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A comprehensive review on *Momordica charantia* Linn (Karela)

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Abstract
Momordica charantia, belonging to the family of *Cucurbitaceae*, also named as bitter melon, balsam pear and bitter gourd. This plant is used for the treatment of various diseases from ancient days to now a day. The fruit of this plant is mainly used as vegetable and can cure small pox infection. It has also been utilized in different Asian traditional medicines for the treatment of bronchitis, cholera, anemia, ulcer, blood diseases, diarrhea, gonorrhea rheumatism, gout, colic, worms, dysentery, disease of liver and spleen, cancer and diabetes etc. The main constituents of of this plant include protein, triterpene, alkaloid, steroid, inorganic, lipid, and phenolic compounds, which are responsible for biological and pharmacological activities such as anti-diabetic, anti-cancerous and anti-tumorous, anti-microbial, anti-helmintic, antimalarial, anti-ulcerative and immunomodulatory. The present study gives pool information about the botany, phytochemical constituents and pharmacological actions of different parts of *Momordica charantia* Linn (Karela).

Keywords: *Momordica charantia*, phytochemical constituents, pharmacological properties

1. Introduction
Momordica charantia Linn. (Bengali name Karela), belonging to the family Cucurbitaceae commonly known as Bitter melon or Bitter gourd and widely distributed in Bangladesh, Malaysia, China, India and tropical Africa. The Latin name *Momordica* means "to bite". This plant contains a bitter compound called momordicinso that all parts of the plant taste very bitter and it is believed to have a stomachic effect [1]. Different parts of Karela are used for the treatment of many diseases such as bronchitis, cholera, anemia, ulcer, diarrhea, blood diseases, sexual tonic dysentery and as a cure for gonorrhea [2]. Karela contains some biologically active chemical compounds including proteins, triterpens, steroids, saponins, alkaloids, flavonoids and acids. This plant have been reported to have different therapeutic activities like anti-bacterial, anti-fungal, anti-viral, anti-parasitic, anti-fertility, hypoglycemic, antidiabetic, anti-tumorous and anti-carcinogenic properties [3-8]. Fruits are used as traditional medication to cure different diseases such as gout, rheumatism, worms, colic, liver diseases and spleen [9]. It possesses a potent hypoglycemic effect due to the presence of alkaloids and insulin like peptides and a mixture of steroidal sapogenins known as charantin [10]. The following is a comprehensive and up-to-date review about the distribution, phytochemistry, and pharmacological properties of *Momordica charantia* Linn. with an urge of further advancements in the medicinal uses of the herb worldwide.

Common Names
Bitter melon, Balsam pear, Bitter cucumber, Bitter pear, Karalla, Balsam apple, Cerasee, Carillacundeamor, Papailla, Melao de saoceatano, Bitter gourd, Sorosi, Karela, Kurela, Kor-kuey, Pava-aki, Salsamino, Sorossies, Pare, Peria, Karla, Margose, Goo-fah, Mara chean.

Scientific Classification
Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Cucurbitales
Family: Cucurbitaceae
Genus: Momordica
Species: *M.charantia*

Botanical Description
Momordica charantia is a vine in Cucurbitaceae family which mainly found in Africa, Asia and Australia. Leaves of *M. charantia* are unbranched or sometimes two branched. Vine is 5 m long and three to seven lobes separated deeply. Flowers are yellow in color. Flowers occurs in the month of June to July and fruits in the month of September to November. Fruits are oblong or spindle shaped. They are generally long, narrow and 20 to 30 cm long. Some small fruits are 6 to 10 cm long only. It is green in color but the completely ripe fruit turns orange. The skin of the fruit is breakable and nutritive. It is hollow in cross-section, with a relatively thin layer of flesh surrounding a central seed cavity filled with large flat seeds and pith. Seeds and pith appear white in unripe fruits, ripening to red; the flesh is crunchy and watery in texture [11]. Leaf of *M. charantia* has nutritious value and it is used for the development of human being. The products of this vine proved to be safe for the consumption of human [12].

Fig: Plant of *Momordica charantia*

Phytochemical constituents

A number of reported clinical studies have shown that bitter melon extract from the fruit, seeds, and leaves contain several bioactive compounds that have hypoglycemic activity in both diabetic animals and humans [13]. The main constituents that are responsible for the anti-diabetic activities are triterpene, protein, steroid, alkaloid, lipid and phenolic compounds [14]. Several glycosides have been isolated from *M. charantia* under the genera of cucurbitane- type terpenoids [15-16]. *M. charantia* fruits consists glycosides, saponins, alkaloids, reducing sugars, resins, phenolic constituents, fixed oil and free acids. *M. charantia* consists the following chemical constituents those are alkaloids, charantin, charine, cryptoxanthin, cucurbitins, cucurbitacins, cucurbitanes, cycloartenols, diosgenin, elaeostearic acids, erythrodiol, galacturonic acids, gentisic acid, goyaglycosides, goyasaponins, guanylatecyclase inhibitors, gypsogenin, hydroxytryptamines, karounidiols, lanosterol, lauric acid, linoleic acid, linolenic acid, momorcharasides, momorcharins, momordenol, momordicilin, momordicins, 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, stigmasta-diols, stigmasterol, taraxerol, trehalose, trypsin inhibitors, uracil, vacine, v-insulin, verbascoside, vicine, zeatin, zeatinriboside, zeaxanthin, zeinoxanthin Amino acids-aspartic acid, serine, glutamic acid, thscinne, alanine, g-amino butyric acid and pipecolic acid, ascorbigen, b-sitosterol-d-glucoside, citrulline, elasterol, flavochrome, lutein, lycopene, pipecolic acid. The fruit pulp has soluble pectin but no free pectic acid. Research has found that the leaves are nutritious sources of calcium, magnesium, potassium, phosphorus and iron; both the edible fruit and the leaves are great sources of the B vitamins [17].

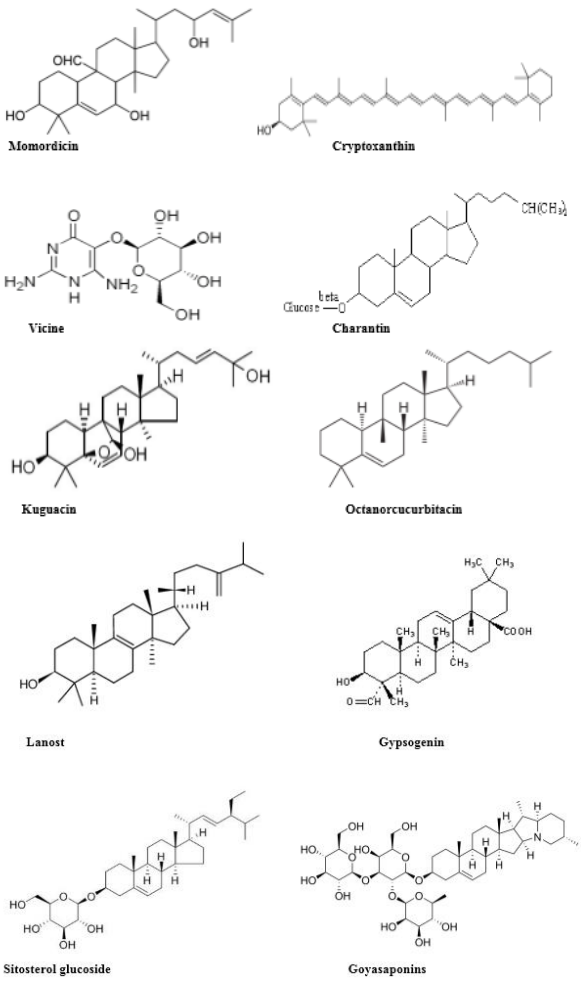

Fig 2: Structures of some phytoconstituents isolated from *M. charantia L.* [13, 18]

Pharmacological properties of *Momordica charantia*

Anti-Diabetic Activity

Xu showed that the isolation of the fruit of *Momordica charantia provide a polysaccharide which is water soluble and has antidiabetic effect when it given orally at the dose of* 300 mg/kg [19]. Wang said in his study that charantin is a chemical substituent found in *M. charantia* which has anti-hyperglycemic activity. At the dose of 200 mg/kg *M. charantia* shows antidiabetic effect after 8 days in mice when administered orally [20]. Again, another study also proved the antidiabetic effect at 300 mg/kg dose when administered orally [21]. Lo in this study just used the protein constituent of *M. charantia* at the dose of 1g/mg which showed antidiabetic effect in mice [22]. At the dose of 50 mg/kg of *Momordica charantia* decrease the blood glucose level when administered orally [23]. At 0.5unit/kg dose, polypeptide-p which is isolated

from the fruit and seed of *Momordica charantia* lowerd the blood glucose level when injected subcutaneously [24]. A constituent Charantin showed antidiabetic effect which was found in *Momordica charantia* [25] and it also increase the release of insulin and inhibit the formation of glucose [26] oral administration of 4g/kg for 2 months *Momordica charantia* fruit showed antidiabetic activity in mice [27]. Orally administered ethanol extraction of *Momordica charantia* decreases the glycemic activity in diabetic rat. Oleanolic acid and momordin of *Momordica charantia* showed antihyperglycemic effect by inhibiting glucose transport in intestine of rat. Aqueous extraction of *Momordica charantia* fruits decrease the blood glucose level in type 2 diabetic rats [28]. Aqueous extraction of this plant seed showed antidiabetic property by reducingblood glucose, glycosylated hemoglobin, lactate dehydrogenase, glucose-6-phosphatase, fructose-1, 6-bisphosphatase and glycogen phosphorylase along with increased hemoglobin, glycogen content and hexokinase, glycogen synthase activity [29], charantin, vicine and polypeptide-p from *Momordica charantia* have been proved to have antidiabetic property [30].

Cardiovascular effect

Sonal *et al.* reported that the cardiovascular effects of *Momordica charantia* has been reported due to the presence of charantin. In anesthetized cat, it was determined that 5-10% blood pressure can be declined at a dose of 800mg/kg. Additionally, at a dose of 5-10 mg/kg, the contraction was increased in an isolated heart of a frog as well as the action of acetylcholine was terminated effectively [31]. Olivier *et al*. reported the effect of charantin (a pure chemical from *Momordica charantia*) in the cardiovascular system. In addition, it also observed that at the dose of 800 mg/kg, 5-10% of blood pressure was reduced in anaesthetized cat [32]. Sheriff *et al.* indicated that *M. charantia* plant extract increased significantly ($P<0.05$) the low density lipoprotein levels in the experimental group B (100 mg/kg), and significantly reduced low density lipoprotein levels ($P<0.05$) in the experimental group A (80 mg/kg), when compared to the control group. This study showed that M. charantia plant extract has cardio-protective properties by its dose-dependent effects on blood cholesterol [33].

Antioxidant Activities

Thenmozhi *et al.* reported that at the dose of 300 mg/kg body weight the *Momordica charantia* fruit extract (MCE) exerts the antioxidant potentials as well as maintaining the cellular integrity of the liver tissue, which could offer protection against ammonium chloride (AC) (100 mg/kg body weight) induced hyperammonemia [34]. Qader *et al*., reported that the antioxidant activity of ethanol extract is higher than the aqueous extract. A strong correlation between antioxidant activity and the total phenol contents has been exhibited [35]. Aljohi *et al*., reported that though *Momordica charantia* pulp (MCP) showed the highest metal-chelating activity, the antioxidant activity of *Momordica charantia* flesh (MCF) was higher than that of *Momordica charantia* pulp (MCP). MCF had the highest phenolic and flavonoid contents, on the other hand, MCP had the highest flavonol content [36]. Rezaeizadeh *et al*., reported that the total antioxidant activity results indicated that, the inhibition percent of methanolic extract was significantly higher compare to the inhibition percent of chloroformic extract in both of the ferric thiocyanate (FTC) and thiobarbituric acid (TBA) methods. For free radical scavenging, a higher IC50 value was found for methanolic extract than chloroformic extract. Methanolic extract contained a significantly higher concentration of total phenols and flavonoids than chloroformic extract. In addition, methanolic extract contained more potent antioxidant and high polyphenol compounds than chloroformic extract [37]. Hamissou *et al*., reported that in inhibiting the free radical DPPH, bitter gourd was 82.05% as effective as ascorbic acid and average total phenolic compounds were recorded 13.28 GAE/g fresh weights. This study also found that the bitter gourd was significantly higher in antioxidant content and in β-glucosidase activities ($P<0.05$) [38].Wu *et al*., (2007) reported that the extracts of wild bitter gourd, grown in Taiwan, possessed higher antioxidant along with free radical-scavenging activities than the normal ones. Leelaprakash *et al*., reported that the in vitro antioxidant activities of methanolic extracts of leaves were more potent than aqueous extracts in both DPPH and ABTS methods [39]. Horax *et al*., reported the antioxidant activity of extracted phenolic compound from bitter melon in Total Phenolic contents and phenolic acid constituents in four varieties of bitter melons (*Momordica charantia*) and antioxidant activities of their extracts [40]. Antioxidant properties of *Momordica charantia* (Karela) Seeds, on Streptozotocin induced-diabetic rats, has been studied and results clearly suggest that seeds of *Momordica charantia*(Karela) may effectively regularize the impaired antioxidant status in streptozotocin induced-diabetes. Sathishsekar *et al*., reported that the antioxidant properties of *Momordica charantia* (bitter gourd) seeds, on Streptozotocin induced diabetic rats [41].

Antiobesity Activity

Obesity or excessive body fat is a major risk factor for developing type-2 diabetes. Therefore, many overweight diabetics can improve their blood glucose levels by losing weight through proper nutrition and regular exercise [42]. Another way for diabetics to lose weight is by using herbal supplements such as bitter melon. Researchers have discovered that the bioactive compounds in bitter melon have hypolipidemic actions that can lower serum and liver cholesterol, which improves glucose tolerance [43].

Hypolipidemic Activity

Traditionally *Momordica charantia* has been used as a treatment for diabetic patient. *Momordica charantia* has antidiabetic and hypolipidemic activity due to its various phytochemical constituents. *Momordica charantia* has insulin receptor binding protein (mcIRBP) which turns into mcIRBP-9 after digesion of the protein. McIRBP-9 is a unique gastro-resistant bioactive peptide which has hypolipidemic property. So, a study by Lodemonstrated that oral administration of *Momordica charantia* decrease 23.62 ± 6.14% fasting blood glucose level and 24.06 ± 1.53% glycated hemoglobin (HbA1c) level [44]. Another study proved that oral administration of 200mg/kg fruits of *Momordica charantia* with methanol extract decrease 35.6% of the level of blood

glucose and 400mg/kg reduce 38.8% blood glucose level in mice [45]. Further, ethanolic extraction of 200 mg of *Momordica charantia reduces the level of cholesterol and triglyceride (P < 0.05) in mice when given orally with fat and regular food* [46]. *Furthermore, orally administered aqueous extraction of Momordica charantia for 30 days showed hypolipidemic activity and increase the insulin conc. (*14.4 ± 0.05 mU/mL to 23.7 ± 1.2 mU/mL) [47]. Again, a study by Al-Bahrani proved the hypolipidemic activity of mice in serum when given orally at the dose of 0.30mg/ml with aqueous extraction. This study did not showed any effect of serum glucose level with methanol extraction of *Momordica charantia* [48]. Constituents of *Momordica charantia decrease liver secretion of Low density lipoprotein and very low density lipoprotein which are known as bad cholesterol but increase high density lipoprotein which is called good cholesterol.* Several in vivo studies showed the hypolipidemica ctivity of *Momordica charantia* fruits and seeds. Friuts and seeds have been proved to reduce the cholesterol and triglyceride level [49-50].

Anticancer and Antitumor activity

A study by Ali proved that the methanol extract of 40mg/kg of *Momordica charantia* showed anticancer effect in mice after injecting them with 200mg/kg Diethylnitrosamine [51]. Again Gu demonstrated that MCP30 protein of *Momordica charantia* decreased the cell proliferation and the S-phase of cell cycle and prevent Endometrial carcinoma [52]. MAP30 protein from the plant *M. charantia* exhibited antitumor property against various tumors. Qian in his study, extract MAP30 protein from *M. charantia* and proved that this protein have the ability to inhibit acute myeloid leukemia. Zhang proved the anticancer activity of *Momordica charantia* by using colony formation, animal model etc.and their data suggested that *M. charantia* has chemotherapeutic activity [53]. Further an in vivo study conducted by Kabir which showed the positive result. *Momordica charantia* showed anticancer property when it was given at the dose of 1.2, 2.0, and 2.8 mg/kg/day *intraperitoneally* [54]. Furthermore Ray proved that *Momordica charantia can suppress the proliferation of cell in breast cancer of human cancer cell.* The phytochemical momordin has clinically demonstrated cytotoxic activity against Hodgkin's lymphoma in vivo, and several other in vivo studies have demonstrated the cytostatic and antitumor activity of the entire plant of bitter melon. Further studies reported that, a water extract blocked the growth of rat prostate carcinoma and a hot water extract of the entire plant inhibited the development of mammary tumors in mice. Numerous in vitro studies have also demonstrated the anti-cancerous and anti-leukemic activity of bitter melon against numerous cell lines including liver cancer, human leukemia, melanoma and solid sarcomas [55].

Anti-sialogogue activity

Charantin at dose of 10-15 mg/kg delayed the onset of tremors but did not affect salivation produced by tremorine [56].

Antifertility

The fruit and leaf of bitter melon has demonstrated an in vivo antifertility effect in both male and animals. It reduced the production of sperm. Bitter melon is contraindicated during pregnancy and traditionally has been used as an abortive. It also has been documented to have weak uterine stimulant activity. Different extracts (ether, benzene and alcohol) of M. charantia seeds reduced the availability of pituitary gonadotrophs necessary for spermatogenesis [57]. Aqueous extract of *Momordica charantia* significantly decrease plasma levels of estrogen and progesterone of the female Wistar rats [58]. Extract of *Momordica charantia* decreases the mean testicular volume and weight, seminiferous tubular diameter and cross sectional area of tubules [59].

Antimicrobial activity

Ethanol extraction of the fruit and seed of *Momordica charantia showed antimicrobial activity against P. aeruginosa, E. coli, Staphylococcus aureus, Salmonella typhi, Aspergillus niger* and *C. albicans* in disc diffusion method. Oil and seed showed this activity for *A. niger* and, *E. coli* [60]. The leaves also have antimicrobial property specially for *E. coli.* Ethyl acetate extraction of the leaves were showed their effect against *E. coli (MIC:* 128 µg/mL) *and B. cereus* [61]. At the dose of 100mg/ml, the methanol extraction of plant extract showed antimicrobial property against *E. coli* (ZOI=6mm) [62]. β- sitosterol of *Momordica charantia showed antimicrobial effect in agar disk diffusion method and Zone of inhibition was 10 to 14 mm for E. coli, P. aeruginosa, S. aureus and K. pneumonia* [63]. At100 mg/ml dose, Aqueous and ethanol extraction of *Momordica charantia inhibited the bacterial growth against S. aureus, B. subtilis, E. coli,* and *P. aeruginosa. For ethanol extraction ZOI was* 17 to 14 mm and MIC value was 6.5 to 12.5 mg/ml. Again, for aqueous extraction ZOI was 15 to 11 mm and MIC value was 50 to 100 mg/ml [64]. Plumericin is a constituent of Momordica charantia plant showed antimicrobial activity against Enterococcus faecalis and Bacillus subtilis [65]. Various water, ethanol, and methanol extracts of the leaves have demonstrated in vitro antibacterial activities against E. coli, Staphylococcus, Pseudomonas,Salmonella, Streptobacillus and Streptococcus; an extract of the entire plant was shown to have antiprotozoal activity against Entamoebahistolytica. The fruit and fruit juice has demonstrated the same type of antibacterial properties and, in another study, a fruit extract has demonstrated activity against the stomach ulcer-causing bacteria Helicobacter pylori. Long-term use of this plant may result in the die-off of friendly bacteria with resulting yeast/candida opportunistic overgrowth [66].

Antifungal activity

Again, seed extract of *M. charantia* showed activity against *Fusarium solani* (MIC=108.934 µg/ml) [67]. Ethanol extraction of M. charantia leaves showed antifungal activity against Candida tropicalis, and Candida krusei ((MIC ≤ 1024 µg/mL) [68]. Ethanolic extract of fruit and seed of *Momordica charantia* showed moderate activity against *A.alternata* (41.17%) and *F. oxysporum* (35.7%). Leaves of this plant also showed antifungal activity [69-71]. Wang in his study isolated the antifungal ribosome inactivating protein from *Momordica charantia* which showed its effect against *Fusarium oxysporum* and *Pythium aphanidermatum* [72].

Anti HIV Agents

Laboratory tests suggest that compounds in bitter melon might be effective for treating HIV infection. The proteins (alpha and beta momorcharin) appeared to modulate the activity of both T and B lymphocytes and significantly suppressed the macrophage activity [73].

Antimalarial and Larvicidal activity:

Orally administered methanol extraction of *M. charantia at the dose of* 200 mg/kg showed antimalarial activity in animal test [74]. Again, Adeyi showed this activity in mice at the dose of 100 mg/kg with methanol extract which also showed effective result against P. berghei-induced malaria infection [75]. Chloroform extraction of *M. charantia fruit coat showed this effect against* P. falcipuram malaria parasite (IC50=1.83 ± 0.029 µg/ml [76]. Ethanol extract of 500 mg/Kg M. charantia leaves showed an effective result against malarious mice when administered orally [77]. Again in vivo study of this plant extract also showed effective activity *P. vinckeipetteri* and in vitro study showed effect on *Plasmodim falciparum* [78]. M. charantia has shown good larvicidal activity against three container breeding mosquitoes— *An. stephensi, Cx. quinquefasciatus and Ae.aegyptin* [79].

Analgesic and antipyretic activity

Ethanol extraction of 250 and 500 mg/kg of Momordica charantia fruits showed analgesic and antipyretic activity due to its presence of various constituent [80].

Anti-Genotoxic Activity

Momordica charantia decreased the genotoxic activity of methylnitrosamine, methanesulfonate and tetracycline, as shown by the decrease in chromosome breakage [81].

Anthelminthic activity

Ethanol (95%) extract of fruits of *Momordica charantia* (Karela), was found active on *Ascaridia galli*, whereas, hot water extract of seed at concentration of 1:50 was active on *Haemonchus contortus* [82]. *Momordica charantia* (Karela) is utilized in the treatment of *Ascaridia galli* [83].

Wound Healing Activity

Fruit powder of Momordica charantia Linn., in the form of an ointment (10% w/w dried powder in simple ointment base), showed a statically significant response ($P < 0.01$), in terms of wound contracting ability, wound closure time, period of epithelization, tensile strength of the wound and regeneration of tissues at wound site in an excision, incision and dead space wound model in rats [84]. *Momordica charantia* extract showed a significant reduction in wound area and period of epithelization [85]. At the dose of 100 mg/kg, olive oil macerate of *Momordica charantia* showed significant wound healing activity both in incision (45.1%) and excision (89.8%) wound models [86].

Conclusion

Though the relatively low toxicity of all parts of the *Momordica charantia* Linn. (Karela) have been demonstrated in vivo clinical studies, it is a potential herbal plant which is used as vegetable and medicine. It is a good source of various medicinally important biochemical like, protein, steroid, triterpene, alkaloid, and phenolic which possesses different biological and pharmacological activities including antioxidant, anti-diabetic, anti-cancerous and anti-tumorous, anti-fertility, antimicrobial, anti-viral, antimalarial, anti-helmintic, anti-ulcerative and immunomodulatory etc. *Momordica charantia* Linn. (Karela) can be utilized as a good source of nutritional, medicinal and pesticidal agent on the basis of all these properties.

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