

A REVIEW ON PHYTOCHEMICAL AND PHARMACOLOGICAL PROPERTIES OF *MOMORDICA CHARANTIA* LINN.

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Summary

Pharmacognosy is one of the oldest scientific disciplines is now has undergone major changes. Currently plant based drugs are researched and formulated in modern framework in new ways of medicine. many of the thousands of plant species growing throughout the world have medicinal uses, containing active constituents that have a direct pharmacological action on the body. Karela (*Momordica charantia*) is being medicinally used since antiquity and was a part of therapeutic regimen for a variety of maladies. The main objective of this review is to highlight the origin, morphology, cultivation, phytochemistry, and pharmacological aspects of Karela (*Momordica charantia*).

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Introduction

Momordica charantia is a tropical and subtropical vine of the family *Cucurbitaceae*, widely grown for edible fruit, which is among the most bitter of all vegetables. English names for the plant and its fruit include bitter melon or bitter gourd (pinyin: kǔguā), in hehe it is generally known as cerasee, in Indonesia, it is known as pare. The original home of the species is not known, other than that it is a native of the tropics. It is widely grown in South and Southeast Asia, China, Africa, and the Caribbean (25).

Vernacular names:

According to country:-Bitter gourd,Bitter melon,Bitter cucumber (English),Karela, Balsamina(India), Karavila(Chinese),Futoreishi(Japanese),Prriya(Malaysia).

According to language:- English:- bitter gourd,Hindi:- karela,Sanskrit:- karvellak,Gujrati:- kareli(2).

Taxonomy:

Kingdom: *Plantae*
Division: *Magnoliophyta*
Class: *Magnoliosida*
Order: *Viales*
Family: *Cucurbitaceae*
Genus: *Momordica*
Species: *Charantia(2)*

Morphology:

Herbaceous, slender climber with slightly pubescent stems and leaves; petiole = blade; leaves to 10-12 cm long, palmately 5-7-lobed; the lobes " sinuate-dentate; flowers yellow; peduncle with a reniform bracteole; corolla 1.5-2 cm long; fruit obovoid or oblong-cylindric, coarsely ridged and bumpy-tuberculate, to 20 cm, orange or dark yellow when ripe, splitting open to reveal the seeds, these black but covered with a soft, fleshy red aril, 12-16 mm long. Seeds and pith appear white in unripe fruits, ripening to red. The bitter melon more typical of India has a narrower shape with pointed ends, and a surface covered with jagged, triangular "teeth" and ridges. Coloration is green or white. Some bear miniature fruit of only 6 - 10 cm in length. It is an annual creeper. Leaves 1-3 inch in width and are parted in 5-7 parts. Flowers yellow in color and monoceous. Fruits 2-10 inch long having green color and barrel shape having thick middle part and sharp at the edges .

Origin and distribution:

Originally found only in the tropics of old world, it has been spread by man throughout all the tropical regions of the world and is commonly found on fences and shrubs and in hedgerows (1). It is widely found in India, South Africa, Srilanka and Mediterranean countries. Bitter melon grows in tropical areas, including parts of the

Amazon, east Africa, Asia, and the Caribbean, and is cultivated throughout South America as a food and medicine.

Photo of *Momordica charantia* :(29)



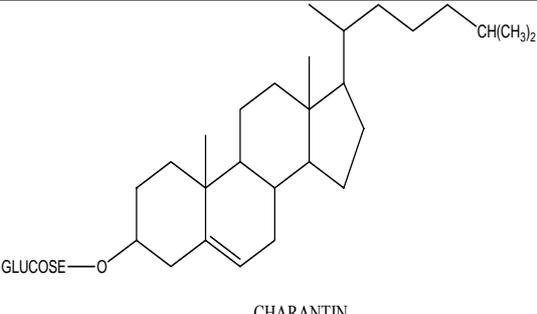
Phytochemistry (24)

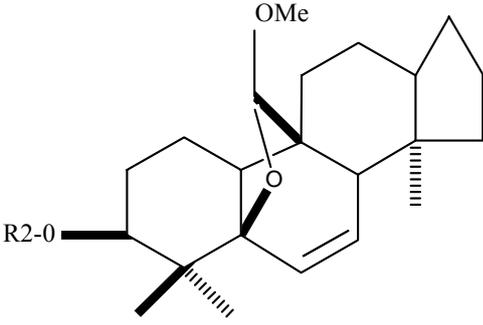
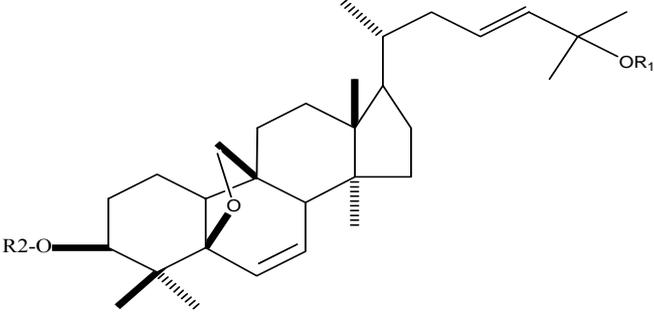
Bitter melon contains an array of biologically active plant chemicals including triterpenes, proteins, and steroids. One chemical has clinically demonstrated the ability to inhibit the enzyme guanylate cyclase that is thought to be linked to the cause of psoriasis and also necessary for the growth of leukemia and cancer cells. In addition, a protein found in bitter melon, momordin, has clinically demonstrated anticancerous activity against Hodgkin's lymphoma in animals. Other proteins in the plant, alpha- and beta-momorcharin and cucurbitacin B, have been tested for possible anticancerous effects. A chemical analog of these bitter melon proteins has been developed, patented, and named "MAP-30"; its developers reported that it was able to inhibit prostate tumor growth. Two of these proteins-alpha- and beta-momorcharin-have also been reported to inhibit HIV virus in test tube studies. In one study, HIV-infected cells treated with alpha- and beta-momorcharin showed a nearly complete loss of viral antigen while healthy cells were largely unaffected. The inventor of MAP-30 filed another patent which stated it was "useful for treating tumors and HIV infections. Another clinical study showed that MAP-30's antiviral activity was also relative to the herpes virus in vitro.

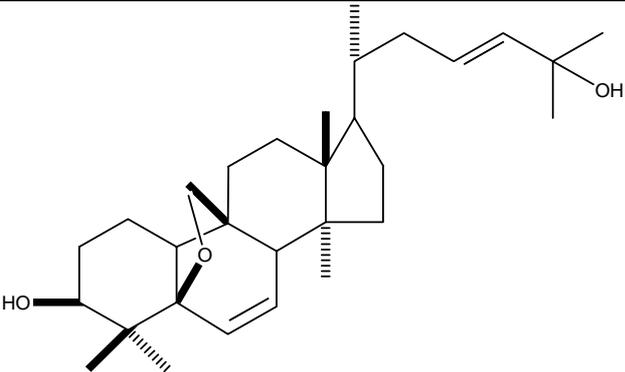
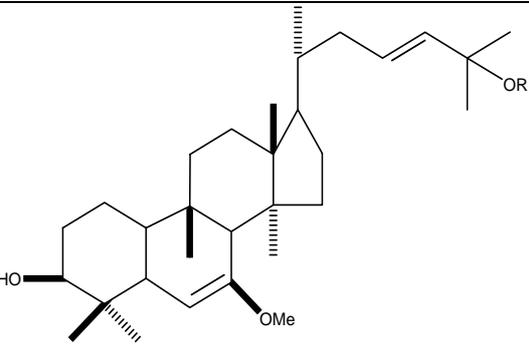
In numerous studies, at least three different groups of constituents found in all parts of bitter melon have clinically demonstrated hypoglycemic (blood sugar lowering) properties or other actions of potential benefit against diabetes mellitus. These chemicals that lower blood sugar include a mixture of steroidal saponins known as charantins, insulin-like peptides, and alkaloids. The hypoglycemic effect is more pronounced in the fruit of bitter melon where these chemicals are found in

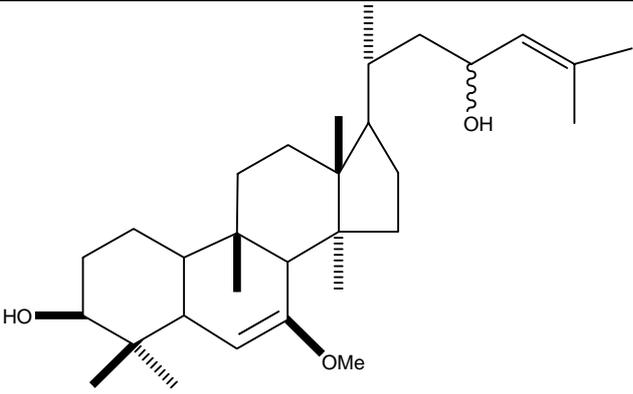
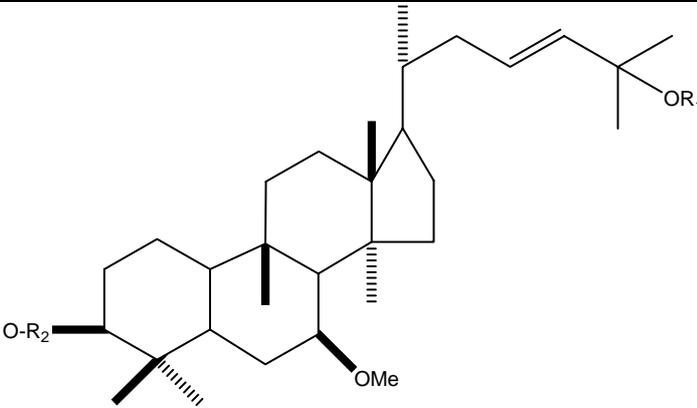
greater abundance. Alkaloids, charantin, charine, cryptoxanthin, cucurbitins, cucurbitacins, cucurbitanes, cycloartenols, diosgenin, elaeostearic acids, erythrodiol, galacturonic acids, gentisic acid, goyaglycosides, goyasaponins, guanylate cyclase inhibitors, gypsogenin, hydroxytryptamines, karounidiols, lanosterol, lauric acid, linoleic acid, linolenic acid, momorcharasides, momorcharins, momordenol, momordicilin, momordicins, momordicinin, momordicosides, momordin, 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-insulin, verbascoside, vicine, zeatin, zeatin riboside, zeaxanthin, and zeinoxanthin are all found in bitter melon. Three new cucurbitane-type triterpene called karavilagenins A, B, and C and five new cucurbitane-type triterpene glycosides called karavilosides I, II, III, IV, and V were isolated from the dried fruit of Sri Lanka *Momordica charantia* L. (Cucurbitaceae) together with two known cucurbitane-type triterpenes, 19(R)-methoxy-5 β ,19-epoxycucurbita-6,23-dien-3 β ,25-diol and 5,19-epoxycucurbita-6,23-diene-3,25-diol, and nine known cucurbitane-type triterpene glycosides, goyaglycosides-b, -c, and -d, and momordicosides F1, F2, G, I, K, and L. The structures of karavilagenins and karavilosides were elucidated on the basis of chemical and physicochemical evidence.

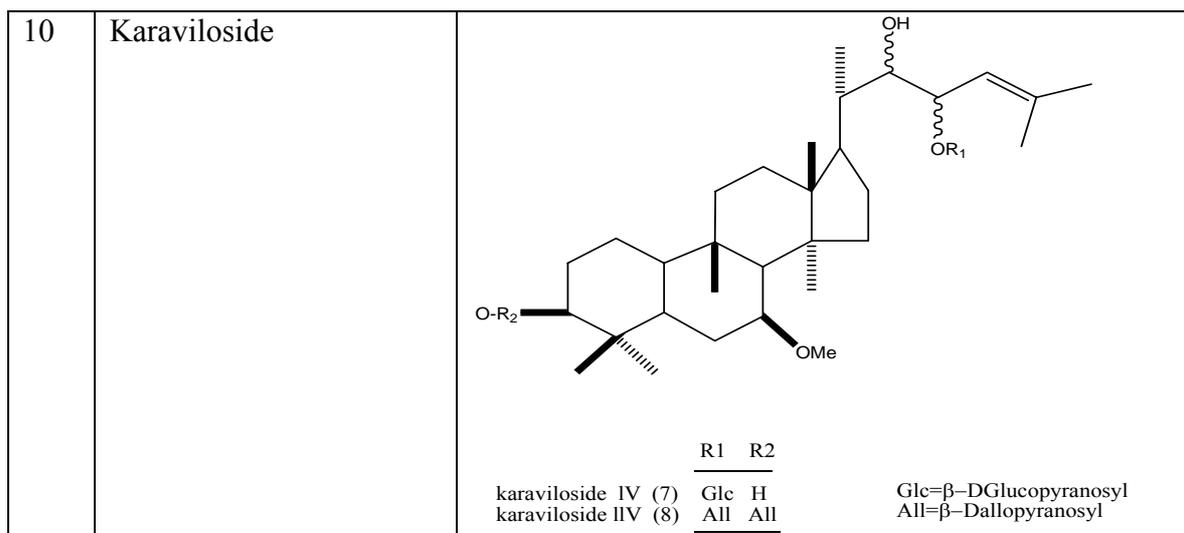
Structures

Sr no.	Name	Structure
1	Charatine	 <p style="text-align: center;">CHARANTIN</p>

2	Goyaglycoside	 <p>The structure shows a complex polycyclic skeleton with a central oxygen atom in a ring. Substituents include a methoxy group (OMe), a methyl group (R2-O), and a methyl group (R1). A double bond is present in one of the rings.</p> <table border="1" data-bbox="767 611 1110 757"> <thead> <tr> <th></th> <th>R1</th> <th>R2</th> </tr> </thead> <tbody> <tr> <td>goyaglycoside-b (11):</td> <td>H</td> <td>All</td> </tr> <tr> <td>goyaglycoside-c (12):</td> <td>Me</td> <td>Glc</td> </tr> <tr> <td>goyaglycoside-d (13):</td> <td>Me</td> <td>All</td> </tr> </tbody> </table>		R1	R2	goyaglycoside-b (11):	H	All	goyaglycoside-c (12):	Me	Glc	goyaglycoside-d (13):	Me	All			
	R1	R2															
goyaglycoside-b (11):	H	All															
goyaglycoside-c (12):	Me	Glc															
goyaglycoside-d (13):	Me	All															
3	Mormodicoside	 <p>The structure is similar to the Goyaglycoside skeleton but includes a long side chain with a double bond and a methyl group, and a substituent labeled OR1.</p> <table border="1" data-bbox="722 1149 1059 1279"> <thead> <tr> <th></th> <th>R1</th> <th>R2</th> </tr> </thead> <tbody> <tr> <td>momordicoside F1 (14)</td> <td>Me</td> <td>Glc</td> </tr> <tr> <td>momordicoside F2 (15)</td> <td>H</td> <td>All</td> </tr> <tr> <td>momordicoside G (16)</td> <td>Me</td> <td>All</td> </tr> <tr> <td>momordicoside I (17)</td> <td>H</td> <td>Glc</td> </tr> </tbody> </table>		R1	R2	momordicoside F1 (14)	Me	Glc	momordicoside F2 (15)	H	All	momordicoside G (16)	Me	All	momordicoside I (17)	H	Glc
	R1	R2															
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momordicoside I (17)	H	Glc															

<p>6</p>	<p>5β,19-epoxycucurbita-6,23-diene-3β,25-diol</p>	 <p>5β,19-epoxycucurbita-6,23-diene-3β,25-diol</p>
<p>7</p>	<p>Karavilagenin</p>	 <p> $\frac{R}{\text{---}}$ karavilagenin A (1): Me karavilagenin B (2): H </p>

<p>8</p>	<p>Karavilagenin</p>	 <p>karavilagenin C (3)</p>
<p>9</p>	<p>Karaviloside</p>	 <p>R1 R2</p> <p>karaviloside I (4): Me Glc karaviloside II (5): Me All karaviloside III (6): H All</p>



General uses:

Other effects of bitter melon include dose-related analgesic activity in rats and mice, (11) anti-inflammatory actions,(7) and treatment for GI ailments, such as gas, ulcer, digestion, constipation, dysentery, (10) , (4) or hemorrhoids. (12) The plant has also been used for skin diseases (eg, boils, burns, infections, scabies, psoriasis),(4) and for its lipid effects (7) and hypotensive actions. (4) , (7) Bitter melon has also been used as an insecticide. (3) , (4) It exhibits genotoxic effects in *Aspergillus nidulans* . (22)

Dose:

Decoction: 1 cup 1-2 times daily

Tincture: 1-3 ml twice daily

Capsules: 1 g twice daily

Pharmacological actions and Pharmacology of *Momordica charantia*:

Antioxidant activity:

The n-hexane extract of seeds of momordica has been reported to contain conjugated octadecatrienoic fatty acids and α-eleostearic acid. These acids have been studied for their anti-oxidant activities and are proven to be successful in an in vitro study. Thus

it may help to reduce the risk of coronary heart diseases in non-diabetic as well as diabetic patients.(26)

Anti-tumor activity:

The in vivo antitumor activity of a crude extract from the bittermelon (*Momordica charantia*) was determined. The extract inhibited tumor formation in CBA/H mice which had been given i.p. injections of 1.0×10^5 CBA/DI tumor cells (77% of the untreated mice with tumors versus 33% of the treated mice with tumors after 6 weeks). The extract also inhibited tumor formation in DBA/2 mice which had been given i.p. injections of either 1×10^5 P388 tumor cells (0% of untreated mice survived after 30 days versus 40% survival of the treated mice) or 1×10^5 L1210 tumor cells (0% survival of untreated mice versus 100% of treated mice after 30 days). The in vivo antitumor effect required both the prior exposure of tumor cells to the extract (2 hr) in vitro and i.p., biweekly injections of the extract into the mice. The optimum dose for tumor inhibition (8 μ g protein, biweekly, i.p.) was not toxic to mice for at least 45 days of treatment. This same treatment caused a marked enhancement of C3H mouse thymic cell response to concanavalin A in vitro. When compared to the untreated control mice, the bitter-melon-injected animals exhibited a 4-fold-higher incorporation of tritiated thymidine into trichloroacetic acid-precipitable material after 48 hr of exposure to 50 μ g of concanavalin A. Nylon wool-purified spleen cells from these same bittermelon-treated mice exhibited an enhanced mixed lymphocyte reaction when exposed to irradiated P388 stimulator cells (186% of the untreated control mice). These data indicate that in vivo enhancement of immune functions may contribute to the antitumor effects of the bitter melon extract.(27)

Antibacterial activity :

Bacillus subtilis, *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* are inhibited by the extract of chloroform and ethanol (95%) of dried fruit at concentration of 250.0 mg/ml on agar plate. *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa* are also inhibited by the extract of water at the concentration of 250.0 mg/ml on agar plate. But this extract can not produce inhibitory action on the *Staphylococcus aureus*. At the concentration of 250.0 mg/ml the extract of petroleum ether does not inhibit the *Staphylococcus aureus* and *Escherichia coli* but it can inhibit *Bacillus subtilis* and *Pseudomonas aeruginosa*. *Sarcina lutea* inhibited by dried fruit on agar plate. Chloroform, ether, water and methanol extracts of dried fruit on agar plate inhibit *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhosa*, *Sarcina lutea*, *Shigella dysenteriae* and it strongly inhibits *Staphylococcus aureus* MIC < 50.0 mg/Disk. *Bacillus subtilis* is strongly inhibited by water and methanol extract, MIC < 50.0 mg/Disk. Ethanol

(95%) and hot water extracts of dried bark on agar plate shows the inhibition of *Staphylococcus aureus* and *Escherichia coli*. Ethanol (95%) extract of dried leaves undiluted on agar plate can't inhibit *Staphylococcus aureus* and *Escherichia coli* but hot water extract can inhibit them. At the concentration of 2.0 mg/ml

The menthol extract of dried leaves on agar plate inhibit the growth of *Corynebacterium diphtheriae*, *Neisseria species*, *Pseudomonas aeruginosa*, *Salmonella species*, *Streptobacillus species*, *Staphylococcus species* but does not inhibit *Staphylococcus aureus*. *Sarcina lutea* inhibited by menthol extract of dried entire plant at the concentration of 15.0 mg/ml on agar plate. *Bacillus subtilis*, *Escherichia coli*, *Proteus species*, *Pseudomonas aeruginosa* and *Staphylococcus albus* are not inhibited and *Staphylococcus aureus* is inhibited by menthol/water (1:1) extracts of leaves in broth culture. Unsaponifiable fraction of seed oil agar plate was inhibit several Gram negative organism(1).

Antimicrobial activity:

Roots and leaf extracts of bitter melon have shown antibiotic activity(3)(4). One study reports cytostatic activity from bitter melon aqueous extract(5), as constituents momorcharins have antitumor properties and can inhibit protein synthesis(6). Similarly, the plant also inhibits replication of viruses, including polio, herpes simplex type 1, and HIV (3)(7). A study on antipseudomonal activity reports bitter melon to be effective, but not promising, in overall results (8). Antiviral and other effects of bitter melon have been reviewed (3). Research reveals no animal or clinical data regarding bitter melon as an antimicrobial agent.

Antifertility action:

A protein in bitter melon was reported to have antifertility activity in male rats (9). Oral administration of the fruit (1.7 g/day extract) to male dogs caused testicular lesions and atrophy of spermatogenic aspects. In female mice, the plant exhibited similar, but reversible, antifertility effects (7). Momorcharins are capable of producing abortions (6). Uterine bleeding has been induced in pregnant rats given the juice, as well as in rabbits, but not in nonpregnant females (7). The ripe fruit has been said to induce menstruation (10). Other effects of bitter melon include dose-related analgesic activity in rats and mice, anti-inflammatory actions(7), and treatment for GI ailments, such as gas, ulcer, digestion, constipation, dysentery(10)(4), or hemorrhoids. The plant has also been used for skin diseases (eg, boils, burns, infections, scabies, psoriasis), and for its lipid effects and hypotensive actions. Bitter melon has also been used as an insecticide. It exhibits genotoxic effects in *Aspergillus nidulans*.

Inhibition of protein:

A haemagglutinating lectin purified from the seeds of *Momordica charantia* by affinity chromatography on Sepharose 4B and on acid-treated Sepharose 6B. It has mol.wt. 115 000 and consists of four subunits, of mol.wts. 30 500, 29000, 28 500 and 27 000. The lectin inhibits protein synthesis by a rabbit reticulocyte lysate with an ID50 (concentration giving 50% inhibition) of approx. 5,ug/ml. Protein synthesis by Yoshida ascites cells is partially inhibited by the lectin at a concentration of 100,ug/ml. From the same seeds another protein was purified which has mol.wt. 23 000 and is a very potent inhibitor of protein synthesis in the lysate system, with an ID50 of 1.8ng/ml. This inhibitor has no effect on protein synthesis by Yoshida cells, and has no haemagglutinating properties. . *Artemia salina* ribosomes preincubated with the lectin or with the inhibitor lose their capacity to perform protein synthesis. The proteins seem to act catalytically, since they inactivate a molar excess of ribosomes. . The lectin and the inhibitor are somewhat toxic to mice, the LD50 being 316 and 340,ug/100g body wt. respectively(13).

Hypoglycemic activity:

Momordica Charantia (bitter gourd) is one of the many plants considered to have a hypoglycemic effect and many diabetic subjects consume it because of its hypoglycemic effect (14). Studies done in animal model, mainly streptozotocin induced diabetic rats and mice have shown significant lowering of blood glucose levels (15)(16). In some clinical trials *Momordica charantia* is shown to have a beneficial effects in diabetic subjects (17) (18).

Glucose tolerance :

The effect of karela (*Momordica charantia*), a fruit indigenous to South America and Asia, on glucose and insulin concentrations was studied in nine non-insulindependent diabetics and six non-diabetic laboratory rats. A water-soluble extract of the fruits significantly reduced blood glucose concentrations during a 50 g oral glucose tolerance test in the diabetics and after force-feeding in the rats. Fried karela fruits consumed as a daily supplement to the diet produced a small but significant improvement in glucose tolerance. Improvement in glucose tolerance was not associated with an increase in serum insulin responses. These results show that karela improves glucose tolerance in diabetes. Doctors supervising Asian diabetics should be aware of the fruit's hypoglycaemic properties.(23)

Insecticide activity:

At the concentration of 1.0 ppm extract of petroleum ether shows the insecticidal activity. Water extract of dried leaves does not show insecticidal activity in case of *Oncopeltus fasciatus* and, but in the case of *Blatella germanica* and *Periplaneta americana* it shows the strong activity (1).

DNA synthesis inhibition:

At the concentration of 0.1mg/ml hot water extract of entire plant shows the DNA synthesis inhibition on sea urchin ova. Chromatographic fraction of dried fruit in cell culture was actively show DNA synthesis inhibition on BKH-21 cells and Vesicular stomatitis virus. Ethanol (100%) extract of seed

In cell culture was actively show DNA synthesis inhibition on Sarcoma 180(solid)(1).

CNS depressant activity:

Extract of ethanol of fresh fruit administered intraperitoneally to mice of both sexes at variable doses and then CNS depressant activity was observed(1).

Cytotoxic activity:

In the cell culture dried fruit extract shows the cytotoxic activity on CA-755 and Leuk-CML (Human). At the concentration of 0.14mg/ml fresh fruit juice in cell culture shows the cytotoxic activity on Melanoma-B cell-M9. Viable cells decreased from 100% to 5% between 18 and 26 hours. The juice was also shows the cytotoxic activity on human lymphocytes and leukemic lymphocytes. At the concentration of 0.4mg/ml hot water extract of entire plant shows the cytotoxic activity on HEP2 cells. Water extract of dried fruit in cell culture shows this activity on CBA/D1 cells. The activity was highly dose dependent. In cell culture water extract of fresh fruit was actively show this activity on human lymphoblast and lymphocytes(1).

Antihyperglycemic activity:

At the dose of 250.0mg/kg acetone extract of dried fruit in ration of rats shows the antihyperglycemic activity. Fall in sugar of 49% in 30 days. Blood sugar in maintained within normal limits for two weeks after treatment ceased vs alloxan induced hyperglycemia. At the dose of 1.0mg/kg of benzene extract of dried fruit administered intragastrically to rabbits it shows the antihyperglycemic activity. Alloxan recovered rabbits were tested for glucose tolerance following sample treatment vs glucose induced hyperglycemia. Decoction of dried fruit taken orally by the human adult at dose of 500.0mg/person it was show the antihyperglycemic activity. Ethanol (95%) extract of dried fruit administered intragastrically to female rats at the dose of 250.0mg/kg was show the antihyperglycemic activity vs streptozotocin induced hyperglycemia. Dried powder fruit, taken orally once daily

for 11 days by ten male patients with mild diabetes (23-28 years of age), at a dose of 2.0gm/person was shows the antihyperglycemic activity(1).

Hepatotoxic Activity:

Infusion of dried entire plant taken orally by human children at variable dosage levels was equivocal. May be associated with the development of veno-occlusive disease of the liver in Jamaican children(1).

Adverse reaction:

Bitter melon's hepatotoxic effects have been demonstrated in animals, in which enzymes became elevated following plant administration. The momorcharin constituents may induce morphological changes in hepatocytes as well. (7) Because of the plant's ability to reduce blood sugar, caution is warranted in patients who may experience hypoglycemia. (10) Two small children experienced hypoglycemic coma resulting from intake of a tea made from the plant. Bitter melon extract is said to be nontoxic. (3)The plant is relatively safe at low doses and for a duration of 4 weeks or less. (10)There are no published reports of serious effects in adults given the usual oral dose of 50 mL. In general, bitter melon has low clinical toxicity, with some possible adverse GI effects. (7)

The seed constituent, vicine may induce “favism,” an acute condition characterized by headache, fever, abdominal pain, and coma. (3) , (7)

Drug interaction:

Both recovered upon medical treatment. (7) Increased hypoglycemic effect was noted in a 40-year-old woman taking *M. charantia* (a curry ingredient) and chlorpropamide. (21)

Standardisation

Charantin is one of the phytoconstituent present in *Momordica charantia* Linn. *M. charantia* is known for its hypoglycemic activity from ancient times. Standard charantin showed single peak in HPTLC chromatogram. The calibration curve of charantin was obtained by spotting standard charantin on HPTLC plate. After development the plate was scanned at 536 nm . The calibration curve was prepared

by plotting the concentration of charantin versus average area of the peak . PHFs were analysed by the proposed method. We found little less amount of charantin in Diabecone and Mersina. It may be due to varied factors like time of collections, age of the plant, processing conditions, incorrect identification of the plant, improper selection of the herb variety, addition of exhausted material and genetic variety of the plant material.(28)

Discussion

Alternative systems of medicine viz. Ayurveda, Siddha, and Chinese Medicine have become more popular in recent years (30,31,32).As the global scenario is now changing towards the use of nontoxic plant products having traditional medicinal use, development of modern drugs from *Momordica charantia* should be emphasized for the control of various diseases. In the present review we have made an attempt to congregate the botanical, phytochemical, ethnopharmacological, pharmacological and toxicological information on *Momordica charantia*, a medicinal herb used in the Indian system of medicine.

Acknowledgement

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