Anti-Diabetic Properties and Phytochemistry *Momordica charantia L.* (Cucurbitaceae)

Author: **A. Raman, C. Lau.**
Type of Publication: Review
Date of Publication: 1996
Publication: Phytomedicine Vol. 2, pp 349-362, 1996
Organization/s: King's College London
Abstract: Unripe fruits, seeds and aerial parts of Momordica charantia Linn. (Cucurbitaceae) have been used in various parts of the world to treat diabetes. Oral administration of the fruit juice or seed powder causes a reduction in fasting blood glucose and improves glucose tolerance in normal and diabetic animals and in humans. Animal and in vitro data support both insulin secretagogue and insulinomimetic activity of the fruit. However, enhanced insulin levels in vivo in response to its administration have not been observed. Although a wide range of compounds has been isolated from Momordica charantia, notably steroidal compounds and proteins, the orally active anti-diabetic principle has not been adequately identified. A polypeptide, p-insulin, produces hypoglycaemic effects in humans and animals on subcutaneous injection, but oral activity is questionable. Other reported hypoglycaemic principles from Momordica charantia include the sterol glucoside mixture charatin (fruit) and the pyrimidine nucleoside vicine (seeds). However these are only effective at doses too high to account for all the activity of the plant extract. Principal toxicity of Momordica charantia in animals is to the liver and reproductive system. These effects have not been reported in humans despite widespread use of the fruit medicinally and as a vegetable.

Contents

Introduction

Many plants have been used for the treatment of diabetes mellitus in traditional systems of medicine throughout the world. Indeed, along with dietary measures, plant preparation formed the basis of the treatment of the disease until the introduction of insulin in 1922. A number of review article have been published on the traditional use of plants in diabetes (Swanston-Flatt et al., 1991; Bailey and Day, 1989) and on plants and phytochemicals whose reputed hypoglycaemic effects have been scientifically investigated (Perl, 1988; Handa et al., 1989; Day, 1990; Marles and Farnsworth, 1995).

The unripe fruit and seeds of *Momordica charantia L*. (Cucurbitaceae) have been the subject of over a hundred scientific articles describing their pharmacological or phytochemical properties. The aim of this review is to summarize the evidence for the

anti-diabetic properties of *Momordica charantia*, present its known phytochemical constituents and discuss the possible correlation between the two.

Habitat and traditional uses

The native country of *Momordica charantia* is uncertain, but the plant is cultivated throughout the tropics, particularly in India, China, East Africa and Central and South America (Walters and Decker-Walters, 1988). It is occasionally grown as an ornamental creeper, but more commonly cultivated for the use of the unripe fruit as a vegetable. The fruit has a number of different local names – bitter gourd, bitter-melon, balsam-pear, cundeamor (South America), karela (India), carilla or goo-fah (Jamaica); the reported spelling of the local names is often variable. The wild variety (*M. charantia* var. abbreviata) grows as a weed in the West Indies, where the plant is known as cerasee (Jamaica) or sorossie (Dominican Republic). This variety has smaller fruit than the Indian one. The term karela is used throughout this review to denote all varieties of the fruit since in the majority of studies the type used has not been specified.

In addition to its major use as an anti-diabetic agent, karela has been used in India and Sri Lanka as a tonic, emetic and laxative (Nadkarni, 1982). Both the cultivated and wild forms are used for this purpose (Bailey et al., 1986). In South / Central America, cerasee fruit or tea (see below) is used for diabetes, colds and fevers, stomach aches, constipation in children and the induction of abortion (Arvigo and Balick, 1993; West et al., 1971). Traditional Chinese uses for the fruit, seeds, vines and leaves include gastroenteritis, diabetes, tumors and some viral infections (Zhang, 1992a).

When used as an anti-diabetic remedy, karela juice prepared by crushing and straining the unripe fruit (ea. 50 ml) is taken once or twice a day. Fried karela may also be consumed. Cerasee on the other hand, is taken as a decoction or "tea" (hot water extract) of the aerial parts of the plants, free of large fruit (Bailey et al., 1986).

Studies in human subjects

Karela fruit. To date, no large-scale clinical trial has been reported on the anti-diabetic effects of karela, but a number of studies using small groups of diabetic patients have been conducted. Both non-insulin-dependent diabetes mellitus (NIDDM, Type II, maturity onset) and insulin-dependent (IDDM, Type I, juvenile onset) patients have participated.

Kirti et al. (1982) have described some early studies (1950-1974) carried out in India and the Caribbean, in which karela's anti-diabetic activity was observed. More recent interest was aroused when Aslam and Stockley (1979) reported a case of a possible interaction, in the form of decreased glycosuria, between a curry containing karela and the anti-diabetic drug chlorpropamide taken by the Asian NIDDM patient. Following this, Leatherdale et al. (1981) carried out a study in 9 Asian NIDDM outpatients living in the United Kingdom. Acute administration of karela juice with a glucose load resulted in a significant improvement in glucose tolerance without increasing the insulin levels in the blood. Daily consumption of fried karela for 8 to 11 weeks had a similar, through not statistically significant, effect. Nevertheless, there was a significant reduction in glycosylated haemoglobin, indicating an improved control of blood glucose levels over this period.

Further evidence for a beneficial chronic effects is that an improvement in both glucose tolerance, and fasting blood glucose levels was observed in 8 NIDDM patients following 7 weeks of daily consumption of powdered karela fruit (Akhtar, 1982). Srivastava et al. (1993) reported that 3-7 weeks treatment of diabetics with powdered fruit, led to a mean fall of 25% (range 11-48%) in post-prandial blood glucose levels. There was a marked fall in both blood and urine sugar over 7 weeks in a group treated

with an aqueous extract of the fruit. Glycosylated haemoglobin showed a significant reduction by the end of the trial.

By contrast, Kirti et al. (1982), reported that whilst karela (acute or chronic) resulted in a reduction in glycosuria, there was no effect on blood glucose. However in their experiments, blood glucose levels were measured two hours after the administration of karela extract and by this time any effects of the fruit may have diminished. The earlier work of Leatherdale et al. (1981), suggested that improved glucose tolerance is most marked within the first 90 minutes of karela administration. Inter-patient variation may also explain a poor response to karela; Welihinda et al. (1986) reported that karela juice significantly improved glucose tolerance in only 13 of the 18 patients tested.

***P-insulin*.** In 1974, Khanna et al., isolated a polypeptide (p-insulin or v-insulin) from karela. A significant hypoglycaemic effect was observed in 6 IDDM, 1 NIDDM and 2 asymptomatic diabetics administered p-insulin subcutaneously (Baldwa et al., 1977). In a later study by Khanna et al. (1981) subcutaneous p –insulin led to a significant fall in blood glucose in 11 IDDM patients, whereas a similar effect in 8 NIDDM patients did not reach statistical significance. One IDDM patient was reported to have been maintained on p-insulin for 5 months with no complaints of side effects.

***Karela seeds*.** Oral administration of powdered karela seeds produced a significant reduction in post-prandial blood sugar values in 14 NIDDM and 6 IDDM patients (Grover and Gupta, 1990).

In vivo studies in laboratory animals

Studies using laboratory animals have included normal animals of various species, and those in which diabetes mellitus has been induced by administration of alloxan or streptozotocin (STZ). These two drugs are known to selectively damage beta cells of the pancreas, resulting in partial or virtual loss of insulin production (Fischer, 1985).

***Karela juice or extract*.** The three main animals species in which the effects of karela juice or karela solvent extracts have been investigated are the rabbit, rat and mouse.

***Rabbit Model*.** One of the earliest reports of karela's activity was by Sharma et al. (1960) who reported trhat the juice caused an improvement in glucose tolerance in alloxan diabetic but not normal animals. Somewhat in contrast to this, Akhtar et al. (1981) found that dried karela fruit caused a significant dose dependent decrease in blood glucose and that a higher minimum dose was required for alloxan-treated rabbits than normal ones. However, Kulkarni and Gaitonde (1962) saw no reduction in fasting glucose levels on either acute or chronic administration of dried karela juice to normal rabbits. These conflicting results may be due to variations in blood sampling times and dosages of both karela and alloxan.

A number of solvent extracts of karela have also been tested. Intravenous administration of a chloroform soluble extract of the juice resulted in a marked hypoglycaemic effect in alloxan-treated but not normal rabbits. (Tiangda et al., 1987). This may be an indication of greater pancreatic β-cell sensitivity to karela in alloxan treated animals. Glucose tolerance in alloxan recovered rabbits was improved by oarl administration of a benzene extract of karela, but not an ethanolic one (Venkanna Babu et al., 1988). Three non-sapogenic hypoglycaemic and 1 hyperglycaemic principles were reported to have been isolated from karela, but their identities were not given.

***Rat model*.** Rat models have been widely used to study the effects of karela juice and its extracts. Improved glucose tolerance on acute administration of the juice has been demonstrated in normal rats (Karunanayake et al., 1984; Chandrasekar et al., 1989) and in rats anterior pituitary extract-induced hyperglycaemia (Gupta, 1963).

Chronic administration over 30 days lowered the mean glucose tolerance in a group of STZ-treated rats, but this did not reach statistical significance (Karunanayake et al., 1990).

Higashino et al. (1992) found that a polar solvent extract of karela improved tolerance of both orally and intraperitoneally administered glucose, suggesting that a mechanism involving impaired glucose absorption from the gastro-intestinal tract was involved. Ali et al. (1993a) demonstrated that improved glucose tolerance only occurred in NIDDM-model STZ-treated rats and not those in which IDDM had been induced with a higher dose of STZ. This suggests an insulin secretagogue activity by karela. However, Leatherdale et al. (1981) found no significant increase in insulin levels in response to karela treatment in normal rats.

As well as improved glucose tolerance, a hypoglycaemic effect on acute administration of karela juice in fasted rats has been demonstrated in both normal (Leatehdale et al., 1981; Karunanayake et al., 1984; Chandrasekar et al., 1989) and STZ-treated animals (Higashino et al., 1992). However, Ali et al. (1993) found that very high doses of STZ can abolish the effect of karela. In alloxan induced diabetic rats, chronic administration of karela for 20 days was found to lower blood glucose significantly in a dose dependent manner (Srivastava et al., 1987, 1988, 1993). However, Platel et al. (1993) found that 8 weeks administration of freeze-dried fruit to normal animals did not affect blood glucose levels, possibly due to the operation of normal homeostatic mechanism. Karela juice administered prior to alloxan did not protect the animals from the induction of hyperglycaemia (Sharma et al., 1960).

Other potential beneficial effects of karela administration include lowering of serum cholesterol in normal rats (Platel et al., 1993) and delayed cataractogenesis in STZ-diabetic animals (Srivastava et al., 1987, 1988, 1993).

Mouse model. In normal mice, treatment with karela extracts resulted in improved glucose tolerance using either orally or intraperitoneally administered glucose. There was no significance difference observed between insulin levels in treated and control animals. (Day et al., 1990). A hypoglycaemic effect of the juice in STZ-treated animals was also demonstrated. The results of fractionation studies implied the presence of more than one active component, possibly alkaloidal in nature (structure not given).

***P-insulin*.** Subcutaneous administration of polypeptide, p-insulin, isolated from karela to fasted gerbils and langurs caused a significant fall in blood glucose (Khanna et al., 1981).

***Charantin*.** Charantin (Fig. 1), a mixture of sitosterol and stigmastadienol glucosides was isolated fro karela by Lotlikar and Rajarama Rao (1960/61) in approximately 0.01% yield. A decrease in blood glucose concentration was found when charantin was administered to fasted normal rabbits orally or intravenously. However, the data was obtained using only one or two animals at each dosage level and no controls were carried out. In a more elaborate study (Lotlikar and Rajarama Rao, 1966), charantin administered to normal rabbits intravenously or orally produced a gradual but significant fall in blood sugar. In alloxan diabetic rabbits, the effects were more erratic. Pancreatectomy was found to reduce but not abolish the hypoglycaemic effect of charantin (Lotlikar and Rajarama Rao, 1966), indicating a dual mechanism of action.

Karela seed. As in human subjects (Grover and Gupa, 1990), karela seed was found to lower blood glucose levels in STZ induced diabetic RABBITS (Kedar and Chakrabarti, 1982). The seed also reversed low muscle and liver glycogen and elevated serum cholesterol, fatty acids and triglycerides induced by STZ. Polar solvent (methanol, 50% aqueous ethanol, normal saline) extract of karela seed showed a significant hypoglycaemic effect in fasted albino rats (Dubey et al., 1987). The methanol and saline extracts were also able to reduce adrenaline-induced hyperglycaemia. In both cases, the methanol extract was the most potent. However, Ali et al. (1993a) reported that a methanolic extract of the seed did not reduce blood glucose levels in fasting or post-prandial states in normal and STZ-treated IDDM rats.

***Vicine*.** Vicine (Fig. 2) has been isolated from the seeds of karela in 0.6% yield (Handa et al., 1990). Intraperitoneal administration of vicine caused a hypoglycaemic response in normal fasting albino rats. The dose used was equivalent to about five times the amount of seed administered orally by Kedar and Chakrabarti (1982) to obtain a response.

***Karela vines and aerial parts*.** Cerasee tea (prepared from the vines) was found to lower basal glucose concentrations and to improve glucose tolerance in normal mice (Bailey et al., 1985), with no significant change in the plasma insulin level. A hypoglycaemic response was also observed in STZ-treated mice. When cerasee tea substituted for drinking water for 12 days, glucose tolerance measured on day 13 was improved. More recently, Ali et al. (1993a) tested methanolic and saponin-free methanolic extract of the whole plant of *Momordica charantia* in normal rats. Not effects were seen on fasting blood glucose.

Effects on tissue and enzymes; possible mode of action

Attempts have been made to obtain further information on the mode of action of karela fruit and seeds through experiments using enzymes, tissues or cells in *vitro* or examining organs isolated from karela treated animals. Karela fruit and seed preparation have a number of biological effects in *vitro* (Table 1), which may give an indications of their mode of action.

***Glucose absorption*.** A theoretical means by which glucose tolerance can be improved is by decreased absorption of glucose from the gut. Meir and Yaniv (1985) reported that glucose uptake by inverted gut was inhibited in the presence of extracts of karela fruit. However, from the *in vivo* work of Day et al. (1990) and Higashino et al. (1992) it would appear that this in not the mechanism involved in the action of karela since tolerance of intraperitoneally administered glucose is also improved. There have been no studies reported to date on effects of karela on enzymes involved in the digestion of carbohydrates, e.g. α-amylase.

***Insulin secretion*.** In a number of *in vitro* studies (Welihinda et al., 1982a, b; Ali et al., 1993 b; Mosihuzzaman et al., 1994), extract from the fruit have been found to stimulate insulin release from isolated pancreatic islet cells. The responsiveness of STZ and alloxan treated animals to karela, would seem to suggest that pancreatic stimulation is not involved. However, it must be noted that STZ and alloxan treatment may not result in complete destruction of pancreatic β-cells. For instance, in the study by Kedar and Chakrabarti (1982), STZ-treated animals were responsive to glibenclamide, which acts by stimulation of insulin release from the pancreas. In addition, Ali et al. (1993a) found that the effects of karela could be abolished by treating the animals with a higher dose of STZ. In some studies (Sharma et al., 1960; Tiangda et al., 1987) alloxan treated rabbits were more responsive to karela extracts than normal animals. This may include a sensation of the β-cells to karela by alloxan. However, it should be noted that increased insulin levels have not been observed in karela treated mice (Day et al., 1990), rats or humans (Leatherdale et al., 1981) *in vivo*.

***Insulinomimetic effects*.** Karela juice shows certain insulinomimetic effects such as increased glucose uptake into muscle, stimulation of lipogenesis, and inhibition of lipolysis on tissue preparation *in vitro* (Table 1). *In vitro* tests on tissues taken from animals treated with karela have also shown a depression of hepatic gluconcogenetic enzymes, and increased liver and muscle glycogen.

There is conflicting data on effects of karela extracts on tissue respiration. Welihinda and Karunanayake (1986) found that karela juice did not show any effect on tissue respiration by diaphragm muscle *in vitro*. However. Meir and Yaniv (1985) reported that karela inhibited the oxidation of glucose by liver tissue, possibly at the first step in glycolysis i.e. phosphorylation by hexakinase. These contradictory results may be due to

difference in the tissue, methodology and type of karela preparation used. A more reliable indicator of effect of karela on tissue respiration may be that demonstrated by Shibib et al. (1993). Liver glucose –6-phosphate dehydrogenase (G6PD-6-PDH) activity was elevated on *in vivo* administration of karela ethanolic extract by gastric intubation. This would enhance the utilization of glucose by the liver leading to a lower in blood glucose.

The lipogenic and anti-lipolytic effects of karela juice *in vitro* are shared by seed extracts. A saponin (not identified) and proteins have been found to account for the *in vitro* effects of the seeds. The proteins are believed to be lectins; the abortifacient proteins α- and β-momorcharin also found in the seeds are not active in this assay (Wong et al., 1985 a, b). However, against this, Welihinda and Karunanayake (1986) reported that adipose tissue of karela treated rats did not differ significantly in triglyceride content from that of control animals.

Thus, inhibition of glucose absorption, insulin secretagogue activity and insulinomimetic effects have been attributed to karela in *in vitro* tests. However, not all of these have been fully supported by *in vivo* data, probably due to the compounds showing activity *in vitro* not being bioavailable *in vivo*.

Phytochemicals isolated from *Momordica charantia* and their relationship to its anti-diabetic effects

Since the early 1960's a number of phytochemicals have been isolated from *Momordica charantia* fuit, seeds and whole plants. A review of the known constituents was published in 1989 (Fiche Espece, 1989). This data and supplementary information are given in Tables 2-4. In some cases biological activities such as insulinomimetic properties, protein synthesis inhibition, or insect attractant effects have been associated with the pure compounds e.g. saponins or proteins. Possible identities, which emerge for the hypoglycaemic principle in Momordica charantia, are steroidal glycosides, insulinomimetic kectins and alkaloids: the evidence relating to each of these is discussed below.

Steroidal glycosides. The earliest reported active constituent of karela fruit was "Charantin" (Fig. 1), a mixture of glucosides of sitosterol and 5.25 stigmastadien-3β-ol (Lotlikar and Rajarama Rao, 1960/61, 1966). However, it is important to note that the dose of charantin required to elicit a hypoglycaemic response in rabbits was equivalent to 180 to 315 g of fruit orally and 81 g fruit intravenously, whereas the hypoglycaemic effect can be seen in rabbits with about 10 to 15 g of the fruit per kg body weight.

In 1975, Olaniyi isolated a substance "foetidin," from the whole plant of *Momordica foetida,* which was found to be identical in composition to charantin. Marquis et al. (1977) claimed that at 18 hours from administration, foetidin lowered blood glucose in fasting rats in an effect comparable to insulin. This claim is often quoted in the literature as support that the steroidal mixture is the active principle of *Momordica charantia.* However, a closer examination of the original data presented in the paper shows that foetidin was not significantly different from control at time points other than the 18-hour sample.

It is known that *Momordica charantia* fruit, seeds and vines contain other steroidal glycosides (momordicosides and momordicines; Table 2-4, Fig. 3 and 4). A saponin fraction from the seeds of karela showed insulinomimetic effects in vitro (Wong et al., 1985; Ng et al., 1986 b). The contribution of steroidal constituents other than charantin to the in vivo anti diabetic effects of *Momordica charantia* has not been evaluated.

Insulinomimetic proteins. In vitro insulinomimetic effects have been observed with fruit proteins (Table 3). The active seed protein is believed to be a galactose binding lectin (Table 3). Khanna et al., (1981) reported that an 11 k Dalton protein (p-

insulin or v-insulin) caused hypoglycaemia in man and laboratory animals on parenteral administration.

Proteins are generally considered to be inactive when administered by the oral route, as they would undergo extensive digestion by proteolytic enzymes. Thus the possibility of a polypetide being responsible for the hypoglycaemic effects of the fruit or seeds when given orally must be viewed with some skepticism. However, against this, there is some evidence (Pusztai, 1986) that lectins may be absorbed into the bloodstream from the gasto-intestinal tract. Khanna et al., (1985) has stated without any supporting data that p-insulin is also effective orally.

Alkaloids. Day et al., (1990) reported that hypoglycaemic activity of fractionated karela fruit juice resided in an alkaloid-rich fraction. The alkaloids have not been isolated or characterized. The pyrimidine nucleoside vicine (Fig. 2) has been isolated from the seeds (Dutta et al., 1981; Barron et al., 1982). This "alkaloid" has been found to induce hypoglycaemia in rats in an intraperitoneal dose equivalent to 16 g seeds per kg body weight. Thus vicine may not account for all the activity of the seeds.

Kakra compounds. Srivastava et al., (1993) isolated three non-steroidal hypoglycaemic compounds (Kakra 1 b, 111 a and 111 b) from the fruit which differ from earlier reported principles, ie. p-insulin or charantin. The structure of these compounds was not elucidated.

Other pharmacological and toxicological properties

A number of effects of *Momordica charantia* unrelated to diabetes have been investigated. No data is available on standard toxicity parameters e.g. $I.D._{50}$ values of the juice, seeds or plants. However some information on toxicity is available from observations made during experimental or clinical use of *Momordica charantia* extracts in animals or humans.

Anti-cancer. Protein fractions obtained from the fruit and seed of *Momordica charantia* have the ability to inhibit cell growth, guanylate eyelase activity and ribosomal activity (Table 2,3). West et al., (1971) demonstrated inhibitory effects of whole plant extracts on seedling root growth, division of fertilized sea urchin eggs, rat foetal growth (if injected on day of mating) and the growth of Hep_2 cells in culture. They also report a single case study of a leukemia patient in whom regular intake of the extract led to a fall in white blood cell count, and an increase in blood haemoglobin.

Antivirals. The growth of herpes simplex virus I (Foa Tomasi et al., 1982) and human immunodeficiency virus I (Lifson et al., 1988; Lee-Huang et al., 1990) is inhibited by karela extracts. Increased T-cell count and a normalization of the CD 4/CD 8 ratio seemed to occur in three HIV positive patients given regular doses of karela juice (Zhang, 1992 b). The juice was administered as a retained enema i.e. rectally. This may explain its apparent effectiveness since the active anti-viral components of *Momordica charantia* are believed (Zhang, 1992 b) to be the proteins α and β-momorcharin and MAP (Table 3), which would be expected to undergo hydrolysis by pancreatic enzymes if administered by the oral route.

Analgesic Effects. A methanolic extract of the seeds from unripe fruit has been shown to produce a marked dose-dependent analgesic effect in mice and a much weaker effect in rats (Biswas et al., 1991), but using different test systems for the two species. Naloxone pretreatment failed to modify the analgesic response, suggesting the opioid receptors were not involved.

Anti-inflammatory effects. A dose related anti-inflammatory effect has been demonstrated using carageenin-induced rat hind-paw oedema (Lal et al., 1990). Free radical seavenging activity of the juice in vitro (Rao, 1991) may be involved.

Hypotensive action. "Cerasee" (aerial parts of *Momordica charantia*) extract showed a marked transient depressor effect on injection to the anesthetized dog (Feng et al., 1962). Gamma amino butyric acid has been suggested to be responsible for this effect (Durand et al., 1962).

Anti-fertility effects. Oral administration of karela fruit extract (1.75 g/day for 60 days) to male dogs resulted in testicular lesions and mass atrophy of spermatogenic elements (Dixit et al., 1978). Serumenzyme were normal implying that an infertility state was induced without altering general metabolic activity in the animal.

A study by Stepka et al. (1974) found that daily oral administration of the fresh juice *Momordica* (species not stated) leaves to a group of female mice reduced the fertility rate. This was reversed on withdrawal of the treatment. No pathological changes were seen in any of the maternal organs, but in some cases, concepti were seen as necrotic masses. In more recent work proteins capable of inducing abortions (α and β momorcharins) and necrosis of placental trophoblasts have been isolated from *Momordica charantia* seeds (Table 3). It is possible that similar proteins occur in the leaves. Uterine bleeding has been induced in pregnant rats given karela juice (6 ml/kg) orally (Zhang 1992 b), while 2 pregnant rabbits given karela juice (6 ml/kg) suffered uterine haemorrhage and death within a few hours (Sharma et al., 1960). No such effect was noted in non-pregnant females.

Effects on growth, blood and serum lipids. Chronic administration of karela extract (1.75 g orally per day for 20-60 days) to dogs resulted in elevated levels of serum cholesterol and non-esterified fatty acids, but no significant changes in body weight or serum enzymes (dixit et al., 1978). Rats maintained on a diet containing freeze-dried karela for 8 weeks showed no change in food consumption rate or growth rate (Platel et al., 1993). At the end of this period, organ weights (liver, kidney, testes, spleen, adrenals and heart) were similar to those of control animals. Blood cell counts, cell volume and haemoglobin parameters showed no significant difference to controls and remained within the normal range. However in this study, there was a significant decrease in blood cholesterol.

Hepatotoxicity. Following the administration of karela juice and seed extract to rats (10 ml/kg body weight daily for 30 days), serum γ-glutamyl transferase and alkaline phosphatase was significantly elevated, but consistent histopathological defects were not observed in the liver (Tennekoon et al., 1994). Therefore the eleated enzymes could either be due to mechanisms not obvious at the histological level or to enzyme induction. The prevalence of dilatation and/or congestion in the hepatic central veins and associated sinusoids was twice as high in the juice treated group as in the seed extract treated and control groups. Ng et al. (1994) have found that α- and β-momorcharins can induce cytoplasmic blebs and other morphological changes in rat hepatocyte *in vitro*. Secretion of various enzyme markers of cell damage is also raised.

Fatal doses in animals. Continuous single or twice daily oral administration of karela juice (6 ml/kg body weight) to 6 rabbits, died within a few hours of receiving this dose (Sharma et al., 1960). Rats given karela juice (18-40 ml/kg body weight, by intraperitoneal route) became sluggish and died within 6-18 hours. Zhang (1992 b) reported that pregnant rats died within a few hours of receiving karela juice (6 ml/kg body weight) orally. In normal and alloxan diabetic rats given the same dose daily, 80-90% died within 5-23 days. Abdominal injection of the juice at (15 ml/kg body weight) caused death in 6-18 hours. In rabbits receiving 10 ml/kg orally per day, the majorities were reported to have shown toxic effects, although the nature of these effects was not given in the paper.

Toxicity in humans. Although toxicity has been observed in some animal studies, if extrapolated to humans, the relevance of the dose and route of administration

must be considered. A dose of 6-10 ml/kg would represent a dose of 400 ml-1000 ml for an adult. The normal adult dose is 50 ml, given orally. There are no published reports of fatal or serious effects in adults at this dose.

Patel et al. (1968) reported that administration of the juice or dried juice powder 9equivalent to 250-500 g of the fruit) to diabetic patients led to abdominal pain and diarrhea. Zhang (1992) has used orally or rectally administered fruit juice to treat HIV-positive patients. He reports that there is very low clinical toxicity. A patients who had been given the juice daily for over three years did not show any change in the blood chemistry or any other untoward effect. Liver, kidney, heart or blood abnormalities have not been reported in any of Zhang's patients despite long term use of *Momordica charantia* fruit juice.

The only report of a potential fatal reaction in humans is hypoglycaemic coma induced in two small children (Hulin et al., 1988a b). The children aged three and four required urgent medical attention following ingestion of a water extract of *Momordica charantia* leaves and vines. In both cases, the Sorrosi (cerasee) tea had been administered by their mothers early in the morning, before any other food was consumed. Between 1-2 hours after ingestion, the children experienced convulsions followed by coma. Blood glucose was in the region of 1 mM (normal range 3.8-5.5 nM). Both patients recovered following treatment.

Conclusion

The fruit seeds and aerial parts of *Momordica charantia Linn* have been used as an anti-diabetic remedy in a number of areas of the world notably India, Sri Lanka, China and the West Indies. Limited studies on humans have shown that karela fruit juice reduces fasting blood glucose and improves glucose tolerance on acute administration. Prolonged administration causes a lowering of glycosylated haemoglobin in the blood and decreasing glycosuria and basal glycaemia. The hypoglycaemic and anti-hyperglycaemic effects of karela fruit and seeds have also been demonstrated in animal models. Through evidence from animal and *in vitro* studies, there is support for both insulin secretagogue and insulinomimetric activity of the fruit. However, enhanced insulin levels *in vivo* in response to administration of karela have not been observed.

A wide range of compounds has been isolated from *Momordica charantia* fruit, seeds and vines, notably saponins and proteins. Suggested hypoglycaemic compounds include a polypeptide (p-insulin), a steroid mixture (charantin) and a pyrimidine nucleoside (vicine). However, none of these is fully supported as a sole active constituent by the scientific data available. It is possible that a number of active constituents with a range of biological effects beneficial to diabetes are present in the fruit.

Principal toxic properties of karela juice noted in animals are anti-fertility effects and hepatoxicity, with death occurring on chronic oral treatment with doses of the order of 6 ml/kg body weight. Pregnant females were particularly susceptible. Encouragingly, similar effects have not been reported in humans despite widespread use of the fruit juice both as a medicinal plant and as a vegetable.

References

Akhtar,M.S.: Trial of *Momordica charantia Linn* (karela) powder in patients with maturity onset diabetes. J.Pak.Med.Assoc. 32: 106-107, 1982.sihu

Akhtar, M.S.,Arhar,M.A. and Yaqub,M: Effect of *Momordica charantia* on blood glucose level of normal and alloxan-diabetic rabbits. Planta Med. 42: 205-212, 1981.

Ali,L.,Khan,A.K.A.,Mamun,M.I.R.,Mosihuzzaman,M.,Nahar,N.,Nur-e-Alam,M. and Rokeya,B.: Studies on the hypoglycaemic effects of fruit pulp, seed and whole plant of *Momordica ch*arantia on normal and diabetic model rats. Planta Med. 59: 408-412, 1993a.

Ali,L.,Azad,Khan,A.K.,Hassan,Z.,Mamun,M.I.R., Mosihuzzaman, M., Nahar, N., Nur-e-Alam, M, and Rokeya, B,: Insulin releasing properties of fractions from *Momordica charantia* fruit on isolated rat islets. Diabetologia 36 (1): 181, 1993b.

Arvigo, R. and Balick, M. in: "Rainforest remedies. One hundred healing herbs of Belize." Lotus Press, Twin Lakes, WI USA p. 165, 1993.

Aslam, M. and Stockley, I.H.: Interaction between curry ingredient (karela) and drug (chlorpropamide). Lancet 1: 607, 1979.

Bailey, C.J. and Day, C.: Traditional plant medicines as treatments for diabetes. Diabetes Care 12 (8): 553-564, 1989.

Bailey, C.J. and Day, C. and Leatherdale, B.A.: Traditional treatments for diabetes from Asia and the West Indies. Practical Diabetes 3 (4): 190-192, 1986.

Bailey, C.J. and Day, C., Turner, S.L. and Leatherdale, B.A.: Cerasee, a traditional treatment for diabetes. Studies in normal and streptozotocin diabetic mice. Diabetes Res. 2: 81-84, 1985.

Baldwa, V.S., Bhandari, C.M., Pangria, A. and Goyal, R.K.: Clinical trial in patients with Diabetes Mellitus of an insulin-like compound obtained from plant source. Ups. J. Med. Sci. 82: 39-41, 1977.

Barron, D., Kaouadji, M. and Mariotte, A.M.: Etude comparative de deux cucurbitacees a usage medicinal. Planta Med. 46: 184-186, 1982.

Barbieri, L., Lorenzoni, E. and Stirpe, E.: Inhibition of protein synthesis in vitro by a lectin from *Momordica charantia* and by other haemagglutinins. Biochem. J. 182: 633-635, 1979.

Barbierui, L., Zamboni, M., Lorenzoni, E., Montanaro, L. Sperti, S. and Stirpe, E.: Inhibition of protein synthesis in vitro by proteins from seeds of *Momordica charantia* (bitter pear melon). Biochem. J. 186: 443-452, 1980.

Biswas, A.R., Ramaswamy, S. and Bapna, J.S.: Analgesic effect of *Momordica charantia* seed extract in mice and rats. J. Ethnopharmacol. 31: 115-118, 1991.

Chan, W.Y., Tam, P.P.L. and Yeung, H. W.: Biological effects of β-momorcharin on early mouse embryos and endometrial cells in "Advances in Chinese Medicinal Materials Research." Eds Chang, H.M., Yeung, H.W., Tso, W. W. and Koo, A. World Scientific Publiching Co PLC Ltd. Singapore, Philadelphia, p. 679, 1985.

Chandrasekar, B., Mukherjee, S.K.: Blood sugar lowering pontentiality of selected Cucurbitaceae plants of Indian origin. Indian J, Med. Res. 90: 300-305, 1989.

Chandravadana, M.V.: Identification of triterpenoid feeding deterrent of red pumpkin beetles (Anlacophora foveicollis) from *Momordica charantia.* J. Chem. Ecol. 13 (7): 1689-1694, 1987.

Claflin, A.J., Vesely, D.L., Hudson, J.L., Bagwell, C.B., Lehotay, D.C., Lo, T.M., Fletcher, M.A., Block, N.L. and Levey, G.S.: Inhibition of growth and guanylate eyelase activity Of an undifferentiated prostate adenocarcinoma by an extract of the balsam pear (*Momordica charantia abbreviata)*. Proc. Natl. Acad. Sci. USA, 75 (2): 989-993, 1978.

Cunnick, J.E., Fortner, G.W. and Takemoto, D.J.: In vitro modulation of immune responses by the bitter melon (*Momordica charantia).* J. Cell. Biol. 99 (4): part 2, 333a, 1984.

Day, C.: "Hypoglycaemic compounds from plants" in New antidiabetic drugs. ED. C.J. Bailey and P.R. Flatt, Smith-Gordon , UK, p. 267-278, 1990.

Day, C., Cartwright, T., Provost, J. and Bailey, C.J.: Hypoglycaemic effect of *Momordica charantia* extracts. Planta Med. 56: 426-429, 1990.

Dhalla, N.S., Gupta, K.C., Sastry, M.S. and Malhorta, C.L.: chemical composition of the fruit *Momordica charantia.* Indian P. Pharm. 23: 128-129, 1961.

Dixit, V.P., Khanna, P. and Bhargava, S.K.: Effects of *Momordica charantia L.* fruit extract on the testicular function of dog. Planta Med. 34: 280-286, 1978.

Dubey, D.K., Biswas, A.R., Bapna, J.S. and Pradhan, S.C.: Hypoglycaemic and antihypoglycaemic effects of *Momordica charantia* seed extracts in albino rats. Fitoterapia, LVIII (6): 387-3290, 1987.

Dutta, P.K., Chakravarty, A.K., Chowdhury, U.S. and Pakrashi, S.C.: Vicine, a favism-inducing toxin from *Momordica charantia Linn.* seeds. Indian J. Chem. 20 B, August: 669-671, 1981.

Endo, Y., Tsurugi, K. and Lambert, J.M.: The site of action of six different ribosome inactivating proteins from plants on eukaryotic ribosomes: the RNA N-glycosidase activity of the proteins. Biochem. Biophys. Res. Commun. 150 (3): 1032-1036, 1988.

Falasca, A., Gasperi-Campani, A., Abbondanza, A., Barbieri, L. and Stirpe, E.: Properties of the ribosome-inactivating proteins gelonin, *Momordica charantia* inhibitor and dianthins, Biochem. J. 207: 505-509, 1982.

Fatope, M.O., Takeda, Y., Yamashita, H., Okabe, H. and Yamauchi, T.: New cucurbitane triterpenoids from *Momordica charantia.* J. Nat. Prod. 53 (6): 1491-1497, 1990.

Feng, P.C., Haynes, L.J., Magnus, K.E., Plimmer, J.R. and Sherratt, H.S.A.: Pharmacological screening of some West Indian medicinal plants. J. Pharm. Pharmacol. 14: 556-561, 1962.

Fiche, espece. Fiche espece on *Momordica charantia L.* Medecine tradionelle et pharmacopee 3 (2): 177-194, 1989.

Fischer, L.J.: Drugs and chemicals that produce diabetes. Trends Pharmacol. Sci. 6 (2): 72-75, 1985.

Fletcher, M.A., Caldwell, K.E., Kozlovskis, P., Claflin, A.J., Rubin, R.W. and Lehotay, D.: An inhibitor of tubulin polymerization from *Momordica charantia* var. abbreviata. Fed. Proc. 42 (3): 362, 1983.

Foa-Tomasi, L., Campadelli-Fiume, G., Barbieri, L. and Stirpe, E.: Effect of Ribosome inactivating proteins on virus infected cells. Inhibition of virus multiplication and of protein synthesis. Arch. Virol. 71: 323-332, 1982.

Go, T.T.M., Yeung, H.W. and Fong, W.P.: Deoxyribonucleolytic activity of α- and β-momorcharins. Life Sci. 51: 1347-1353, 1992.

Grover, J.K. and Gupta, S.R.: Hypoglycaemic activity of seeds of *Momordica charantia*. Eur. J. Pharmacol. 183: 1026-1027, 1990.

Guevara, A.P., Lim-Sylianco, C.Y., Dayrit, F.M. and Finch, P.: Acylglucosyl sterols from *Momordica charantia.* Phytochemistry 28 (6): 1721-1724, 1989.

Gupta, S.S.: Experimental studies on pituitary diabetes. Part III. Effect of indigenous anti-diabetic drugs against the acute hyperglycaemic response of anterior pituitary extract in glucose fed albino rats. Indian J. Med. Res. 51: 716-724, 1963.

Handa, G., Singh, J., Sharma, M.L., Kaul, A. and Zafar, R.: Hypoglycaemic principle of *Momordica charantia* seeds. Indian J. Nat. Prod. 6 (1): 16-19, 1990.

Handa, S.S., Chawla, A.S. and Maninder, A.S.C.: Hypoglycaemic plants – a review. Fitoterapia, IX (3): 195-224, 1989.

Higashino, H., Suzuki, A., Tanaka, Y. and Pootakham, K.: Hypoglycaemic effects of Siamese *Momordica charantia* and Phyllanthus urinaria extracts in streptozotocin-induced diabetic rats (the 1st report). Nippon Yakurigaku Zasshi (Folia pharmacol. japon.) 100: 415-421, 1992.

Huang, Q., Liu, S., Tang, Y., Zeng, F. and Qian, R.: Amino acids sequencing of a trypsin inhibitor by refined 1.6 A X-ray crystal structure of its complex with porcine β-trypsin. FEBS Lett. 297 (1,2): 143-146, 1992.

Hulin, A., Wavelet, M. and Desbordes, J.M.: Intoxication aigue par *Momordica charantia* (sorrossi). A propos de deux cas. Semaine des hospitaux 64 (44): 2847-2848, 1988a.

Hulin, A., Wavelet, M. and Desbordes, J.M.: Intoxication aigue par *Momordica charantia* (sorrossi). A propos de deux cas. Medecine d'Afrique Noir 35 (9): 671-674, 1988b.

Ide, H., Kimura, M., Arai, M. and Funatsu, G.: The complete amino acid sequence of ribonuclease from the seeds of the bitter gourd (*Momordica charantia).* FEBS Lett., 284: 161-164, 1991.

Ishikawa, T., Kikuchi, M., Iida, T., Seto, S., Tamura, T. and Matsumoto, T.: Fatty acids and sterols from seed oils of *Momordica charantia*. Chem. Abstr. 105 (7): 57906 r, 1986.

Iyer, R.I., Nagar, P.K. and Sircar, P.K.: Endogenous cytokinins in seeds of bittergourd *Momordica charantia L.* Indian J. Exp. Biol. 18: 766-767, 1981.

Jilka, C., Strifler, B., Fortner, G.W. Hays, E.E. and Takemoto, D.J.: In vivo antitumor activity of the bitter melon (*Momordica charantia)*. Cancer Res. 43: 5151-5155, 1983.

Karunanayake, E.H., Jeevathayaparan, S. and Tennekoon, K.H.: Effect of *Momordica charantia* fruit juice on streptozotocin induced diabetes in rats. J. Ethnopharmacol. 30: 199-204, 1990.

Karunanayake, E.H., Welihinda, J., Sirimanne, S.R. and Sinnadorai, G.: Oral hypoglycaemic activity of some medicinal plants of Sri Lanka. J. Ethnopharmacol. 11: 223-231, 1984.

Kedar, P. and Chakrabarti, C.H.: Effects of bittegourd (*Momordica charantia*) seed and glibenclamide in streptozotocin induced diabetes mellitus. Indian J. Exp. Biol. 20: 232-235, 1982.

Khan, M.I., Mazumder, T., Pain, D., Gaur, N. and Surolia, A.: Binding of 4-methylumbelliferyl β-D galactopyranoside to *Momordica charantia* lectin. Eur. J. Biochem. 113: 471-476, 1981.

Khanna, P., Jain, S.C., Panagariya, A. and Dixit V.P.: Hypoglycaemic activity of polypeptide-p from a plant source. J. Nat. Prod. 44 (6): 648-655, 1981.

Khanna, P., Nag, T.N., Jain, S.C. and Mohan, S.: Indian Patent No. 136565, 1974.

Khanna, P.: Insulin from Bitter gourd. The Eastern Pharmacist, July 1985: p. 101-102, 1985.

Kikuchi, M., Ishikawa, T., Iida, T., Seto, S., Tamura, T. and Matsumoto, T.: Triterpene alcohols in the seed oils of *Momordica charantia L.* Agri. Biol. Ch. 50 (11): 2921-2922, 1986.Kirti, S., Kumar, V., Nigam, P. and Srivastava, P.: Effect of *Momordica charantia* (karela) extract on blood and urine sugar in diabetes mellitus – study from a diabetic clinic. Clinician 46 (1): 26-29, 1982.

Kulkarni, R.D. and Gaitonde, B.B.: Potentiation of tolbutamide action by jasad bhasma and karela (*Momordica charantia).*Indian J, Med. Res. 50 (5): 715-719, 1962.

Lakshminarayana, G., Kaimal, T.N.B., Mani, V.V.S., Sita Devi, K. and Chandrasekhara Rao, T.: Fatty acid changes during maturation of *Momordica charantia* and Trichosanthes anguina seeds. Phytochemistry 21 (2): 301-303, 1982.

Lal, J., Chandra, S., Gupta, S. and Tandan, S.K.: Studies on anti-convulsant and anti-inflammatory actions of extracts of *Momordica charantia.* Indian Vet. J. 67: 82-83, 1990.

Leatherdale, B.A., Panesar, R.K., Singh, G., Watkins, T., Bailey, C.J. and Bignell, A.H.: Improvement in glucose tolerance due to *Momordica charantia* (karela). M.M.J. 282: 1823-1824, 1981.

Lee-Huang, S., Huang, P.L., Nara, P.L., Chen, H.C., Kung, H.E., Huang, P., Hunag, H.L., and Huang, P.L.: MAP 30: a new inhibitor of HIV-1 infection and replication. FEBS Lett. 272 (1,2): 102-18, 1990.

Li, S.S.L.: Purification and characterization of seed storage proteins from *Momordica charantia*. Experientia 33: 895-896, 1977.

Li, S.S.L.: Purification and partial characterization of two lectins from *Momordica charantia.* Experientia 36: 524-527, 1980.

Lifson, J.D., McGrath, M.S., Yeung, H.W. and Hwang, K.: International Patent No. W088/0912 (1988).

Lin, J.Y., Hou, M.J. and Chen, Y.C.: Isolation of toxic and nontoxic lectins from the bitter pear melon *Momordica charantia Linn.* Toxicon 16: 653-660, 1978.

Lodikar, M.M. and Rajarama Rao, M.R.: Note on a hypoglycaemic principle isolated from the fruits of *Momordica charantia.* J. univ. Bombay 29: 223-4, 1960-1961.

Lodikar, M.M. and Rajarama Rao, M.R.: Pharmacology of a hypoglycaemic principle isolated from the fruits of *Momordica charantia Linn*. Indian J. Pharm. 28 (5): 129-133, 1966.

Marles, R.J. and Fansworth, N.R.: Antidiabetic plants and their active constituents. Phytomedicine 2 (1): 137-189, 1995.

Marquis, V.O., Adanlawo, T.A. and Olaniyi, A.A.: The effect of Foetidin from Momordica Foetida on blood glucose level of albino rats. Planta Med. 31: 367-374, 1977.

Mazumder, T., Gaur, N. and Surolia, A.: The physicochemical propertiets of the galactose-specific lectin from *Momordica charantia.*_Eur. J. Biochem. 113: 463-470, 1981.

Meir, P., and Yaniv, Z.: An in vitro study on the effect of *Momordica charantia* on glucose uptake and glucose metabolism in rats. Planta Med. 3: 12-16, 1985.

Minami, Y. and Funatsu, G.: The complete amino acid sequence of momordin-a, a ribosome inactivating protein from the seeds of bitter gourd (*Momordica charantia)*. Biosci. Biotech. Biochem. 57 (7): 1141-1144, 1993.

Minami, Y., Nakahara, Y. and Funatsu, G.: Isolation and characterization of two momordins, ribosome-inactivating proteins from the seeds of bitter gourd (*Momordica charantia)*. Biosci. Biotech. Biochem. 56 (9): 1470-1471, 1992.

Miyahara, Y., Okabe, H. and Yamauchi, T.: Studies on the constituents of *Momordica charantia L*. II. Isolation and characterisation of minor seed glycosides, Momordicosides C, D and E. Chem. Pharm. Bull. 29 (6): 1567-1579, 1981.

Mosihuzzaman, M., Nahar, N., Mamun, I.R. and Nasrin, T.: Hypoglycaemic agents from *Momordica charantia* fruit pulp. Abstract from Eight Asian Symposium on Medicinal Plants, Species and other Natural Products, held in Malaysia, p. 109, 1994.

Nadkarni, A.K.: Indian Materia Medica (3rd ed). Publ. Popular Prakashan PVT Ltd., Bombay. Volume 1, p. 805-807, 1982.

Ng, T.B., Liu, W.K., Tsao, S.W. and Yueng,. H.W.: Effect of trichosanthin and momorcharins on isolated rat hepatocytes. J. Ethnopharmacol. 43: 81-87, 1994.

Ng, T.B., Wong, C.M. and Li, W.W.: Effects of acid ethanol-extractable compounds from *Momordica charantia* fruits and seeds on lipid metabolism in isolated rat adipocytes, in

"Advances in Chinese Medicinal Materials Research." Eds Chang, H.M., Yeung, H.W., Tso, W.W. and Koo, A. World Scientific Publishing Co PLC Ltd. Singapore, Philadelphia, p. 685, 1985.

Ng, T.B., Wong, C.M. and Li, W.W. and Yeung, H.W.: Insulin-like molecules in *Momordica charantia* seeds. J. Ethnopharmacol. 15: 107-117, 1986 a.

Ng, T.B., Wong, C.M. and Li, W.W. and Yeung, H.W.: A steryl glycoside fraction from *Momordica charantia* seeds with an inhibitory action on lipid metabolism in vitro. Biochem. Cell Biol. 64: 766-771, 1986 b.

Ng, T.B., Wong, C.M. and Li, W.W. and Yeung, H.W.: Isolation and characterization of a galactose binding lectin with insulinomimetic activities. Int. J. Pept. Protein. Res. 28: 163-172, 1986 c.

Ng, T.B., Wong, C.M. and Li, W.W. and Yeung, H.W.: Peptides with antilipolytic and lipogenic activities from seeds of the bitter gourd *Momordica charantia* (family Cucurbitaceae). Gen. Pharmacol. 18 (3): 275-281, 1987 a.

Ng, T.B., Li, W.W. and Yeung, H.W.: Effects of ginsenosides, lectins and *Momordica charantia* insulin-like peptide on corticosterone production by isolated rat adrenal cells. J. Ethnopharmacol. 21: 21-29, 1987 b.

Okabe, H., Miyahara, Y., Yamauchi, T., Miyahara, K. and Kawasaki, T.: Studies on the Constituents of *Momordica charantia L.* I. Isolation and characterization of Momordicosides A and B, glycosides of a pentahydroxy-cucurbitane triterpene. Chem. Pharm. Bull. 28 (9): 2753-2762, 1980.

Okabe, H., Miyahara, Y. and Yamauchi, T.: Studies on the constitutuents of *Momordica charantia L.* III. Characterisation of new cucurbitacin glycosides of the immature fruits (I). Structures of Momordicosides G, F_1, F_2 and I. Chem. Pharm. Bull. 30 (11): 3977-3986, 1982 a.

Okabe, H., Miyahara, Y. and Yamauchi, T.: Structure of Momordicosides F_1 F_2 G, I, L, novel cucurbitacins in the fruits *of Momordica charantia L.* 23 (1) : 77-80, 1992 b.

Okabe, H., Miyahara, Y. and Yamauchi, T,: Studies on the constituents of Momordica charantia *L.*, IV. Characterization of the new cucurbitacin glycosides of the immature fruits (2). Structure of the bitter glycosides, Momordicosides K and L. Chem. Pharm. Bull. 30 (12): 4334-4340, 1982 c.

Olanilyi, A. A.: A neutral constituent of Momordica foetida. Lloydia 38 (4): 361-362, 1975.

Pan, Q. C., Xian, L.J. and Yeung, H.W.: Anticancer effects of protein fractions from *Tricosanthes kirilowii* and *Momordica charantia* , in "Advances in Chinese Medicinal Materials Research" , Eds. Chang, H.M., Yeung, H.W., Tso, W.W. and Koo, A. World Scientific Publishing Co PLC Ltd. Singapore, Philadelphia, p. 674, 1985.

Patel, J.C., Dhirawani, M.K. and Doshi, J.C., "Karella" in the treatment of diabetes meliitus. Idian J. Med. Sci. 22: 30-32, 1968.

Perl, M.: "The biochemical basis of the hypoglycemic effects of some plants extract" in Herbs, spices and medicinal plants: recent advances in botany, horticulture and

pharmacology, Volume 3, p.49-70. Eds Lyle E. Craker, James E. Simon. Oryx Press, 1988.

Platel , K., Shurpalekar, K.S. and Srinivasan, K.: Influence of bitter gourd (*Momordica charantia*) on growth and blood constituents in aibino rats. Die Nahrung 37 (2): 156-160, 1993.

Pusztai, A.: The biological effects of lectins in the diet of animals and man in "Lectins", Vol V. Walter de Gruyter and Co. Berlin. New York, 1986.

Rao, S.M.A.: Oxygen free radical scavenging activity of the juice of *Momordica charantia* fruits. Fitoterapia LXII (4) : 344-346, 1991.

Rivera, G.: Preliminary chemical and pharmacological studies on "Cundeamor," *Momordica charantia L.* (Part 1). Am. J. Pharm. 113(7): 281-296, 1941.

Saito, T. and Kato, N.: Linolenoyglucopyranosylclerosterol as a *Dacus cucubitae* attractant. Japan Kokai Tokkyo Koho JP. 62-26295 (Japanese patent), 198 b.

Saito, T. and Kato.: Galactopyranosyldilinolenoylglycerol as a *Dacus cucurbitae* attractant. Japan Kokai Tokkyo Koho JP. 62-26292 (Japanese), 1987 b.

Sharma, V.N., Sogani, R.K. and Arora, R. B.: Some observations on hypoglycaemic activity of *Momordica charantia.* Indian J. Med. Res. 48: 471-477, 1960.

Shibib, B. A., Khan, L. A. and Rahman, R.: Hypoglycaemic activity of *Coccinia indica* and *Momordica charantia* in diabetic rats : depression of the hepatic gluconcogenic enzymes glucose-6-phosphatase and fructose-1,6-bisphosphatase and elevation of bothe liver and red-cell shunt enzyme glucose-6-phosphate dehydrogenase. Biochem. J. 292: 267-270. 1993.

Shum, L.K. W., Ooi, V.E.C. and Yeung, H. W.: Effects of *Momordica charantia* seed extract on the rat mid-term placenta, in "Advances in Chinese Medicinal Materials Research". Eds Chang, H.M., Yeung, H.W. Tso, W.W. and Koo,A. World Scientific Publishing Co. PLC Ltd. Singapore, Philadelphia, p.679, 1985.

Spreafico, E., Malfiore, C., Moras, M. L., Marmonti, L., Filippeschi, S., Barbieri, L., Perocco, P. and Stirpe, E.: The immunomodulatory activity of the plants proteins *Momordica charantia* inhibitor and pokeweed antiviral protein. Int. J. of immunopharmacol. 5 (4): 335-343, 1983.

Srivastava, Y., Venkatakrishna-Bhatt, H., Verma, Y. and prem, A. S.: Retardation of retinopathy by *Momordica charantia L.*, (bitter gourd) fruit extract in alloxan diabetuc rats. Indian J. Exp. Biol. 25: 571-572, 1987.

Srivastava, Y., Venkatakrishna-Bhatt, H. and Verma, Y.: Effects of *Momordica charantia Linn*. pomous aqueous extract on cataractogenesis in murrin alloxan diabetic. Pharmacol. R. Commun. 20 (3): 201-209, 1988.

Srivastava, Y., Venkatakrishna-Bhatt, H., Verma, Y., Venkaiah, K. and Raval, B. H.: Antidiabetic and adaptogenic properties of *Momordica charantia* extract: An experimental and clinical evaluation. Phytother. Res. 7: 285-289, 1993.

Stepka, W., Wilson, K. E. and Madge, G. E.: Antifertility investigation on *Momordica charantia*. Lloydia 37: 645, 1974.

Sucrow, W.: Uber Sterlingglucoside und ein neues Stigmastadienol aus *Momordica charantia*. Tetrahedr. L. 26: 2217-2221, 1965.

Sucrow, W.: Inhaltsstoffe von *Momordica charantia L*., I.-5.25-Stigmastadienol-(3β) und sein β-D-glucosid. Chemische Berichte 99: 2765-2777, 1966.

Swanston-Flatt, S. K., Flatt P., Day, C. and Bailey, C. J.: Traditional dietary adjuncts for the treatment of diabetes mellitus. Proc. Nutr. Soc. 50; 641-651, 1991.

Takemoto, D.J., Jilka, C. and Kresie, R.: Purification of a cytostatic factor from the bitter melon (*Momordica charantia*). Fed. Proc. 41 (4): 1392, 1982 a.

Takemoto, D. J., Jilka, C. and Kresie.: Purification and characterization of a cytostatic factor from the bitter melon *Momordica charantia*. Prep. Biochem. 12 (4): 355-375, 1982 b.

Takemoto, D. J., Jilka, F., Fortner, W. and Cunnick, J.: Characterization of an anti-lymphoma factor from the bitter melon (*Momordica charantia*). Fed. Proc. 43 (4): 950, 1984.

Tennekoon, K. H., Jeevathayaparan, S., Angunawala, P., Karunanayake, E. H. and Jayasinghe, K. S. A.: Effect of *Momordica charantia* on key hepatic enzymes. J. Ethnopharmacol. 44: 93-97, 1994.

Tiangda, C., Mekmanee, R., Praphapraditchote, K., Ungsurungsie, M. and paovalo, C.: The hypoglycaemic activity of *Momordica charantia Linn*. in normal and alloxan-induced diabetic rabbits. Journal of the National Research Council 19 (1): 1-11, 1987.

Ulubelen, A. and Sankawa, U.: Steroids and hydrocarbons of the leaves of *Momordica charantia*. Revista latinoamericana de quimoterapia 10 (4): 171-173, 1979.

Venkanna Babu, B., Moorti, R., Pugazhenthi, S., Prabhu, K. M. and Murthy, P. S.: Alloxan recovered rabbits as animals model for screening for hypoglycaemic activity of compounds. Indian J. Biophys. 25; 714-718, 1988.

Venkataramaiah, C. and Rao, K. N.: Studies on indolyl-3-acetic acid oxidase and phenolic acid pattern in Cucurbitaceous fruits. Z. Pflanzenphysiologic 111 (5): 459-463, 1983.

Vesely, D. L., Graves, W. R., Lo, T. M., Fletcher, M. A. and Levey, G. S.: Isolation of a guanylate cyclase inhibitor from balsam pear (*Momordica charantia abbreviata*). Biochem. Biophys. Res. Commun. 77 (4): 1294-1299, 1997.

Walters, W. and Decker-Walters, D. S.: Notes on Economic plants. Econ. Botan 42 (2) : 286-292, 1988.

Welihinda, J., arvidson, G., Gylfe. E., Hellman. B. and Karlsson, E.: The insulin-releasing activity of the tropical plant *Momordica charantia*. Acta Biologica et Medica 41 (12): 1229-1240, 1982 a.

Welihinda, J., Glylfe, E., Karlsson, E., and Hellmann, B.: Effects hypoglycemic plant extract (*Momordica charantia*) on isolated pancreatic islets rich in β-cells. Act. Endoer. 100: 5247, 1982 b.

Welihinda, J. and Karunanayake, E, H.: Extrapancreatic effects of *Momordica charantia* in rats. J. Ethnopharmacol. 17: 247-255, 1986.

Welihinda, J., Karunanayake, E. H., Sherilf, M. H. R. and Jayasinghe, K. S. A.: Effects of *Momordica charantia* on the glucose tolerance in maturity onset diabetes. J. Ethnopharmacol. 17: 277-282, 1986.

West, M. E., Sidrak, G. H. and Street, S. P. W.: The anti-growth properties of extract from *Momordica charantia L*. West Indian J. Med. XX: 25-34, 1971.

Wong, C. M., Ng, T. B., Li, W. W. and Yeung, H. W.: Compounds of *Trichosanthes kurilowii* roots and *Momordica charantia* fruits and seeds with antilipolytic activity in isolated rat adipocytes, in "Advances in Chinese Medicinal Materials Research". Eds. Chang, H. M., Yeung, H. W., Tso, W. W. and Koo, A. World Scientific Publishing Co PLC Ltd. Singapore, Philadelphia, p.685, 1985 a.

Wong, C. M., Ng., T. B. and Yeung, H. W. : Screening of *Trichosanthes kurilowii*, *Momordica charantia* and Cucurbita maxima (family Cucurbitaceae) for compounds with antilipolytic activity. J. Ethnopharmacol. 13: 313-321, 1985 b.

Yasuda, M., Iwamoto, M., Okabe, H. and Yamauchi, T.: Structures of Momordicines I, II and III, the bitter principles in the leaves and vines of *Momordica charantia L*. Chem. Pharm. Bull. 32 (5): 2044-2047, 1984.

Yeung, H. W., Li, W. W., Chan, W. Y., Law, L. K. and Ng., T. B.: Alpha and beta momorcharins. Int. J. Pept. Protein Res. 28: 518-524, 1986.

Yuwai, K. E., Sundar Rao, K., Kaluwin, C., Jones, G. P. and Rivett, D. E.: Chemical composition of *Momordica charantia Linn*. fruits. J. Agr. Food Chem. 39: 1762-1763, 1991.

Zhang, Q. C.: Bitter melon: a herb warranting a closer look. PWA Coalition Newsline, October 1992, Issue 81, 48-49, 1991 a.

Zhang, Q. C.: Preliminary report on the use of *Momordica charantia* extract by HIV patients.. J. Naturpath. Med. 3 (1): 65-69, 1992 b.

ADDRESS

A. Raman, Pharmacognosy Research Laboratories, Department of Pharmacy, King's College London, Manresa Road, London SW 3 LX, UK.