica charantia L. Seringe, MCA extracts activated the peroxisome proliferator-activated receptor (26), as well as having anti-inflammatory and antioxidant properties 27,28).

Momordica charantia plants are high in minerals including Cu, Fe, Mg, Zn, and Ca. Some fatty acids are also present, including lauric, myriaatic, pal- mitic, stearic, and linolaic acids (29).

Momordica charantia Linn. (Karela) is known by numerous names, including M. chinensis, M. elegans, M. indica, M. operculata, M. sinensis, and Sicyos fauriei. In several languages, it is known by different common names, such as Karela in Hindi, Bitter gourd in English, Karavelli in Sanskrit, Karli in Gujarati, Baramasiya in Bangali, Kannada in Kannada, Kaypa in Malayalam, Pakar in Tamil, and Kakara in Telugu (30).

Botanical Description:

MomordicacharantiaLinn. (Karela) (Figure 1) is a cucurbitaceae blooming climber. The herbaceous, tendrilbearing plant can reach a height of six meters or more. The leaves are 4-12 cm long and have 3-7 deeply separated lobes (Figure 1).

Figure 1: plant of Bitter melon bearing fruit.

The lobes are primarily blunt, with a few tiny points at the edges. There are no stipules. Flowers are usually actinomorphic and unisexual.

The epigynous zone of the perianth is brief to protracted; yellow on short (female) or long (male) peduncles that are short-lived. Fruit is ovoid, ellipsoid, or spindle shaped with a pronounced warty appearance and an oblong form (Figure2).

Figure 2 : Fruits of Bitter melon.

In cross-section, it is hollow, with a thin layer of flesh surrounding a central seed chamber filled with huge flat seed and pith (31). 8-13mm long compressed seeds with a corrugated border and sculptured on both faces (32).

Components utilized

Bitter melon fruits are used as vegetables, while the entire plant, including the fruits, leaves, roots, and seeds, is used as medicine.

Bitter melon's biological activity

The following biological activities are demonstrated by various plant parts:

• Root: Astringent and acrid.

• Leaf: Analgesic, bitter, emetic, and purgative.

• Fruits are astringent, anthelmintic, anti-diabetic, anti-inflammatory, bitter, depurative, digestive, purgative, stimulant, stomachic, and thermogenic [33].

Chemical components

Bitter melon's principal ingredients are triterpene, protein, steroid, alkaloid, inorganic, lipid, and phenolic chemicals.

Alkaloids, momordicin and charantin (Fig. 3), charine, cryptoxanthin, cucurbitins, cucurbitacins, cucurbitanes, cycloartenols, diosgenin, elaeostearic acids, erythrodiol, galacturonic acids, gentisic acid, goyaglycosides, goyasaponins, guanylate hydroxytryptamines, karounidiols, lanosterol, lauric acid, linoleic acid, linolenic acid, momorcharasides, momorcharins, momordenol, momordicillin, momordicinin, momordicicosides, momordin, momordolo, multiflo- renol, myristic acid, nerolidol,

Aspartic acid, serine, glutamic acid, thscinne, alanine, gammo butyric acid, and pipecolic acid, ascorbigen, bsistosterol-d-glucicide, citruline, elasterol, flavochrome, lutein, lycopene, pipecolic acid, pipecolic acid (34,35).

The fruits and leaves of Mo- mordica charantia (Karela) contain the majority of the pharmacologically active chemical components.

Fruits contain glycosides, saponins, alkaloids, reducing sugars, resins, phenolic constituents, fixed oil, and free acids (31), and leaves contain minerals such as calcium, magnesium, potassium, phosphorus, and iron; fruits and leaves are high in B vitamins (thiamine, riboflavin, niacin, vitamin B6, folate) (30,34).

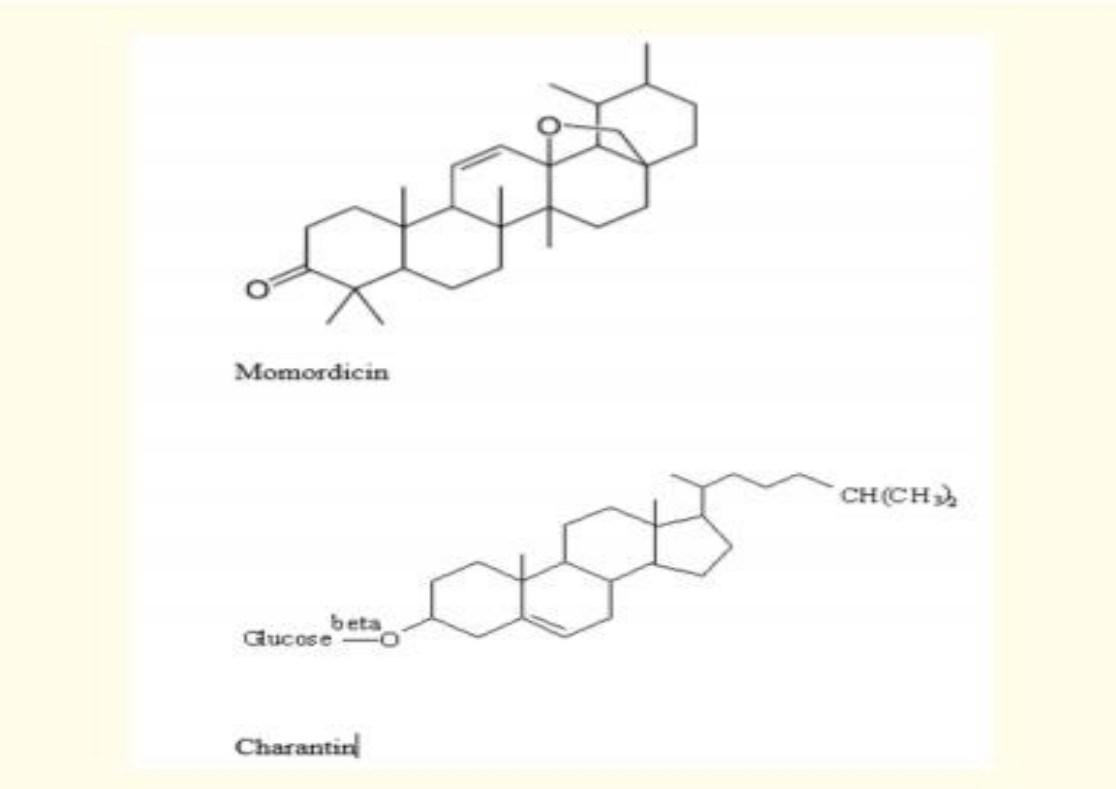

Figure 3: Chemical structure of momordicin and charantin.

Momordica charantia Traditional Use

Bitter melon has long been utilized in several Asian traditional medicine systems to prevent and treat various ailments.

Bitter melon fruits are used to treat asthma, burns, constipation, cough, diabetes, fever, gout, helminthiases, inflammation, leprosy, skin illnesses, ulcers, and wounds. It has hypoglycemic characteristics in both animal and human trials. The juice of the leaves was used to heal piles, purify blood, and was even used to treat liver damage, dyspepsia, jaundice, and cholera [36-38].

Melon juice that is bitter

Bitter melon leaves are washed and sanitized before being sliced. Two glasses of water are filled with six tablespoons of chopped leaves.

In an uncovered pot, bring this mixture to a boil for about 15 minutes. It is then allowed to cool. The recommended dose is 1/3 cup three times a day. This mixture is particularly efficient in the treatment of type 2 diabetes (38),

Bitter melon is used on a regular basis to reduce diabeties.

Momordica Charantia's Anti-Diabetic Properties:

J. Virdi et colleagues. demonstrated that oral administration of fresh fruit juice (dosage, 6 cc/kg body weight) decreased blood sugar levels in normal and alloxan-diabetic rabbits (39).

P. B. Aswar et al. demonstrated that Momardica charantia fruit juice is effective in diabetes. The anti-diabetic activity of Momardica charantia fruit extracts established the scientific basis for this plant's value in the treatment of diabetes (40), Alcoholic extracts of the fruit were reported to have anti-diabetic and hepatoprotective properties in rats (41,42). Bitter gourd bioactive components activate a protein called AMPK (AMP-activated protein kinase), which regulates fuel metabolism and enables glucose uptake mechanisms that are impaired in patients with diabetes.

Because it connects two insulin receptors, lectin from Momardica charantia possesses insulin-like action. This lectin decreases blood glucose concentrations by acting on peripheral tissues and decreasing hunger in the same way that insulin does in the brain. Lectin is most likely a substantial contribution to the hypoglycemic effect that develops after eating bitter gourd, and it could be used to manage adult-onset diabetes. Lectin binding is non-

protein specific, which is probably why bitter gourd has been linked to immunostimulatory activity - by joining receptors that affect the immune system and thereby stimulating those receptors (44).
Vijayalakshmi et al. investigated the alterations in glycolconjugate metabolism that occur throughout the progression of diabetes problems, as well as their regulation by administering bitter gourd and wasted turmeric(45).
Sureshkumar et al. investigated the effect of bitter gourd on streptozotocin-induced diabetic rats, with a focus on kidney heparin sulfate (HS). Bitter gourd exhibited a partial reversal of all diabetes-induced symptoms in this study. Bitter gourd feeding considerably reduced the increase in glycol-conjugate components during diabetes. Bitter gourd treatment significantly reduced diabetes-related el- evation in the activity of enzymes involved in the synthesis and breakdown of glycosaminoglycans (GAGs). The composition of GAGs revealed a drop in amino sugar and uronic acid concentrations during diabetes, and bitter gourd feeding was helpful in compensating for this decline.
Bitter gourd consumption reduced sulfate content in GAGs during diabetes, indicating a beneficial role for bitter gourd in controlling glyco-conjugate and heparin sulfate related kidney complications during diabetes, thus prolonging late complications of diabetes (46).
Charantin, a hypoglycemic molecule composed of (1:1) sitosteryl glucoside (C35H60O6) and stigmasteryl glucoside (C35H58O6), belongs to the class of steroidal saponins. Charantin produces hypoglycemia effects in rabbits when administered orally or intravenously, according to Lolitkar and Rao Protein P-insulin is another polypeptide hypoglycemic agent found in nature, with a molecular weight of around 11,000 Da and 166 amino acids. A clinical trial indicated that the polypeptide-pZnCl2 reduced blood sugar levels. (47).Khanna and Mohan discovered p-insulin in Momordica charantia seeds and tissue cultures in addition to the fruits According to Dutta et al. and Barron et al., bitter gourd seeds contain vicine, a pyrimidine nucleoside that has been shown to induce hypoglycemia in rats when injected intraperitonially. (48).Charantin-rich extract has been shown to improve insulin sensitivity in type 2 diabetic (T2D) patient(49,51). Recently, bioactivity-guided fractionation was used to identify 8 novel cucurbitanetype glycosides that also demonstrated a hypoglycemic impact in vitro Karela includes bitter compounds such as charantin, vicine, glycosides, and karavilosides, as well as polypeptide-p a plant insulin, all of which are hypoglycemic and enhance blood sugar levels by increasing glucose uptake and glycogen synthesis in the liver, muscles, and fat cells (52,30).
According to reports, they also improve pancreatic beta cell insulin release and repair or induce new proliferation of insulin-secreting beta cells. P-Insulin, a polypeptide derived from fruits and seeds, reduced and stabilized blood sugar levels in rats. Bitter melon also includes lectin, a bioactive molecule with insulin-like action.The insulin-like bioactivity of lectin is caused by its ability to connect two insulin receptors. This lectin decreases blood glucose concentrations by acting on peripheral tissues and suppressing appetite in the same way that insulin does in the brain. This lectin plays a significant role in the hypoglycemic impact that arises after consuming Karela. Charantin, an alcohol-extracted hypoglycemic medication made of mixed steroids, is sometimes used in the treatment of diabetes to lower blood sugar levels (31,53,54). Nkambo W. et al. confirmed in vivo hypoglycemic efficacy of the methanolic fruit extract of Mo- mardica charantia in their experimental investigation [55].Momordica charantia extract, according to Eman A. Moussa and Maliha A. Almarzooq, caused a considerable drop in creatinine and cholesterol levels in the blood. Momordica charantia juice reduced cholesterol levels in diabetic alloxan mice. The juice may have immediate anti-lipid peroxidation effects by scavenging free radicals, lowering the risk of diabetes complications (56). Bittergourd fruit juice administration may be useful as an adjunct therapy with oral hypoglycaemic agents in the management of diabetes mellitus, as demonstrated by Kaushal Parmar., et al. (57). Sonal Desai and Pratima Tatke's investigation confirmed that charantin, a natural steroidal glycoside found in the fruits of this medicinal plant,(58).
Baldwa et al. investigated the effects of bitter melon on blood sugar levels in diabetic patients. Nineteen people with type 1 or type 2 diabetes mellitus were included in the study. To isolate vegetable insulin, an extraction process was used, which was then 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. On a sliding scale, nine diabetic patients received 10 units of this suspension if their fasting blood glucose concentration was 180 mg/dL, 20 units for 180-250 mg/dL, and 30 units for >250 mg/dL. A placebo was given to five diabetic patients and five healthy volunteers. The major goal was to reduce fasting.

The authors reported a mean decrease in serum glucose levels in diabetic patients who were given bitter melon, with effects observed 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, both diabetic patients and healthy controls saw a 5% drop in serum glucose during the research period. Although these findings sound encouraging, no statistical analysis was carried out, and the study was not blinded or randomized. The diabetic individuals who received bitter melon had significantly lower mean baseline serum glucose concentrations than the placebo group (295 versus 210 mg/dL, respectively).Furthermore, the study included both type 1 and type 2 diabetes mellitus, which have different etiologies and processes. Because of these flaws, the findings may only be regarded preliminary (59).

Leatherdale et al. conducted a case-series analysis on nine patients with type 2 diabetes mellitus, eight of whom were taking sulfonylureas concurrently. The patients were given a baseline glucose tolerance test (GTT), a GTT after consuming 50 mL of bitter melon juice (obtained from about 200 g of fresh fruit), and another GTT after 8-11 weeks of daily consumption of 0.23 g of fried bitter melon fruit. The GTT done following the fried fruit eating demonstrated a 6% drop in glucose levels on average.After one hour, the GTT performed after the period of fried fruit eating demonstrated a mean drop in glucose levels of roughly 6%. This outcome does not appear to be statistically significant. After one hour, the GTT after juice consumption revealed a significant drop in glucose of around 12%. Furthermore, eating fried bitter melon for 8-11 weeks lowered glycosylated hemoglobin (HbA1c) levels by 8% compared to baseline. Firm conclusions cannot be reached due to methodological flaws such as a lack of controls, failure to specify patients' baseline characteristics, and insufficient explanation of statistical procedures (60).

Welihinda et al. published a case series research comprising 18 people with newly diagnosed type 2 diabetes. Each patient was given 100 mL of bitter melon fruit juice 30 minutes before the glucose loading for the GTT. The results were compared to the subjects' own answers to a GTT administered as a control the day before. Thirteen (73%) of the patients improved their GTT results somewhat or significantly after ingesting bitter melon. It is unclear what baseline differences occurred among the five nonresponders. These findings, while intriguing, cannot be called conclusive. Confounding is increased when there are no actual controls or randomization. Again, the investigation was not blinded, and the baseline characteristics of the patients were poorly defined (61).

Srivastava conducted a 21-day case series research with 12 individuals with type 2 diabetes mellitus.

Aside from diabetic diets, the patients were not receiving any other treatments. Each subject was given one of two bitter melon preparations: (1) an aqueous extract made by boiling 100 g of chopped bitter melon in 200 mL of water until the volume was decreased to 100 mL, which was given daily as a single morning dose, and (2) 5 g of dried fruit powder, which was given three times daily. The powder group (n = 5) demonstrated a nonsignificant 25% drop in mean blood glucose level after three weeks of medication. The mean blood glucose level was reduced by 54% in the aqueous extract group (n = 7), and the mean Hb A1c level fell from 8.37% to 6.95% (p 0.01).This study was once again inadequately constructed and written. The statistical analysis was not correctly stated, and controls, a description of the patients' baseline characteristics, and a fasting glucose level measurement were all missing (62).

The Phytochemistry of Momordica charantia:

The MC fruit is 932 percent water, whereas protein and fats constitute for 1802 and 076 percent of its dried weight, respectively(63). On the contrary, about 45% of MC seed oil is constituted of 63-68% eleostearic acid and 22-27% stearic acid(64). Several glycosides have been extracted from the MC stem(65) and fruit(66-68), and they are classified as cucurbitane-type triterpenoids.

Four triterpenoids in particular have AMP-activated protein kinase activity, which is a possible hypoglycemic mechanism of MC(68).

Animal research on Momordica charantia

MC seeds, fruit pulp, leaves, and whole plant have been demonstrated in numerous animal experiments to produce hypoglycemic effects in normal animals(69- 73). MC, in particular, boosts glucose levels In rats, MC extract improves tolerance(74) and reduces postprandial hyperglycemia(75), and it can improve insulin sensitivity and

lipolysis(76-78). According to certain investigations, the hypoglycemic impact of MC was comparable to that of oral drugs such as tolbutamide(72), chlorpropamide(78), and glibenclamide(79).
A wealth of pharmacological evidence has thrown light on putative mechanisms of MC's anti-diabetic activities, with the AMP-activated protein kinase pathway being a repeating theme(80-83). Other research has suggested that the a- and g-peroxisome proliferator-activated receptors (PPARa and PPARg) have a function in lipid and glucose homeostasis and may help to reduce insulin resistance(84-86).
A Zn-free protein with insulinomimetic properties was recently obtained from MC(85).echoing the notion of'vegetable insulin' discovered by Baldwa et al. some 30 years ago(88).

Momordica charantia clinical trials

Clinical investigations on the hypoglycemic effects of MC have been limited and infrequent as compared to animal trials.
In 1956, Lakholia, a physician, was perhaps the first to establish the medicinal effect of bitter melon on himself(89). As we analyzed the studies that fulfilled our search criteria, we discovered that the majority lacked suitable controls or had poor procedures that lacked baseline characteristics(74,88,90,100), as shown in Table 1. Five of these have been chosen for further debate, as follows. Four were clinical trials, and the fifth, albeit a case series, was chosen due to its huge sample size.
The research of John et al.
John et al. (98) assigned fifty type 2 diabetes (T2D) patients (twenty-six trials and twenty-four controls) to receive either dried MC fruit or riboflavin. There were clear inclusion criteria based on fasting blood sugar (FBS) and postprandial sugar (PPS) levels. The sample size was estimated using a sugar level reduction of 300 mg/l (30 mg/dl) for both FBS and PPS. All subjects' baseline characteristics were equivalent. Dried MC fruit was given at a dose of 2 g three times per day, with riboflavin serving as a placebo.All subjects were told to keep their current oral hypoglycemic treatment and food habits. FBS and PPS levels were assessed with fructosamine levels at baseline, 2 weeks, and 4 weeks after therapy. The authors attributed the lack of a statistically significant impact attributable to intervention to the possibility of using dried MC rather than fresh fruit, or to an inadequate dose. There was no mention of the randomization protocol in this trial, nor was it a double-blind design due to the non-matching placebo. Furthermore, the authors simply reported the lack of negative effects and did not account for dropouts. As a result, the Jadad score(101) for this randomised study is 1 (on a scale of 0 to 5).
Dans and colleagues conducted research.
Dans et al. (100) conducted a randomized double-blind placebo-controlled experiment on forty participants with newly diagnosed or poorly treated T2D with HbA1c values ranging from 7 to 9%. The sample size was obtained using a 1% reduction in HbA1c as the aim and an estimated power of research of 088. All respondents' baseline characteristics were not significantly different. For three months, the trial group was given a brand-name product containing a standardized quantity of dried MC extract at a dose of two capsules three times per day (precise amount per capsule unclear). The placebo group followed the identical protocol as the experimental group. Before beginning treatment, baseline HbA1c and other biochemical testing were done. Subjects were then followed up on monthly for three months, with blood glucose checked and compliance or adverse effects documented. All baseline tests were redone at the end of treatment. The trial group had a mean reduction in HbA1c of 0217%, which was not statistically significant (P140483) and was insufficient to reject the null hypothesis.
In conclusion, the authors proposed a follow-up investigation with a bigger sample size. Nonetheless, this study deserves credit for its appropriate design, comprehensive documentation of detrimental effects, and individual accounting for dropouts. As a result, the Jadad score for this study is 5.
The research of Tongia et al.
Tongia et al. (99) gathered fifteen T2D patients and divided them into three equal groups. Aside from the diagnostic diagnosis and age, no inclusion criteria were specified. Subjects' FBS and PPS levels were assessed prior to intervention, and the results served as controls. The three groups were subsequently given metformin, glibenclamide, and metformin glibenclamide for 7 days before the FBS and PPS values were assessed. Over the next 7 days, individuals were given half-dosage oral hypoglycemic medicines, as well as a standard dose of MC fruit extract twice per day (200 mg twice day), and FBS and PPS levels were assessed again.

FBS and PPS levels were reduced after oral hypoglycemics, and this was further reduced with MC extract. Although significant, the cited P values must be weighed against the limited sample size of fifteen participants. It's worth mentioning that this study used a within-subject design and made no mention of the inclusion criteria.FBS and PPS levels were reduced after oral hypoglycemics, and this was further reduced with MC extract. Although significant, the cited P values must be weighed against the limited sample size of fifteen participants. It's worth mentioning that this study used a within-subject design and made no mention of the inclusion criteria.
Furthermore, the sample size and study power were not justified. This study cannot be rated with a Jadad score because it is not a randomized trial.
The research of Baldwa et al.
Baldwa et al. (88) studied the effect of an insulin-like compound isolated from MC fruit that was dubbed "vegetable insulin" on fourteen diabetic people (T1D and T2D) and five healthy volunteers. The'vegetable insulin' was administered subcutaneously to nine diabetic individuals on a sliding scale (precise dosage not specified). Five other diabetic patients and five healthy volunteers served as controls, each receiving a placebo injection (the type of the placebo was not specified). When compared to pre-injection levels, there was a 215% reduction in blood glucose at 30 minutes, a 492% reduction at 4 hours, and a 28% reduction at 12 hours in the trial group. Regardless of treatment, those who got placebo had a 5% drop in glucose levels.There was no clear randomization protocol; investigators and subjects were not blinded; and baseline characteristics of the subjects were not uniform, either in pathology (both T1D and T2D in the trial group) or severity (baseline glucose levels ranged from 2100 to 2950 g/l (210 to 295 mg/dl). Furthermore, the control arm was diverse (it included both healthy and diabetic individuals). Again, because this is not a randomized experiment, a Jadad score cannot be assigned.
Ahmad et al. conducted research
Ahmad et al. (96) investigated the effect of MC in a case series of 100 T2D patients (58 males and 42 females).
The inclusion criteria were explicit, and all subjects' baseline characteristics were statistically equivalent. As a washout period, subjects were told to discontinue their existing oral drugs for three days before to the trial. On day 1, fasting (s1) and postprandial blood sugar (s2) levels were measured. On day 2, fasting blood sugar was tested again (s3), and all subjects drank a drink made from freshly blended MC fruit (dosage adjusted depending on subject body weight). Blood sugar was checked 1 hour (s4) later, followed by a postprandial measurement 2 hours later (s5).The modes of MC administration (from methanol extract to dried powder to fresh fruit), the actual dosage (time and dose per kg body weight), and the outcome assessments (from HbA1c to postprandial sugar levels to oral glucose tolerance test) are clearly different in these five trials.
As a result, meta-analysis and between-study comparisons are unfeasible. For simplicity of administration, MC should be taken as an encapsulated powder; however, existing research suggest that MC is more effective when given fresh or juiced(90,94,96,98). Furthermore, existing data appear to support an acute or single dosage effect of MC(88,92,94,96) rather than a long-term effect lasting more than 4 weeks(91-98-100). The authors recommend a well-designed randomised controlled clinical trial with a large sample size to assess the hypoglycemic effects of MC. It will use various arms (fresh MC juice, dry MC powder, and corresponding matching placebos) with cross-over and washout over a 6-12 month period with interim analysis.

Conclusions

There are strong signs that bitter melon may be quite beneficial in the treatment of diabetes. The seeded fruit has a long history of use as a meal, and bitter melon aqueous preparations appear to have a strong hypoglycemic impact.
Furthermore, there are some (although very faint) signs that bitter melon extracts may protect patients from various diabetes complications.
We are confident in offering seeded bitter melon as a meal or tea to elderly people with NIDDM. To make a daily dose of bitter melon tea, boil 100 g diced fruit in 200 ml water until the liquid is reduced by half. However, due to the plant's potential abortifacient effects and capacity to impair fertility in animals, we would not recommend daily usage of bitter melon to younger patients or patients who may be interested in having children at this time.

Reference:

1. D Sathish Kumar., et al. "A Medicinal Potency of Momordica Charantia". International Journal of Pharmaceutical Sciences Review and Research 1 (2010): 95-100.

2. Nesar Ahmad., et al. "Momordica Charantia: For traditional uses and pharmacological actions". Journal of Drug Delivery and Therapeutics 6 (2016): 1-5.

3. Abdel-Barry JA., et al. "Hypoglycaemic and antihyperglycae-mic effects of Trigonella foenum-graecum leaf in normal and alloxan induced diabeticrats". Journal of Ethnopharmacology58 (1997): 149-155.

4. National bitter Melon Council.

5. Beloin N., et al. "Ethnomedicinal uses of Momordica charantia (Cucurbitaceae) in Togo and relation to its phytochemistry and biological activity". Journal of Ethnopharmacology 96 (2005): 49-55.

6. Grover JK and Yadav SP. "Pharmacological actions and potential uses of Momordica charantia". Journal of Ethnopharmacology 93 (2004): 123-132.

7. Ng TB., et al. "Proteins with abortifacient, ribosome inactivating, immunomodulatory, antitumor and anti-AIDS activities from Cucurbitaceae plants". Genetic Pharmacology 23 (1992): 579-590.

8. Scartezzini P and Speroni E. "Review on some plants of Indian traditional medicine with antioxidant activity". Journal of Eth-nopharmacology 71 (2000): 23-43.

9. Zafar R., et al. "Momordica charantia - a review". Hamdard Medicine 34 (1991): 49-61.

10. Nazimuddin S and Naqvi SS. "Flora of Pakistan No 154, Cucur-bitaceae Deptt Botany University Karachi 1984 56.

11. Duke JA. Handbook of medicinal herbs. CRC Press, Boca Raton FL (1985): 315-316.

12. Agrawal M and Kamal R. "In vitro clonal propation of Mo-mordica charantia L". Indian Journal of Biotechnology (2004): 426-430.

13. Longo D., et al. Harrison's Principles of Internal Medicine 18th ed. USA: Mcgraw-hill (2011).

14. Shaw JE., et al. "Global estimates of the prevalence of diabetes for 2010 and 2030". Diabetes Research and Clinical Practice 87 (2010): 4-14.

15. Zimmet P. "Globalization, coca-colonization and the chronic disease epidemic: can the Doomsday scenario be averted?" Journal of Internal Medicine 247 (2000): 301-10.

16. Zimmet P., et al. "Preventing Type 2 diabetes and the dysmeta-bolic syndrome in the real world: a realistic view". Diabetic Medicine 20 (2003): 693-702.

17. Yeh-Lin LU., et al. "Antioxidant activities of different wild bitter gourd (Momordica charantia L. var. abbreviata Seringe) culti-vars". Botanical Studies 53 (2012): 207-214.

18. Miura T., et al. "Hypoglycemic activity of the fruit of the Mo-mordica charantia in type 2 diabetic mice". Journal of Nutri-tional Science and Vitaminology 47 (2001): 340-344.

19. Rathi SS., et al. "The effect of Momordica charantia and Mucuna pruriens in experimental diabetes and their effect on key metabolic enzymes involved in carbohydrate metabolism". Phytotherapy Research 16 (2002): 236-243.

20. Kar A., et al. "Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan diabetic rats". Journal of Ethnopharmacology 84 (2003): 105-108.

21. Omoregbe RE., et al. "Antimicrobial activity of some medicinal plants extracts on Escherichia coli, Salmonella paratyphi and Shigella dysenteriae". African Journal of Medicine and Medical Sciences 25 (1996): 373-375.

22. Lee-Huang., et al. "MAP-30: a new inhibitor of HIV-1 infection and replication". FEBS Letter 272 (1990): 12-18.

23. Lee-Huang S., et al. "Anti-HIV and anti-tumor activities of re-combinant MAP30 from bitter melon". Gene 61 (1995): 151-156.

24. Senanayake., et al. "The effects of bitter melon (Momordi-cacharantia) on serum and liver triglyceride levels in rats". Journal of Ethnopharmacology 91 (2004): 257-262.

25. Kobori M., et al. "Bitter gourd suppresses lipopolysaccharide-induced inflammatory responses". Journal of Agricultural and Food Chemistry 56 (2008): 4004-4011.

26. Chao CY and CJ Huang. "Bitter gourd (Momordica charantia) extract activates peroxisome proliferators-activated receptors and upregulates the expression of the acyl CoA oxidase gene in H4IIEC3 gepatoma cells". Journal of Biomedical Science 10 (2003): 782-791.

27. Lii CK., et al. "Suppressive effects of wild bitter gourd (Momordica charantia Linn. var. abbreviata Ser.) fruit extracts on inflammatory responses in RAW 264.7 macrophages". Journal of Ethnopharmacology 122 (2009): 227-233.

28. Wu SJ and LT Ng. "Antioxidant and free radical scavenging ac-tivities of wild bitter melon (Momordica charantia Linn. var. abbreviata Ser.) in Taiwan". LWT-Food Science Technology 41 (2008): 323-330.

29. KE Yuwai., et al. "Chemical composition of Momordica charantia L. fruits". Journal of Agricultural and Food Chemistry 39 (1991): 1762-1763.

30. Madhu Gupta., et al. "Momordica charantia Linn. (Karela): Nature's Silent Healer". International Journal of Pharmaceutical Sciences Review and Research 11 (2011): 32-37.

31. Kumar DS., et al. "A medicinal potency of Momordica charantia". International Journal of Pharmaceutical Sciences Review and Research 1 (2010): 95-111.

32. Kirtikar KR and Basu BD. Indian medicinal plant (1987): 1130.

33. Jadhav D. Medicinal plants of Madhya Pradesh and Chhattis-garh (2008): 213-214.

34. Dhalla NS., et al. "Chemical composition of the fruit of Mo-mordica charantia Linn". Indian Journal of Pharmacology 23 (1961): 128-140.

35. Braca A., et al. "Chemical composition and antimicrobial ac-tivity of Momordica charantia seed essential oil". Fitoter 79 (2008): 123-125.

36. Agharkar SP. Medicinal plants of Bombay Presidency. Scien-tific Publishers, Jodhpur (1953): 37.

37. Garau C., et al. ‘‘Beneficial effect and mechanism of action of Momordica charantia in the treatment of diabetes mellitus a mini review’’. International Journal of Diabetes and Metabolism 11 (2003): 46-55.

38. KP Sampath Kumar., et al. ‘‘Traditional Medicines and Thera-peutic benefits of Momordica charantia Linn’’. International Journal of Pharmaceutical Sciences Review and Research 3 (2010): 23-28.

39. Virdi J., et al. ‘‘Antihyperglycemic effects of three extracts from Momordica charantia’’. Journal of Ethnopharmacology 88 (2003): 107-111.

40. PB Aswar and BS Kuchekar. ‘‘Photochemical, Microscopic, Antidiabetic, BiochemicalandHistopathological Evaluation of Momordica charantia’’. International Journal of Pharmacy and Pharmaceutical Sciences 4 (2012): 325-331.

41. Yakaiah Vangooti., et al. ‘‘Antidiabetic Effect of Momordica Charantia (Bitter Melone) On Alloxan Induced Diabetic Rabbits’’. International Journal of Medical Research and Health Sciences 2 (2013): 137-142.

42. Batran., et al. ‘‘Some toxicological studies of Momordica charantia L. on albino rats in normal and alloxan diabetic rats’’. Journal of Ethnopharmacology 108 (2006): 236-242.

43. Wehash FE., et al. ‘‘Some physiological effects of Momordica charantia and Trigonella foenum-graecum extracts in diabetic rats as compared with Cidophage® World’’. Academy of Science, Engineering and Technology 64 (2012): 1206-1214.

44. Joseph B., et al. ‘‘Antidiabetic effects of Momordica charantia (bitter melon) and its medicinal potency’’. Asian Pacific Jour-nal of Tropical Disease 3 (2013): 93-102.

45. Vijayalakshmi B., et al. ‘‘Effect of bitter gourd and spent tur-meric on glycoconjugate metabolism in streptozotocin-induced diabetic rats’’. Journal of Ethnopharmacology 11 (2003): 276-283.

46. Suresh kumar G., et al. ‘‘Modulatory effect of bitter gourd (Momordica charantia Linn.) on alterations in kidney heparin sulfate in streptozotocin-induced diabetic rats’’. Journal of Ethnopharmacology 115 (2003): 276-283.

47. Lolitkar MM., et al. ‘‘Pharmacology of a hypoglycaemic principle isolated from the fruits of Momordica charantia. Linn’’. Indian Journal of Pharmaceutical Sciences 28 (1966): 129-133.

48. Khanna P and Mohan S. ‘‘Isolation and identification of diosgenin and sterols from fruits and in vitro cultures of Momordica charantia Linn’’. Indian Journal of Experimental Biology 11 (1973): 58-60.

49. Dutta PK., et al. ‘‘Vicine a favism-inducing toxin from Momordica charantia Linn’’. Indian Journal of Chemistry 20B (1981): 669-667.

50. Barron D., et al. ‘‘Etude comparative de deux cucurbitacees a usage medicinal’’. Planta Medica 46 (1982): 184-186.

51. Wang H., et al. ‘‘Differential anti-diabetic effects and mechanism of action of charantin-rich extract of Taiwanese Momordica charantia between type 1 and type 2 diabetic mice’’. Food and Chemical Toxicology 69 (2014): 347-356.

52. Zhang L., et al. "Cucurbitane-type glycosides from the fruits of Momordica charantia and their hypoglycaemic and cytotoxic activities". Journal of Functional Foods 6 (2014): 564-574.

53. Virdia J., et al. "Antihyperglycemic effects of three extracts from Momordica charantia". Journal of Ethnopharmacology 88 (2003): 107-111.

54. Lotlikar MM and Rao MRR. "Pharmacology of a hypoglycae-mic principle isolated from the fruits of Momordica charantia Linn". Indian Journal of Pharmacology 28 (1966): 129-135.

55. Nkambo W., et al. "In vivo hypoglycemic effect of methanolic fruit extract of Momordica charantia L". African Health Sciences 13 (2013): 933-939.

56. Eman A., et al. "Hypoglycemic Effect of Momordica charantia (Karela) on Normal and Alloxan Diabetic Albino Mice". Egyptian Journal of Experimental Biology (Zool.), 5 (2009): 487-493.

57. Kaushal Parmar., et al. "Effects of bittergourd (Momordica Charantia) fruit juice on glucose tolerance and lipid profile in type-l l diabetic rats". International Journal of Drug Development and Research 3 (2011): 139-146.

58. Sonal Desai and Pratima Tatke. "Charantin: An important lead compound from Momordica charantia for the treatment of diabetes". Journal of Pharmacognosy and Phytochemistry 3 (2015): 163-166.

59. Baldwa VS., et al. "Clinical trials in patients with diabetes mellitus of an insulin-like compound obtained from plant source". Upsala Journal of Medical Sciences 82 (1977): 39-41.

60. Leatherdale BA., et al. "Improvement in glucose tolerance due to Momordica charantia (karela)". British Medical Journal (Clinical research ed.) 282 (1981): 1823-1824.

61. Welihinda J., et al. "Effect of Momordica charantia on the glucose tolerance in maturity onset diabetes". Journal of Ethno-pharmacology 17 (1986): 277-282.

62. Srivastava Y. "Antidiabetic and adaptogenic properties of Momordica charantia extract: an experimental and clinical evaluation". Phytotherapy Research 7 (1993): 285-289.

63.Yuwai, KE, Rao, KS, Kaluwin, C, et al. (1991) Chemical composition of Momordica charantia L. fruits. J Agric Food Chem 39, 1762–1763.

64.Chang, MK, Conkerton, EJ, Chapital, DC, et al. (1996) Chinese melon (Momordica charantia L.) seed: composition and potential use. J Am Oil Chem Soc 73, 263–265.Google Scholar

65.Chang, CI, Chen, CR, Liao, YW, et al. (2006) Cucurbitane-type triterpenoids from Momordica charantia. J Nat Prod 71, 1327–1330.

66.Harinantenaina, L, Tanaka, M, Takaoka, S, et al. (2006) Momordica charantia constituents and antidiabetic screening of the isolated major compounds. Chem Pharm Bull (Tokyo) 54, 1017–1021.

67.Li, QY, Chen, HB, Liu, ZM, et al. (2007) Cucurbitane triterpenoids from Momordica charantia. Magn Reson Chem 45, 451–456.

68.Tan, MJ, Ye, JM, Turner, N, et al. (2008) Antidiabetic activities of triterpenoids isolated from bitter melon associated with activation of the AMPK pathway. Chem Biol 15, 263–273.

69.Day, C, Cartwright, T, Provost, J, et al. (1990) Hypoglycaemic effect of Momordica charantia extracts. Planta Med 56, 426–429.

70.Shibib, BA, Khan, LA & Rahman, R (1993) Hypoglycaemic activity of Coccinia indica and Momordica charantia in diabetic rats: depression of the hepatic gluconeogenic enzymes glucose-6-phosphatase and fructose-1,6-bisphosphatase and elevation of both liver and red-cell shunt enzyme glucose-6-phosphate dehydrogenase. Biochem J 15, 267–270.

71.Ali, L, Khan, AK, Mamun, MI, et al. (1993) Studies on hypoglycemic effects of fruit pulp, seed, and whole plant of Momordica charantia on normal and diabetic model rats. Planta Med 59, 408–412.

72.Sarkar, S, Pranava, M & Marita, R (1996) Demonstration of the hypoglycemic action of Momordica charantia in a validated animal model of diabetes. Pharmacol Res 33, 1–4.

73.Jayasooriya, AP, Sakono, M, Yukizaki, C, et al. (2000) Effects of Momordica charantia powder on serum glucose levels and various lipid parameters in rats fed with cholesterol-free and cholesterol-enriched diets. J Ethnopharmacol 72, 331–336.

74.Leatherdale, BA, Panesar, RK, Singh, G, et al. (1981) Improvement in glucose tolerance due to Momordica charantia (karela). BMJ 282, 1823–1824.

75.Uebanso, T, Arai, H, Taketani, Y, et al. (2007) Extracts of Momordica charantia suppress postprandial hyperglycemia in rats. J Nutr Sci Vitaminol (Tokyo) 53, 482–488.

76.Chen, Q, Chan, LL & Li, ET (2003) Bitter melon (Momordica charantia) reduces adiposity, lowers serum insulin and normalizes glucose tolerance in rats fed a high fat diet. J Nutr 133, 1088–1093.

77.Chen, Q & Li, ET (2005) Reduced adiposity in bitter melon (Momordica charanita) fed rats is associated with lower tissue triglyceride and higher plasma catecholamines. Br J Nutr 93, 747–754.

78.Ojewole, JA, Adewole, SO & Olayiwola, G (2006) Hypoglycaemic and hypotensive effects of Momordica charantia Linn (Cucurbitaceae) whole-plant aqueous extract in rats. Cardiovasc J S Afr 17, 227–232.

79.Virdi, J, Sivakami, S, Shahani, S, et al. (2003) Antihyperglycemic effects of three extracts from Momordica charantia. J Ethnopharmacol 88, 107–111.

80.Miura, T, Itoh, C, Iwamoto, N, et al. (2001) Hypoglycemic activity of the fruit of the Momordica charantia in type 2 diabetic mice. J Nutr Sci Vitaminol (Tokyo) 47, 340.

81.Zheng, D, MacLean, PS, Pohnert, SC, et al. (2001) Regulation of muscle GLUT-4 transcription by AMP-activated protein kinase. J Appl Physiol 91, 1073–1083.Google Scholar

82.McCarty, MF (2004) Does bitter melon contain an activator of AMP-activated kinase? Med Hypotheses 63, 340–343.

83.Cheng, HL, Huang, HK, Chang, CI, et al. (2008) A cell-based screening identifies compounds from the stem of Momordica charantia that overcome insulin resistance and activate AMP-activated protein kinase. J Agric Food Chem 27, 6835–6843.

84.Chuang, CY, Hsu, C, Chao, CY, et al. (2006) Fractionation and identification of 9c, 11t, 13t-conjugated linolenic acid as an activator of PPARα in bitter gourd (Momordica charantia L.). J Biomed Sci 13, 763–772.

85.Huang, HL, Hong, YW, Wong, YH, et al. (2008) Bitter melon (Momordica charantia L.) inhibits adipocyte hypertrophy and down regulates lipogenic gene expression in adipose tissue of diet-induced obese rats. Br J Nutr 99, 230–239.

86.Shih, CC, Lin, CH & Lin, WL (2008) Effects of Momordica charantia on insulin resistance and visceral obesity in mice on high-fat diet. Diabetes Res Clin Pract 81, 134–143.

87.Yibchok-Anun, S, Adisakwattana, S, Yao, CY, et al. (2006) Slow acting protein extract from fruit pulp of Momordica charantia with insulin secretagogue and insulinomimetic activities. Biol Pharm Bull 29, 1126–1131.

88.Baldwa, VS, Bhandari, CM, Pangaria, A, et al. (1977) Clinical trials in patients with diabetes mellitus of an insulin-like compound obtained from plant source. Ups J Med Sci 82, 39–41.

89.Lakholia, AN (1956) The use of bitter gourd in diabetes mellitus. Antiseptic 53, 608–610.

90.Srivastava, Y, Venkatakrishna-Bhatt, H & Verma, Y (1993) Antidiabetic and adaptogenic properties of Momordica charantia extract: an experimental and clinical evaluation. Phytother Res 7, 285–289.

91.Patel, JC, Dhirawani, MK & Doshi, JC (1968) 'Karella' in the treatment of diabetes mellitus. Indian J Med Sci 22, 30–32.

92.Khanna, P, Jain, SC, Panagariya, A, et al. (1981) Hypoglycemic activity of polypeptide-p from a plant source. J Nat Prod 44, 648–655.

93.Akhtar, MS (1982) Trial of Momordica charantia Linn (Karela) powder in patients with maturity-onset diabetes. J Pak Med Assoc 32, 106–107.

94.Welihinda, J, Karunanayake, EH, Sheriff, MH, et al. (1986) Effect of Momordica charantia on the glucose in maturity onset diabetes. J Ethnopharmacol 17, 277–282.

95.Grover, JK & Gupta, SR (1990) Hypoglycemic activity of seeds of Momordica charantia. Eur J Pharmacol 183, 1026–1027.

96.Ahmad, N, Hassan, MR, Halder, H, et al. (1999) Effect of Momordica charantia (Karolla) extracts on fasting and postprandial serum glucose in NIDDM patients. Bangladesh Med Res Counc Bull 25, 11–13.

97.Yeh, GY, Eisenberg, DM, Kaptchuk, TJ, et al. (2003) Systematic review of herbs and dietary supplements for glycemic control in diabetes. Diabetes Care 26, 1277–1294.

98.John, AJ, Cherian, R, Subhash, HS, et al. (2003) Evaluation of the efficacy of bitter gourd (Momordica charantia) as an oral hypoglycemic agent – a randomized controlled clinical trial. Indian J Physiol Pharmacol 47, 363–365.

99.Tongia, A, Tongia, SK & Dave, M (2004) Phytochemical determination and extraction of Momordica charantia fruit and its hypoglycemic potentiation of oral hypoglycemic drugs in diabetes mellitus (NIDDM). Indian J Physiol Pharmacol 48, 241–244.

100.Dans, AM, Villarruz, MV, Jimeno, CA, et al. (2007) The effect of Momordica charantia capsule preparation on glycemic control in type 2 diabetes mellitus needs further studies. J Clin Epidemiol 60, 554–559.

101.jadad, AR, Moore, RA, Carroll, D, et al. (1996) Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 17, 1–12.

102Hulin, A (1988) Intoxication aigue par Momordica charantia (sorrossi). A propos de deux cas (Acute intoxication due to Momordica charantia (sorrossi). Study of two cases). Sem Hop 64, 2847–2848.

103.Raman, A (1996) Anti-diabetic properties and phytochemistry of Momordica charantia L. (Cucurbitaceace). Phytomedicine 2, 349–362.

104.Heiser, CB (1993) The Gourd Book. Norman, OK: University of Oklahoma Press.

105.Stepka, W (1974) Antifertility investigations on Momordica. Lloydia 37, 645.

106.Saksena, SK (1971) Study of antifertility activity of the leaves of Momordica Linn (Karela). Indian J Physiol Pharmacol 15, 79–80.

107.Dixit, VP, Khanna, P & Bhargava, SK (1978) Effects of Momordica charantia L. fruit extract on the testicular function of dog. Planta Med 34, 280–286.

108.Chan, WY, Tam, PP & Yeung, HW (1984) The termination of early pregnancy in the mouse by β-momorcharin. Contraception 29, 91–100.Google Scholar

109.Leung, SO, Yeung, HW & Leung, KN (1987) The immunosuppressive activities of two abortifacient proteins isolated from the seeds of bitter melon (Momordica charantia). Immunopharmacology 13, 159–171.