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Pharmacological actions and potential uses of *Momordica charantia*: a review

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Abstract

Since ancient times, plants and herbal preparations have been used as medicine. Research carried out in last few decades has certified several such claims of use of several plants of traditional medicine. Popularity of *Momordica charantia* (MC) in various systems of traditional medicine for several ailments (antidiabetic, abortifacient, anthelmintic, contraceptive, dysmenorrhea, eczema, emmenagogue, antimalarial, galactagogue, gout, jaundice, abdominal pain, kidney (stone), laxative, leprosy, leucorrhea, piles, pneumonia, psoriasis, purgative, rheumatism, fever and scabies) focused the investigator's attention on this plant. Over 100 studies using modern techniques have authenticated its use in diabetes and its complications (nephropathy, cataract, insulin resistance), as antibacterial as well as antiviral agent (including HIV infection), as anthelmintic and abortifacient. Traditionally it has also been used in treating peptic ulcers, interestingly in a recent experimental studies have exhibited its potential against *Helicobacter pylori*. Most importantly, the studies have shown its efficacy in various cancers (lymphoid leukemia, lymphoma, choriocarcinoma, melanoma, breast cancer, skin tumor, prostatic cancer, squamous carcinoma of tongue and larynx, human bladder carcinomas and Hodgkin's disease). There are few reports available on clinical use of MC in diabetes and cancer patients that have shown promising results.
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1. Introduction

In developing countries—all over the world—80% of population continues to use traditional medicine in primary medical problems. In the past decade, therefore, research has been focused on scientific evaluation of traditional drugs of plant origin. *Momordica charantia* (MC) is one such plant that has been frequently used as medicine (Giron et al., 1991; Lans and Brown, 1998).

MC, a climber belonging to family Cucurbitaceae, is commonly known as bitter gourd or bitter melon in English and karela in Hindi. *Momordica* means, "to bite"—referring to the jagged edges of the leaf, which appear as if bitten. All parts of the plant, including the fruit, taste bitter. The fruit is oblong and resembles a small cucumber, young fruit is emerald green that turns to orange-yellow when ripe.

The plant grows in tropical areas of Asia, Amazon, east Africa, and the Caribbean. It is cultivated throughout the world for use as vegetable as well as medicine. MC has been used traditionally as medicine in developing countries like Brazil, China, Colombia, Cuba, Ghana, Haiti, India Mexico, Malaya, New Zealand, Nicaragua, Panama and Peru. Some of its common uses in most countries are for diabetes, as a carminative and in treatment of colics (http://www.rain-tree.com/bitmelon.htm; Yesilada et al., 1999; Satyawati et al., 1987). Topically it is used for treatment of wounds, internally as well as externally for management of worms and parasites. It is also used as emmenagogue, antiviral for measles and hepatitis. In Turkish folk medicine, mature fruits of *Momordica charantia* are used externally for rapid healing of wounds and internally for treatment of peptic ulcers.

In India, various medicinal properties are claimed for MC that include antidiabetic, abortifacient, anthelmintic, contraceptive, antimalarial and laxative and is used for treatment of dysmenorrhea, eczema, emmenagogue, galactagogue, gout, jaundice, kidney (stone), leprosy, leucorrhea, piles,

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pneumonia, psoriasis, rheumatism and scabies. However, it is commonly consumed as vegetable.

Its popular medicinal uses focussed research so ever and the last few decades several hundred studies that have been carried with MC, using modern tools, credit MC with antidiabetic, antiviral, antitumor, antileukemic, antibacterial, anthelmintic, antimutagenic, antimycobacterial, antioxidant, antiulcer, anti-inflammatory, hypocholesterolemic, hypotriglyceridemic, hypotensive, immunostimulant, and insecticidal properties (Ng et al., 1992; Raman and Lau, 1996; Basch et al., 2003). This review aims to highlight the main medicinal properties of MC with a view to focus future studies on this plant.

2. Phytochemistry

MC contains biologically active chemicals that include glycosides, saponins, alkaloids, fixed oils, triterpenes, proteins and steroids (Raman and Lau, 1996; http://www.raintree.com/bitmelon.htm). The immature fruits are a good source of Vitamin C and also provide Vitamin A, phosphorus, and iron (http://momordica.allbio.org/).

Several phytochemicals such as momorcharins, momordenol, momordicilin, momordicins, momordicinin, momordin, momordolol, charantin, charine, cryptoxanthin, cucurbitins, cucurbitacins, cucurbitanes, cycloartenols, diosgenin, elaeostearic acids, erythrodiol, galacturonic acids, gentisic acid, goyaglycosides, goyasaponins, multiflorenol, have been isolated (Husain et al., 1994; Xie et al., 1998; Yuan et al., 1999; Parkash et al., 2002). These are reported in all parts of the plant (Murakami et al., 2001).

The hypoglycemic chemicals of MC are a mixture of steroidal saponins known as charantins, insulin-like peptides and alkaloids (Raman and Lau, 1996) and these chemicals are concentrated in fruits of MC, therefore fruit of MC has shown more pronounced hypoglycemic/antihyperglycemic activity (Ali et al., 1993). However, Day et al. (1990) differentiated two types of hypoglycemic substances in MC with different time dependent effects—one with fast antihyperglycemic activity of around 1 h present in the aqueous and the residue after alkaline chloroform extraction of aqueous extract and another with a slow hypoglycemic activity in acidic wash of the chloroform extract remaining after an alkaline water wash.

HIV inhibitory proteins like MRK29 (MW: 28.6 kDa), MAP30 (MW: 30,000 kDa) and lectin are documented (Putnam and Tainer, 2000; Jiratchariyakul et al., 2001; Wang and Ng, 2001a).

The presence of trypsin inhibitors (Miura and Funatsu, 1995; Hamato et al., 1995; Chakraborty et al., 2000), elastase inhibitors (Hamato et al., 1995), guanylate cyclase inhibitors (Vesely et al., 1977; Takemoto et al., 1980) and alpha-glucosidase inhibitor like D-(+)-trehalose are reported (Matsuur et al., 2002).

3. Pharmacological properties of MC

3.1. Antidiabetic activity

3.1.1. Experimental

MC is most widely studied with regard to its antidiabetic effect and all parts of the plant (fruit pulp, seed, leaves and whole plant) have shown hypoglycemic activity in normal animals (Bailey et al., 1985; Day et al., 1990; Shibib et al., 1993; Ali et al., 1993; Cakici et al., 1994; Sarkar et al., 1996; Jayasooriya et al., 2000); and antihyperglycemic activity in alloxan (Akhtar, 1982; Karunanayake et al., 1984; Singh et al., 1989; Pari et al., 2001; Rathi et al., 2002a; Kar et al., 2003) or streptozotocin-induced (Kedar and Chakrabarti, 1982; Bailey et al., 1985; Day et al., 1990; Karunanayake et al., 1990; Higashino et al., 1992; Shibib et al., 1993; Sarkar et al., 1996; Ahmed et al., 1998; Ahmed et al., 2001; Sitasawad et al., 2000; Grover et al., 2002; Rathi et al., 2002a) as well as genetic models of diabetes (Miura et al., 2001).

A poly-herbal preparation containing MC showed a significant reduction in blood glucose, glycosylated haemoglobin, and an increase in plasma insulin and total haemoglobin in animals (Pari et al., 2001). Virdi et al. (2003) demonstrated antihyperglycemic activity of MC fruit that was comparable to glibenclamide in diabetic rats. However, in a recently conducted study, Kar et al. (2003) achieved nearly euglycemic state with ethanolic extracts of MC fruit (250 mg/kg) within 2 weeks of treatment. Chronic treatment with aqueous fruit extract (200 mg/kg, orally) in alloxan diabetic rats caused a significant fall in plasma glucose levels of 64.33, 66.96, 69.7 and 70.53% at 1, 2, 3 and 4 months, respectively, and mean reduction of 15.37, 18.68 and 22.86% in STZ mice at 40, 50 and 60 days, respectively (Rathi et al., 2002a).

Individually, a few Isolated phytochemicals (Charantin, a Polypeptide-p, momordin Ic, oleanolic acid 3-O-monodesmoside, and oleanolic acid 3-O-glucuronide) of MC have shown hypoglycemic activity (Lotlikar and Rao, 1966; Khanna et al., 1981; Matsuda et al., 1998). The pulp juice and saponin free methanolic extract of juice from fruit exerted significant hypoglycemic effect in fasting and post-prandial states of normal and NIDDM rats but not in IDDM rats, effect was most pronounced with latter extract (Ali et al., 1993).

MC has been shown to enhance number of beta cells (Ahmed et al., 1998). In another study, it was shown to act like insulin or promote insulin release (Welihinda et al., 1986; Higashino et al., 1992). However, a few studies have also attributed hypoglycemic activity to an extra-pancreatic effect (Day et al., 1990; Sarkar et al., 1996), which includes increased GLUT4 transporter protein of muscles (Miura et al., 2001), increased glucose utilization in the liver and muscle (Karunanayake, 1986; Sarkar et al., 1996), inhibition of glucose-6-phosphatase & fructose-1, 6-bisphosphatase in liver and stimulation of red-cell and hepatic glucose-6-

phosphate dehydrogenase activities (Shibib et al. (1993). Matsuda et al. (1998) attributed the hypoglycemic activity of MC to inhibition of glucose transport at the brush border of the small intestine. Depressed carbohydrate enzymes activity in liver of diabetic mice was restored with MC treatment (i.e. hexokinase, glucokinase, phosphofructokinase and substrate glucose-6-phosphate) by 74.8, 29.6, 120.5 and 90.55%, respectively ($P < 0.05$, 0.001, 0.001, 0.001) as compared to control (Rathi et al., 2002a).

3.1.2. Effect on diabetic complications

Complications are frequently encountered in diabetes and these are associated with irreversible functional and structural changes in various organs particularly the kidneys, eyes, nerves and blood vessels (American Diabetes Association, 1998).

MC has shown promising effects in prevention as well as delay in progression of diabetic complications (nephropathy, neuropathy, gastroapresis, cataract and insulin resistance) in experimental animals (Grover et al., 2001, 2002; Rathi et al., 2002b; Vikrant et al., 2001).

Diabetic patients are 17 times more prone to kidney disease and diabetes is now the leading cause of end stage renal disease (WHO, 1994). With a view to assessing the effect of *Momordica charantia* treatment on development of nephropathy in diabetic animals certain renal functions parameters were measured. STZ diabetic mice had several times higher mean values of serum creatinine (50.0 μ mol/l), urinary albumin (1411.3 μg/24 h), urine volume (31.9 ml/24 h) and renal weight (0.59 gm) compared to normal mice. However, in parallel, these values were significantly less (47.5 μ mol/l, 1072 μg/24 h, 20.0 ml/24 h & 0.51 g, respectively) in MC treated animals (Grover et al., 2001).

The most frequent and disabling complication of DM is diabetic neuropathy, which causes limb pain, sexual dysfunction along with gastrointestinal, genitourinary and cardiovascular symptoms. In one study, to evaluate the effect of MC on diabetic neuropathy, an aqueous extract of MC (200 mg/kg) was given to diabetic animals for 50 days. The treatment caused reduction in tail flick latency by 43.6% in comparison to diabetic control animals where it increased by 73.6% compared to normal animals (Grover et al., 2002).

Diabetic enteropathy results in dyspepsia, heartburn, nausea, vomiting, abdominal pain, constipation, diarrhea and fecal incontinence, a syndrome that is typically seen in NIDDM. These symptoms were found in 76% of diabetic outpatients evaluated at a tertiary referral center (Feldman and Schiller, 1983). In experimental work, gastric transit ratio in STZ (150 mg/kg i.p.) diabetic mice was reduced 83.00% to that of in normal mice and an aqueous extract of MC (200 mg/kg) normalized this transit time to 90.28%of normal, in addition to causing reduction of plasma glucose (Grover et al., 2002).

Insulin resistance is another important feature of diabetes has been linked to obesity, hypertension, dyslipidemia and atherosclerosis which, together are responsible for substantial morbidity and premature mortality (Reaven, 1988). A fructose rich diet in rats has been shown to induce syndrome X—constituting hyperglycemia associated with hyperinsulinemia, hypertriglyceridemia and obesity (Elliot et al., 2002). Oral administration of aqueous MC extract (400 mg/day for 15 days) to rats fed a fructose rich diet substantially prevented hyperglycemia (63.5 mg/dl versus 75.4 mg/dl in controls; $P < 0.001$) and hyperinsulinemia (7.78 ng/dl versus 15.04 ng/dl in controls, $P < 0.01$) in comparison with fructose control rats (Vats et al., 2001).

Diabetes mellitus has been consistently identified in many studies as the most important risk factor for cataract in Western countries (Hiller et al., 1983; Van-Heyningen and Harding, 1988; Harding et al., 1989). Although surgery is effective, strategies aimed to prevent or delay development of cataract remains the preferred approach to confront the global problem.

In our experiments, MC treatment (aqueous extract 200 mg/kg) of alloxan diabetic rats inhibited development of cataract (observed up to 120 days) that was otherwise seen in non-treated diabetic rats at 100 days (Rathi et al., 2002b).

In another study, daily administration of a high dose (4 gm/kg) of *M. charantia* fruit for 2 months to alloxanized diabetic rats (120 mg/kg) delayed development of cataract to 140–180 days in comparison to 90–100 days in the controls (Srivastava et al., 1988).

3.1.3. Clinical

In a clinical trial, a water-soluble extract of the fruits of *M. charantia* significantly reduced blood glucose concentrations in the nine NIDDM diabetics on OGTT (50 gm). Fried karela fruits consumed as a daily supplement to the diet produced a small but significant improvement in glucose tolerance in diabetic subjects without any increase in serum insulin levels (Leatherdale et al., 1981). In another clinical study, a homogenized suspension of the vegetable pulp of *M. charantia* given to 100 cases of moderate NIDDM subjects caused a significant reduction ($P < 0.001$) of post-prandial serum glucose in 86% cases and fasting glucose in 5% cases (Ahmad et al., 1999). Welihinda and coauthors (1986) observed significant improvement of glucose tolerance in 73% of the maturity onset diabetic patients by MC fruit juice administration.

In a controlled clinical trial, a single subcutaneous injection of pure protein (p-insulin) from MC to nine patients (six with juvenile, one with maturity onset and two with chemical diabetes) produced a mean fall in blood glucose by $45.8 \pm 13.6\%$. The onset of hypoglycemic effect ranged between 30–60 min and maximum effect was observed at 4–8 h in juvenile diabetics; 6–8 h in chemical diabetes and in over 12 h in maturity onset diabetic patients (Baldwa et al., 1976). In another clinical study, an antihyperglycemic peak effect between 4–8 h was achieved with subcutaneous polypeptide P adminstration to nineteen juvenile and maturity diabetics patients (Khanna et al., 1981).

Further clinical work is required to be undertaken before these isolated, purified compounds can be marketed. However, in the developing countries, to cut down costs, intake of MC fruit in form of vegetable should be encouraged as the same has also shown to clinically effective. Keeping the above findings in mind, NIIDM patients should be encouraged to consume MC as it can reduce the blood sugar and more importantly it can keep them away from developing complications associated with diabetes. At the same time safety is assured as the same has been consumed in diet for centuries.

3.2. Antibacterial activity

Leaf extracts (water, ethanol, and methanol) of bitter melon have clinically as well as experimentally demonstrated broad-spectrum antimicrobial activity (Khan et al., 1998). In vitro antimicrobial activity of leaves extract was seen against *Escherichia coli*, *Salmonella paratyphi*, *Shigella dysenterae* and against *Streptomyces griseus* (Omoregbe et al., 1996; Ogata et al., 1991), an extract of the entire plant was also shown to have antiprotozoal activity against *Entamoeba histolytica* (Khan et al., 1998). Fruit extract has also shown activity against *Helicobacter pylori*-organism—MICs ranged between 1.95 and 250 μg/m (Yesilada et al., 1999). In a phase II study, MC leaves extract showed inhibition of *Mycobacterium tuberculosis* growth using the BACTEC 460 susceptibility test method (Frame et al., 1998). It is of great importance that those living in tropical countries be encouraged to consume fruit of this plant as it protects against organisms that cause diseases prevalent in these areas.

3.3. Antiviral activity

MC and several of its isolated phytochemicals, e.g. alpha and beta-momorcharin, lectin and MAP 30, have been documented to have in vitro antiviral activity against Epstein–Barr, herpes, HIV, coxsackievirus B3 and polio—viruses. Promising anti HIV activity has been attributed to a isolated protein known as MAP 30 (MW, 30 kDa).

3.3.1. Anti-HIV activity

Alpha momorcharin, was found to have a combination of abortifacient, tumor suppressive, and anti-HIV properties (Ng et al., 1992). Anti HIV activity of Map 30, recombinant MAP30, and proteolytic fragments of MAP 30 was exhibited in several in vivo and in vitro studies (Lee-Huang et al., 1990; Lee-Huang et al., 1995a,b; Huang et al., 1999). At the same time MAP 30 is non-toxic to normal non-infected cells, as it does not penetrate healthy cells (Lee-Huang et al., 1990). Antiviral activity of MAP30 was attributed to inhibition of HIV-1 integrase (Lee-Huang et al., 1995b). More importantly in a clinical study, combination of MAP 30 with low doses of dexamethasone and indomethacin improved efficacy of anti-HIV therapy (Bourinbaiar and Lee-Huang, 1995). In 1996, Lee-Huang and workers, inventor of MAP-30, obtained US patent for tumor and HIV treatments.

In an in vivo study, the leaf extract of MC demonstrated an ability to increase resistance against viral infections as well as to provide immunostimulant effects in clinical as well as experimental settings (Cunnick et al., 1990). Anti HIV activity of two proteins—alpha- and beta-momorcharin (present in seeds, fruit, and leaves) has been reported in vitro (Zheng et al., 1999; Au et al., 2000) and it was found to be inhibition of HIV-1 integrase (Au et al., 2000). Lectins as well as MRK29 from MC have been shown to act through inhibition of viral reverse transcriptase (Wang and Ng, 2001a; Jiratchariyakul et al., 2001). The salt-precipitated fraction of MRK29 caused 82% reduction of viral core protein p24 expression in HIV-infected cells and an increased in TNF activity (Jiratchariyakul et al., 2001).

3.3.2. Antiherpes activity

Two in vitro studies have shown antiherpes activity of MC ribosome-inactivating proteins and MAP30 against HSV-2 and HSV-1 (Foa-Tomasi et al., 1982; Bourinbaiar and Lee-Huang, 1996). This effect is probably mediated through inhibition of protein synthesis (Foa-Tomasi et al., 1982).

3.3.3. Antipoliovirus activity

MC ribosome-inactivating proteins inhibited poliovirus replication by inhibiting protein synthesis1 (Foa-Tomasi et al., 1982). Schreiber et al. (1999) suggested its use against sexually transmitted diseases, as it had no effect on the motility or vitality of spermatozoa.

3.4. Anticancer activity

Various preliminary studies (in vitro as well as in vivo) with crude MC extract and its various purified fraction—including MAP 30—have shown anticancer activity against lymphoid leukemia, lymphoma, choriocarcinoma, melanoma, breast cancer, skin tumor, prostatic cancer, squamous carcinoma of tongue and larynx, human bladder carcinomas and Hodgkin's disease (Licastro et al., 1980; Ng et al., 1994; Battelli et al., 1996; Ganguly et al., 2000; Sun et al., 2001; Basch et al., 2003;). However, Kusamran et al. (1998) demonstrated chemopreventive potential of Thailand *Momordica charantia* but not by the Chinese variety.

3.4.1. Experimental studies

An aqueous extract of MC caused inhibition of prostatic adencarcinoma growth (Claflin et al., 1978), and exerted cytostatic as well as cytotoxic activities against human leukemic lymphocytes (Takemoto et al., 1982a). The methanol extract as well as momordin I, Id and Ie of MC also showed cell cytotoxicity against human cancer cell lines (Lee et al., 1998). Immunoconjugates of CD30 monoclonal antibody and momordin showed potent in

vitro as well as in vivo antitumor activity (Tazzari et al., 1999).

Alpha-momorcharin showed cytotoxicities against choriocarcinoma and melanoma cells (Tsao et al., 1990) and human placental choriocarcinoma and sarcoma S180 cell lines (Ng et al., 1994). Momordin also inhibited protein synthesis of human trophoblasts and choriocarcinoma cells (Battelli et al., 1996). Alpha-Momorcharin enhanced the tumoricidal effect of mouse macrophages on mouse mastocytomal (P815) cells (Ng et al., 1994). Chronic treatment with hot water extract of MC inhibited uterine adenomyosis and mammary tumor growth in mice (Nagasawa et al., 2002). However, Singh et al. (1998) demonstrated maximal anticarcinogenic activity in the peel of MC.

Alpha- and beta-momorcharin, momordin, and cucurbitacin B from MC have clinically demonstrated ability to inhibit guanylate cyclase linked to pathogenesis and replication of leukemia and other cancers (Takemoto et al., 1982b).

Map 30, as well as its proteolytic fragment exhibited cytotoxicity to tumor cells with almost similar potency (Lee-Huang et al., 1995; Huang et al., 1999).

3.4.2. Clinical

MC has demonstrated the ability to inhibit an enzyme named *guanylate cyclase* in a clinical setting (Takemoto et al., 1982b). A conjugate of momordin, monoclonal antibody (named 8A) and plasma antigen was tried for ex vivo purging in autologous bone marrow transplantation in multiple myeloma patients. The conjugate eliminated minimal residual disease from bone marrow (Dinota et al., 1989). In another study, treatment with *Momordica charantia* for 45 and 90 days in cervical cancer patients showed a significant decrease in P-glycoprotein level ($P < 0.05$) from the basal value, while no such effect was seen in patients given only chemotherapy (Pongnikorn et al., 2003).

3.4.3. Mechanism for anticancer activity

Several studies have reported that phytochemicals of MC to exert anticancer activity through inhibition of DNA, RNA and cellular protein synthesis (Licastro et al., 1980; Zhu et al., 1990; Tsao et al., 1990; Chan et al., 1992; Terenzi et al., 1996).

Detailed studies showed that MC acted through inhibition of cell cycle G2 and M phases (Claflin et al., 1978) through inhibition of incorporation of thymidine, leucine and uridine into DNA (Claflin et al., 1978; Chan et al., 1992; Ng et al., 1994). In addition, inhibition of guanylate cyclase activity (Vesely et al., 1977; Claflin et al., 1978; Takemoto et al., 1980, 1982b), activation of NK cells (Jilka et al., 1983; Cunnick et al., 1990; Porro et al., 1993), induction of apoptosis (Bolognesi et al., 1996; Sun et al., 2001) and modulation of biotransformation and detoxification enzymes of the host were also seen with MC (Kusamran et al., 1998; Singh et al., 1998; Ganguly et al., 2000). Lee et al. (1998) demonstrated inhibition of tumor-promoting signals from the extracellular environment to nuclear transcription machinery as well as protein-DNA interaction with momordin treatment.

Literature at present points to the potential usefulness of MC in cancer treatment. However, it would be interesting to conduct an epidemiological survey with regard to incidence of malignancies among population that consumes MC as vegetable.

3.5. Abortifacient and antifertility

Several experimental studies demonstrated abortifacient properties of *Momordica* proteins (Law et al., 1983; Tam et al., 1984; Chan et al., 1984, 1985, 1986). Momorcharins produced abortifacient activity in early and midterm pregnancy (Chan et al., 1984, 1985, 1986) and it was attributed to its inhibitory effect on the differentiating endometrium. Law et al. (1983) and Tam et al. (1984) attributed abortifacient activity of protein to the effect on implantation of embryos to endometrium, in mouse given on days 4 and 6 of pregnancy. Beta-Momorcharin was shown to have inhibitory effect on decidualization and endometrium & myometrium cell proliferation of pseudopregnant mouse uterus. In addition, beta-Momorcharin also inhibited the biosynthetic activity of the cultured endometrial cells (Chan et al., 1985). The abortifacient activity of beta-momorcharin is seen via (a) blockage of the hatching of embryos from the zona pellucida; (b) decrease in attachment of the blastocyst; (c) reduction in the trophoblast outgrowth and (d) disruption of inner cell mass development (Chan et al., 1984).

However, alpha- and beta-momorcharins treatment prior to pregnancy do not affect follicular recruitment & maturation and the animals underwent pregnancy resulting in a litter size similar to that of controls (Ng et al., 1988).

Studies on male fertility showed alpha-momorcharin as well as beta-momorcharin did not affect luteinizing hormone-induced testosterone production in isolated rat Leydig cells or corticotropin-induced corticosterone production in isolated rat adrenal decapsular cells (Ng et al., 1987). An alcohol extract of MC seeds (25 mg/100 g body weight) showed potent antis-permatogenic, antisteroidogenic and androgenic activities in rats (Naseem et al., 1998). MAP30 had no effect on the motility and vitality of spermatozoa (Schreiber et al., 1999).

Teratogenic effect of momorcharins was seen in the cultured mouse embryos at early organogenesis stage (Chan et al., 1986).

In conclusion, experimental studies demonstrated their ability to induce abortions in rats and mice. Thus, MC produced antifertility in females as well as male animals—sperm production declined, though other studies have shown MC to be safe during pregnancy.

Thus, it is important to undertake detailed work on teratogenic and abortifacient effects of this plant before recommending its use in pregnancy.

3.6. Anti-ulcer activity

MC has been shown to have antiulcer activity observed against two different models of ulcer. In one study, momordin Ic (10 mg/kg, p.o.) potentially inhibited ethanol-induced gastric mucosal lesions (Matsuda et al., 1999). In another study, dried-powdered fruits in filtered honey showed significant and dose-dependent anti-ulcerogenic activity against ethanol-induced ulcerogenesis in rats. In addition, ethanol fruits extract also showed significant anti-ulcer activity against HCl-EtOH induced ulcerogenesis in indomethacin pretreated rats and diethyldithiocarbamate-induced ulcer models (Gurbuz et al., 2000). Interestingly, MC has been shown to have anti *H. pylori* activity, which would also beneficially contribute to anti-ulcer activity (Yesilada et al., 1999).

3.7. Anthelmintic study

Preparations from *Momordica charantia* exhibited in vitro anthelmintic activity against *Ascaridia galli* worms and shown to be more effective than piperazine hexahydrate (Lal et al., 1976).

3.8. Antmalarial activity

Kohler and coauthors (2002) observed weak in vitro antiplasmodial activity of MC extract. Munoz et al. (2000) demonstrated moderate in vivo activity of MC extract against rodent malaria *P. vinckei petteri* 279. However, Amorim et al. (1991) and Ueno et al. (1996) did not observe in vitro antiplasmodial activity of ethanolic MC extract against *P. berghei*.

3.9. Immunomodulatory activity

Studies have shown immunosuppressive as well as immunostimulatory effect by MC components. In vivo study, Leung et al. (1987) observed that microgram injections of *Momordica charantia* inhibitory protein (MCI) to mice delayed H2-incompatible skin allograft rejection, splenocyte responsiveness to concanavalin A (ConA) and phytohemoglobin (PHA). It abrogated PFC response to T-dependent (SRBC) antigen but completely spared response to a T-independent (S III) stimulus. There was reduction in NK cell activity but increased macrophage-mediated spontaneous cytotoxicity. In vitro, MCI inhibited lymphoid cell responsiveness to PHA and ConA, but not to LPS and markedly enhanced macrophage-dependent cytotoxicity (Spreafico et al., 1983). Intraperitoneal administration of alpha-momorcharin and beta-momorcharin (50 μg weekly for 5 weeks) to BALB/cAn or C57BL/6N mice resulted in high levels of IgE production (PCA titer), while no cross-immunological reactivity among these proteins was found (Zheng et al., 1999). Alpha- and beta-momorcharin showed immunosuppressive activity via lymphocytotoxicity or to a shift in the kinetic parameters of the immune response (Leung et al., 1987).

However, its immunostimulant activity has been attributed to increase in interferon production and natural killer cell activity (Cunnick et al., 1990).

In conclusion, MC has a variable effect on the immune system, in some conditions (allograft rejection) it was shown to have immunosuppressive effect (Leung et al., 1987; Spreafico et al., 1983); however, in another situations (HIV), MC exhibited immunostimulant activity.

3.10. Miscellaneous effects

A few preliminary studies have shown various other pharmacological properties of the plant.

3.10.1. Antipsoriasis

MC has been traditionally used in the treatment of psoriasis. Moreover it has guanylate cyclase enzyme inhibiting property (Vesely et al., 1977; Claflin et al., 1978; Takemoto et al., 1982b) that is reported to be helpful in the treatment of psoriasis (http://www.viable-herbal.com/singles/herbs/s; http://www.raintree.com/bitmelon).

3.10.2. Analgesic and antinflammatory activity

Momordin Ic and its aglycone, oleanolic acid are active principles with antirheumatoid activity (Biswas et al., 1991; Choi et al., 2002).

3.10.3. Hypotensive and anti prothrombin activity

Wang and Ng (2001b) observed mild hypotensive response with Momordin. In another study, MC prolonged prothrombin time by inhibiting activation of factor X by factor VIIa-tissue factor complex or factor IXa, (Hayashi et al., 1994).

3.10.4. Hypocholesterolemic and anti-oxidant potential

Several experimental studies carried out in normal as well as diabetic animals have shown hypo-cholesterolemic effect by MC (Platel et al., 1993; Singh et al., 1989; Anila and Vijayalakshmi, 2000; Jayasooriya et al., 2000; Noguchi et al., 2001; Ahmed et al., 2001). Feeding of conjugated octadecatrienoic fatty acid isolated from MC seed for 4 weeks significantly lowered the plasma lipid peroxidation and erythrocyte membrane lipid peroxidation as well as nonenzymatic liver tissue lipid peroxidation, in sunflower oil fed rats (Dhar et al., 1999). However, in another study, total lipids as well as phospholipid concentrations in heart and brain were significantly higher when karela oil was given compared with linseed oil administered rats (Dhar and Bhattacharyya, 1998).

4. Toxicity

MC was shown to be safe (no signs of nephrotoxicity and hepatotoxicity and any adverse influence on the food in-

take, growth organ weights and hematological parameters) in experimental animals when ingested in low doses up to 2 months (Platel et al., 1993; Virdi et al., 2003). However, relatively low toxicity of all parts of this plant are also reported when ingested, although toxicity and even death, in laboratory animals has been reported when extracts in high doses were administered intravenously or intraperitoneally (Kusamran et al., 1998). Traditionally as well as in experiment MC has shown abortifacient activity. The fruit and seeds demonstrated greater toxicity than the leaf or aerial parts of the plant. Documented adverse effects of MC are hypoglycemic coma and convulsions in children, reduced fertility in mice, a favism-like syndrome, increases in gamma-glutamyltransferase and alkaline phosphatase levels in animals, and headaches (Basch et al., 2003).

5. Conclusion

Over the years scientists have verified many of the traditional uses of this bitter plant that continue to be an important natural remedy for various diseases. Concentrated fruit or seed extracts can be found in various herbal preparations (capsules and tablets) that are marketed today. MC preparations are becoming more widely available in the U.S as well as rest of the world and are employed by practitioners of natural health for treatment of diabetes, viral diseases, including flu and psoriasis. Role of MC in diabetes is of paramount importance as this plant serves various purposes in these patients—lowers blood sugar, delays complications (nephropathy, neuropathy, gastroparesis and cataract, atherosclerosis) and is anti-infective (diabetics are known to be more susceptible to infections). Moreover till now there is no pharmacological agent that can control diabetic complications. Most importantly it is cheap and easily available in tropical countries. However, standardization of MC and its antidiabetic component followed by a controlled clinical trial is needed.

Most of the mentioned studies have been conducted using crude preparation of MC and the chemical profile was not mentioned. However, few studies have demonstrated biological activity of MC compounds such as charantin, MAP 30, momordin, alpha and beta momorcharins.

Anticancer activity of MC against numerous cancers suggests that it bears the compounds that have anticancer potential, however, presently further studies are needed.

M. charantia protein (MAP30) has potential for the treatment of HIV and a host of other infections. It would be better if MC or MAP30 are used in combination with current arsenal of antiretroviral drugs. In developing countries like India and Africa where both *M. charantia* and AIDS are ubiquitous, it could bring enormous hope to the suffering and it can be advocated as a dietary aid. Since studies have displayed the abortifacient and weak uterine stimulant activity of MC; therefore use of MC during pregnancy is not advocated. Further, the use of MC by both male and female persons opting for future conception should account the antifertility activity of MC.

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