**REVIEW**

**A Review: *Momordica charantia* L.'s Biological Active Components and Its Potential Use in Traditional Therapies**

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**Abstract**
The use of herbs for therapeutic purposes has been widespread since ancient times. In traditional treatments, plants are applied in a variety of forms, either directly or prepared by isolation and / or enrichment of biologically active ingredients. *Momordica charantia* L. (bitter melon) is a popular bush that has traditional use as a supplement in the treatment of various diseases with its rich bioactive ingredient content. The plant has common pharmacological potential, including antimicrobial, antimutagenic, antifertility, antidiabetic, antioxidant, antilipolytic, hypoglycemic, anticancer, antimicrobial, antiviral and hepatoprotective activities. This review provides a short overview of the in vitro, in vivo and clinical studies conducted to evaluate the therapeutic efficacy and safety of *Momordica charantia*.

**Keywords:** *Momordica charantia*, Bitter melon, Traditional Medicine.

**INTRODUCTION**
The use of medicinal and aromatic herbs in traditional treatments dates back to very old years. There are many of traditional and herbal medicinal products that are used as supplements for the treatment of many diseases. Most known drug active substances are molecules that have been isolated from natural products and have been tested for efficacy. The use of molecules isolated from plants as medicine dates back to the 1800s. The vast majority of drugs approved until 1990 are molecules with natural products or derivatives1. In addition, the mixture of many active substances obtained by extraction of natural products with various solvents can show a synergistic effect and respond much more effectively to traditional treatment than a single chemical molecule will show. Therefore, extraction, purification and efficacy studies of natural products in the field of traditional medicine is an area that is always explored from ancient times until today without losing its importance. Evidence-based assessment of the efficacy and safety of components isolated from medicinal and aromatic plants is important for traditional medicine to be based on safe foundations. For purposeful safe applications of herbal supplements, it is necessary to conduct experiments to determine the effectiveness of natural products commonly known in traditional therapy with in vitro, in vivo and clinical studies. All parts of the *Momordica charantia* L. (bitter melon) plant from the Cucurbitaceae family have bitter taste. Members of the Cucurbitaceae family have medicinal and nutritionally beneficial plants that contain many components with pharmacological activity. *M. charantia* is rectangular like and looks like a small cucumber. The young fruit becomes emerald green and turns orange yellow when it ripens. The seeds are reddish in color. Despite being of Asian origin, it has a wide distribution in various parts of the world, including Central and South America and Africa2. *M. charantia* contains many biologically active compounds such as glycosides, oils, alkaloids, proteins, triterpenes, saponins and steroids.
Unripen fruits are a storage of vitamin C, but also have phosphorus, Vitamin A, and iron content. Bioactive compounds are isolated from fruit, seeds and leaves of the plant. As a result of phytochemical analysis studies on *M. charantia* plant, it was determined that the plant contains cardiac glycoside, alkaloid, tannin, flavonoid, saponin and steroid group chemicals. Phytosterol groups with up to 30 carbon atoms in total have been reported to have anticancer, atherosclerotic, anti-inflammatory and antioxidant activities. Terpenoid derivatives are known to have anti-inflammatory and anticancer activities. Six new triterpenoids isolated from *M. charantia* have been reported to cause up to 72.4% blockade and no cytotoxicity on proliferation of vascular smooth muscle cells. Thus, it has been noted that *M. charantia* is rich in supportive bioactive molecules in the treatment of cardiovascular diseases through inhibition of proliferation of vascular smooth muscle cells. *M. charantia* has high level of fatty acids. It contains fatty acids, that reduce the risk of developing cardiovascular disease such as omega-3. It has been reported that the fatty acid content may act as antimicrobial agents against bacteria and fungi. Phenolic compounds containing coumarins, phenolic acids, lignins, tannins, lignanes and flavonoids are among the secondary metabolites that are abundant in the plant. Phenolic compounds in *M. charantia* have important activities such as antimicrobial, antioxidant, anticancer and anti-HIV-1 activities. These activities of *M. charantia*, which is a plant species rich in biological activity, are thought to originate from rich complex chemical compounds such as flavonoids, tannins, carbohydrates, resins, terpenoids, anthraquinones, saponins, sterols, phlobatamines, amino acids, glycosides, fatty acids and phenolic compounds. Bioactive compounds can be extracted with the help of many different organic solvents using traditional extraction techniques and new technological techniques. Polysaccharides are primary active ingredients that perform various pharmacological activities of *M. charantia*. There are studies investigating the blood sugar levels of the polysaccharides isolated from the plant and their biological activities on the regulation of antioxidant, antibacterial, antitumor and immune system functions. MAP30, a 30 kDa protein isolated from seeds, has been proposed as the agent responsible for antiviral and antineoplastic properties. *M. charantia*’s chemicals responsible for hypoglycemic action are a mixture of steroidal saponins known as charantins, alkaloids and insulin-like peptides. Therefore, it is recommended to consume *M. charantia* fruit extracts for antihyperglycemic activity.

It is known that *M. charantia* provides a very good supportive treatment in the treatment of diabetes in lowering blood glucose levels, in the treatment of inflammatory wounds, in nutritive disorders such as stomach and intestines. It is also known to be used as a supportive in the treatment of various infections, in preventing tumor formation, in the treatment of measles, hepatitis, HIV and AIDS viruses, in the treatment of diseases such as infertility, gastrointestinal cramps, cancer, eczema and psoriasis. α- and β- momarcharin are two proteins in the *M. charantia* that are known to inhibit the AIDS virus. It is known to use both internally and externally for the prevention of worms and parasites locally for the treatment of wounds. Ripe fruits are used for traditional therapies for skin wound healing externally and against to peptic ulcer internally in Turkey. Studies on antidiabetic, antitumor, antioxidant, antileukemic, antibacterial, immunostimulant, anthelmintic, antiviral, antimutagenic, hypocholesterolemic, antivulcer, anti-inflammatory, insecticidal, hypotriglycerideremic, hypotensive and antimycobacterial properties of *M. charantia* are common.

**POSSIBLE BIOLOGICAL ACTIVITIES OF M. CHARANTIA**

**Hypoglycemic activity**

There are numerous in vitro, in vivo and few clinical studies supporting the use of *M. charantia* as whole fruit, extract or dried powder, which can lower blood sugar levels. In line with these studies, it is common to use *M. charantia* as an alternative to decrease blood sugar levels in the treatment of diabetes. There are numerous in vitro, in vivo and few clinical studies supporting the use of *M. charantia* as whole fruit, extract or dried powder, which can lower blood sugar levels. In line with these studies, it is common to use *M. charantia* as an alternative to decrease blood sugar levels in the treatment of diabetes.
type 2 diabetes. In the component analysis of *M. charantia* extract, it has been shown that the components showing structural similarities to animal insulin are responsible for the hypoglycemic effect. In general, it has been suggested that *M. charantia* polysaccharides have a significant effect on hypoglycaemia. Polysaccharides have been reported to have protective and reparative effects on pancreatic islet tissue and the ability to reduce blood sugar. Polysaccharides are thought to exhibit antihyperglycemic activity by improving glucose tolerance, glucose intestinal absorption, or improving glucose metabolism. In addition, a mixture of polypeptides called "polypeptide p" isolated from seeds and two steroid glycosides specified as "charantin" are other chemical molecules reported to have hypoglycemic properties. *M. charantia* aqueous extract has been reported to be a safe alternative for lowering blood sugar levels. Glucosaminoglycans isolated from plant fruits have been found to have beneficial effects on diabetes metabolism. It has been reported that the mixture of maximum molecular weight alkali polysaccharides extracted from *M. charantia* polysaccharides has the best antihyperglycemic effect and can lower blood sugar levels through increased insulin secretion from Beta cells.

A water-soluble polysaccharide isolated from *M. charantia* fruits has been reported to reduce blood glucose levels and increase glucose tolerance in alloxane-induced diabetic mice. Water-soluble polysaccharides can increase insulin secretion in streptozotocin-induced diabetic mice by repairing injured pancreatic islet tissues. Another study has shown that by reducing the amount of *M. charantia* polysaccharides, the glucose level increases significantly and *M. charantia* polysaccharides can be a potential antidiabetic agent. *M. charantia* methanol extract has been shown to exhibit hypoglycemic activity in diabetic albino rats due to alloxan. Various *M. charantia* extracts have been reported to lower high glucose levels in diabetic rats. In diabetic rat models, the ethanol extract of fruit pulp at a dose of 500 mg / kg body weight has been reported to reduce glucose levels 1 hour after administration. It has been reported that aqueous extract and alkaline chloroform extract reduce blood sugar levels 1 hour after application. In diabetic rats and glucose-dependent hyperglycemic rats, it has been reported that the blood sugar levels of the fruit of the plant are lowered half an hour after administration of the methanol extract and water extract. It has also been observed that the extract increases thyroxine levels, normalizes glucose levels, and maintains the normal lipid profile in diabetic rats fed a normal diet or fed a high-fat, low-carb diet. It has been reported that the glucose level is normalized and the effect is protected for 15 days in diabetic rats fed with the acetone extract of the fruit for a long time. Hypoglycemic effects of the aqueous extract of the whole plant have been reported in rats. The plant reduced plasma and hepatic triglyceride content and tissue fat accumulation. It has been noted that plasma and liver lipid parameters improve in diabetic rats fed a cholesterol-rich diet and a high-fat diet. The possible hepatoprotective effect of *M. charantia* in diabetic rats has been investigated. A group of male Sprague Dawley rats were treated with *M. charantia* ethanol extract after treatment according to known protocols. The liver of the animals was examined at 10 weeks, blood was collected by cardiac puncture and centrifuged to collect the serum. While blood glucose levels increased consistently in all groups without *M. charantia* treatment, the increase in blood glucose levels in the group treated with ethanol extract became close to normal. It has been reported that while the markers of liver damage showed a significant increase in the group that did not receive *M. charantia* treatment, it could be used as a supplement in alleviating liver damage in the treatment group. In another study, the mechanisms of the renoprotective effects of *M. charantia* in diabetic rats were investigated. The application of *M. charantia* extract has been reported to restore kidney function, reduce weight loss and restore blood sugar levels to normal levels. The effect of *Lactobacillus plantarum*...
fermentation on the antidiabetic functionality of *M. charantia* was investigated using a type 2 diabetic rat model. Fermented *M. charantia* juice administration has been reported to reduce hyperinsulinemia, hyperglycemia, hyperlipidemia and oxidative stress well than its non-fermented counterpart in diabetic rats. Diabetic rats treated with fermented *M. charantia* juice showed higher concentrations of acetic acid, propionic acid, butyric acid, total short-chain fatty acids and lower pH values in colonic contents than rats treated with unfermented *M. charantia* juice. These results showed that *L. plantarum*-fermentation increases the antidiabetic property of *M. charantia* juice by disrupting the regulation of the intestinal microbiota and the production of short-chain fatty acids. *M. charantia* has been shown to permanently normalize blood sugar levels comparable to healthy rats. In treated rats, the expression of insulin and Pdx1 genes increased, and Glut2 expression decreased. Liver ALT, AST and ALP enzyme activities have fallen to the normal range in the treatment group to support the protective effect of *M. charantia*. These data showed that the plant improves pancreatic function by activating pancreatic beta cells and protecting liver tissue.

The juice of *M. charantia* has been reported to improve glucose tolerance in 73% of patients with beginner diabetes, while 27% of patients are unable to respond. The effects of *M. charantia* PEG and *M. charantia* adsorbed with nanofraction extracts on blood rheological parameters in hyperglycemic patients were clinically investigated. Blood samples of 56 normoglycemic individuals and 26 hyperglycemic patients were collected, their general characteristics, rheological parameters and hematological features were determined. Whole blood viscosity was evaluated after treatment with PEG microspheres adsorbed with *M. charantia* extract, PEG and *M. charantia* nanofraction extracts. Although the viscosity of the blood of hyperglycemic patients is higher than that of normoglycemic individuals, it has been noted that the nanoparticles of *M. charantia* extracts reduce blood viscosity equally in normo and hyperglycemic individuals.

It has been noted that PEG microspheres do not reduce blood viscosity in hyperglycemic patients but PEG microspheres adsorbed with plant nanofraction extract reduce blood viscosity. Based on clinical study data, it has been reported that the use of nanoparticle extract of *M. charantia* and PEG microspheres adsorbed with nanofraction extract may play a role in the treatment of blood disorders in diabetic patients. The effects of *M. charantia* on blood sugar levels in patients with type 1 or type 2 diabetes were investigated. For diabetic patients treated with *M. charantia*, an average decrease in serum glucose levels was noted within 30 minutes. At the end of the 4-hour period, the maximum decrease in serum glucose levels was observed with a rate of 49.2%, while after 12 hours, a permanent 28% decrease was observed. A clinical study was conducted with a group of 9 type 2 diabetic patients, 8 of whom received simultaneous sulfonyl urea.

Subjects were initially given 50 ml of *M. charantia* juice and received 0.23 g of *M. charantia* fruit daily over the next 8-11 week period, and then glucose tolerance tests were performed. The test results, which were applied 1 hour after 50 ml of juice consumption, showed a 12% decrease in blood glucose level. The test, performed 1 hour after the intake of 0.23 g of fruit, showed a decrease of about 6% in glucose levels. It has been noted that after consuming 0.23 g of *M. charantia* for 8-11 weeks, an 8% decrease in glucose levels was observed from the first value. In another clinical study, the effect of *M. charantia* juice on blood glucose levels was investigated in a case series of 18 patients diagnosed with type 2 diabetes. Individuals were given 100 ml of *M. charantia* juice 30 minutes prior to glucose loading. When the glucose tolerance test results before supplementation were compared with the results after treatment, it was observed that 13 patients showed a moderate improvement after taking *M. charantia*. A clinical study was conducted with a group of 12 patients with type 2 diabetes who were not treated other than diabetic diets for 3 weeks. 5 patients received 3 g of dried fruit powder 3 times a day. In 7
patients, 100 ml of the extract of 100 g M. charantia powder prepared by boiling in water was given once every morning. While a 25% decrease in blood sugar level was observed in the patient group receiving dry powder, a significant decrease was observed in the blood sugar level with an average of 54% in the patient group receiving an aqueous extract.

When evaluating in vitro, in vivo and clinical studies, M. charantia extracts have been reported to show a moderate hypoglycemic effect. It is reported that the use of as a supportive therapy in diabetic patients may be an important traditional herbal supplement if it is evaluated and adjusted in dosage with co-consumed drugs.

**Antibacterial activity**

Poultry-related Bacillus spp and α-glucosidase activities and antiobesity properties of M. charantia fruit extract were evaluated. As a result of the test, it was observed that the ethanolic extract showed pronounced antibacterial properties against B. licheniformis. The antiobesity potential of fruit extracts has been shown for porcine pancreatic lipase activity. The ethanolic extract of M. charantia fruits has been observed to cause inhibition of the pancreatic lipase enzyme. When the data obtained in the study were evaluated, it was reported that M. charantia fruits may be effective in inhibition of bacterial pathogens related to poultry.

Polysaccharides isolated from M. charantia have been reported to have significant inhibitory effects on bacteria. It has been shown that the main components of M. charantia responsible for antimicrobial functions are polysaccharides. It has been reported that M. charantia polysaccharides have a good bacteriosis activity in B. subtilis, S. aureus, S. typhimurium and E. coli and the most obvious effect is the effect on S. aureus. In the study conducted to determine different concentrations and pH values of M. charantia polysaccharides acting on S. aureus, A. niger, E. coli and A. oryzae, it was shown that antibacterial effect of polysaccharides was significantly affected by pH value and showed a positive correlation with the concentration.

**Immunomodulatory activity**

In vitro experiments have shown that M. charantia oligosaccharides can increase immunity by stimulating the activation of lymphocytes and macrophages. In another in vitro study, M. charantia polysaccharides have been reported to have significant immunomodulatory activity. It has been reported that the water-soluble polysaccharide isolated from M. charantia may increase endothelium-derived relaxing factor production in the cell proliferation, the development of the inflammatory and immune response, and stimulate splenocytes and thymocytes.

In immunosuppressed mice from cyclophosphamide, it has been reported that carbolic particle clearance index, production of serum hemolysis, spleen index, thymus index and natural killer cell cytotoxicity can be increased compared to normal control levels by M. charantia polysaccharides. It has been reported that the aqueous extract can increase the phagocytic index and the percentage of adhesion of high doses of neutrophils to nylon buffers increased significantly compared to normal control animals.

**Anti-inflammatory activity**

It is known that oxidative stress and inflammation activate each other and oxidative stress plays a role in chronic infectious diseases. The beneficial properties of M. charantia appear to be due to anti-inflammatory and antioxidant activities. M. charantia shows anti-inflammatory effects by acting on several important signal pathways involved in inflammation. Momordicoside G, one of the bioactive components of M. charantia, has been reported to contribute to the repair of lung injuries. The anti-inflammatory properties of BG-4, a new bioactive peptide isolated from M. charantia seed, have been evaluated and reported to have an anti-inflammatory effect by reducing the production of intracellular reactive oxygen species.

The wound-healing activity of the olive oil macerate of M. charantia was investigated in the linear incision and circular excision wound models. It has been noted that M. charantia olive oil...
macerate shows healing activity in incision and excision wound models and shows 31.3% anti-inflammatory activity. Experimental data have shown that *M. charantia* has wound-healing and anti-inflammatory effects. It is known that *M. charantia* plays a role in wound healing by increasing oxygenation by accelerating the production of growth factors, ensuring the proliferation of fibroblast cells and accelerating capillary circulation. The antioxidant and antimicrobial effects of phytochemicals in the plant content are thought to play a role in accelerating the wound healing process. *M. charantia* supplements are thought to play a role in reducing inflammation, obesity and insulin resistance in obese mice by normalizing the serum levels of cytokines. *M. charantia* powder supplementation has been reported to reduce systemic inflammation in obese mice fed a high-fat diet.

The therapeutic role of polysaccharides in *M. charantia* and their mechanisms of action against gastric ulcers from ethanol have been investigated and reported to play a role in suppressing gastric inflammation. *M. charantia* fruit extract supplement has been reported to significantly reduce neuro-inflammation and contribute to the improvement of neurodegenerative diseases.

*M. charantia* extracts have been found to alleviate *P. acnes*-induced bacterial skin inflammation in mice. It has been reported that this effect may be due to the anti-inflammatory effects of phenolic compounds. In mice fed high-fat diets for 16 weeks, it was observed that *M. charantia* juice reduced fat inflammation by 60% and prevented inflammation of colon and intestinal microbial dysbiosis. Based on these, *M. charantia* has been reported to have the potential to be supportive in the treatment of inflammatory diseases such as obesity and type 2 diabetes.

In a clinical study performed by applying *M. charantia* to 38 patients with primary knee osteoarthritis and placebo supplementation to 37 patients for 3 months, the effect of *M. charantia* on reducing pain in patients with primary knee osteoarthritis was evaluated. After 3 months of supplementation, *M. charantia* group significantly reduced body weight, body mass index and fasting blood sugar, and significant improvements in knee osteoarthritis were observed. The study showed that *M. charantia* can offer an alternative to reducing the need for analgesic drug consumption by reducing pain and improving symptoms in diseased individuals.

**Antioxidant activity**

The antioxidant activities of *M. charantia* polysaccharides have been extensively studied and have been shown to exhibit significant antioxidant activity. While polysaccharides are reported to be the main source of antioxidant activity, it has been noted that uronic acid and proteins can strengthen antioxidant activity. It has been reported that pectin polysaccharide isolated from *M. charantia* has a significant effect on the removal of hydroxyl radicals depending on the dose and may prevent lipid peroxidation. The hydroxyl and superoxide radical scavenging capabilities of the three water-soluble polysaccharide fractions isolated from *M. charantia* have been evaluated, all of which have been shown to have powerful hydroxyl radical scavenging and weak superoxide radical scavenging effects. Sulfated modification of *M. charantia* polysaccharides has been reported to show better antioxidant activity in vitro. In addition, it has been shown that polysaccharides can lead to improved antioxidant activity by increasing water solubility by chemical modification.

It has been noted that the treatment of neuroblastoma cells with *M. charantia* extract reduces cytotoxic oxidative stress from H$_2$O$_2$ by increasing intracellular cleansing activity. Triterpene glycosides isolated from *M. charantia* stems and fruits have been reported to significantly inhibit xanthine oxidase activity. Triterpenoids isolated from *M. charantia* bodies exhibited an inhibitory effect on cell activities and xanthine oxidase activity. The antioxidant compounds in *M. charantia* seed powders have been reported to inhibit lipid peroxidation by demonstrating potential natural antioxidant activity. The antioxidant activity of *M. charantia* against oxidative damage caused by peroxynitrite has been
evaluated in vitro and has been clearly shown to contribute to improvement\textsuperscript{103}.

There are also studies evaluating the antioxidant effects of \textit{M. charantia} polysaccharides in mouse models. It has been reported in vivo that water-soluble polysaccharides significantly increase GSH-PX activities in superoxide dismutase and liver homogenate and reduce maleic dialdehyde content by 25.6\% \textsuperscript{104}.

In mouse models treated with \textit{M. charantia} polysaccharides for 28 days, it has been reported that the activity of superoxide dismutase and catalase in serum, liver and cerebrum is significantly increased and maleic dialdehyde level is decreased. The in vivo antioxidant mechanism of \textit{M. charantia} polysaccharides has been linked to its contribution to improving antioxidant enzyme activities against damage caused by free radicals\textsuperscript{98}.

**Antitumor activity**

\textit{M. charantia} extract has been reported to have promising potential as adjuvants in traditional anticancer therapies\textsuperscript{105}. The effectiveness of \textit{M. charantia} extracts and / or components isolated from \textit{M. charantia} against different tumor cells was evaluated. Anti-proliferative and immunomodulatory effects have been reported in most studies\textsuperscript{106}. \textit{M. charantia} has been shown to modulate proteins associated with different cancer pathways\textsuperscript{107}. The cell cycle is stopped by modulation of the signal path and cell cycle proteins, and an antitumor effect is shown by inducing apoptosis or other cell death pathways\textsuperscript{108,109}. \textit{M. charantia} polysaccharides have been reported to inhibit proliferation of human leukemia cell line K562\textsuperscript{110}. Sulfate modification of \textit{M. charantia} extract has been shown to significantly inhibit the growth of HepG2 and Hela cells, and it has been reported that sulfated modification may increase anti-tumor activity\textsuperscript{111}.

The effects of Momordicoside G, an important bioactive component of \textit{M. charantia}, on lung injury and carcinoma lesion were investigated. It is reported that Momordicoside G induces apoptosis with morphological changes in M1-like macrophages by decreasing the amount of reactive oxygen species and promoting autophagy when applied at a dose that has no effect on cell viability in M2-like macrophages\textsuperscript{82}.

Three triterpene glycosides isolated from \textit{M. charantia} have been reported to show significant antitumor activity in cell lines derived from liver carcinoma\textsuperscript{112}. Given the effect of \textit{M. charantia} extracts on several inflammatory-related signaling pathways, it is thought to play an important role as an anti-tumor agent\textsuperscript{107}.

The effectiveness of \textit{M. charantia} juice against PanC pancreatic cancer cells has been demonstrated in vitro. Autophagy inhibitors significantly prevent cell death of cancer cells. \textit{M. charantia} juice has been reported to cause cell death by activating the autophagic pathway in drug-resistant pancreatic cancer (AsPC-1) cells\textsuperscript{113}.

In another study evaluating the effect of \textit{M. charantia} juice on targeting pancreatic cancer-related cancer stem cells (PanC-CSCs), it was reported that the supplement may cause a decrease in the expression of genes and proteins involved in the regeneration and reproduction of PanC-CSC\textsuperscript{114}. 9 compounds containing three cucurbitan-type triterpen glycosides isolated from the immature fruit of \textit{M. charantia} L, antihepatic fibrosis activity against murine hepatic stellate cells (t-HSC / Cl-6) and It was investigated for antihepatoma activity against two types of liver cancer cell line (HepG2 and Hep3B). Karavilosid III has been reported to cause inhibition of the t-HSC / Cl-6 cell line and exhibit cytotoxic activity against the Hep3B and HepG2 cell lines. It has also been developed as a chemotherapy agent for the treatment of liver fibrosis or carcinoma\textsuperscript{112}. MAP30 has been reported to have in vitro antineoplastic effects. These effects are thought to be due to the ability to reduce the expression of growth factor receptors attached to the breast factor, such as the transmutran tyrosine kinase receptor encoded by the HER2 oncogene\textsuperscript{30,115}. It was determined in vivo that tumor growth in S180 sarcoma and H22 liver tumor mice was significantly inhibited by \textit{M. charantia} polysaccharides\textsuperscript{116}.

In another study, \textit{M. charantia} polysaccharides have been shown to suppress the activity of apoptotic markers Bax and caspase-3 and increase
the level of anti-apoptotic protein Bcl-2 that promotes cell survival\textsuperscript{88}. In the study where ribonuclease, which has a molecular weight of 14 kDa isolated from \textit{M. charantia}, is injected daily into mice bearing HepG2 tumors, it was noted that tumor growth was significantly reduced\textsuperscript{117}. Lectin isolated from \textit{M. charantia} has been reported to significantly inhibit tumor growth in mouse cells carrying nasopharyngeal carcinoma\textsuperscript{118}. In vivo study of a mouse model with PC3 prostate cancer, the leaf extract of \textit{M. charantia} was reported to inhibit tumor growth. Cancer has been observed to metastasize to the lymphatic nodes, but no evidence has been found to metastasize to other organs\textsuperscript{119}. The progression of the tumor towards malignancy is strongly associated with chronic inflammation responsible for tumor invasion and angiogenesis of normal tissues in the environment. \textit{M. charantia} components also have the potential to have antitumor effect by modulating the inflammatory state. \textit{M. charantia} extract treatment has been shown to be more effective in inhibiting tumor growth in mouse models with aggressive triple negative breast cancer (TNBC) compared to ER positive breast tumor growth. It has been shown that abnormal irregularity of lipid metabolism is associated with breast cancer progression, and treatment causes decreased esterified cholesterol accumulation in TNBC cell lines compared to control cells. Moreover, expression levels of acyl-CoA and cholesterol acyltransferase 1 (ACAT-1) were evaluated in TNBC cells treated with \textit{M. charantia} extract, and the extract was shown to inhibit ACAT-1 expression in TNBC cells. It has been reported that \textit{M. charantia} therapy may have therapeutic potential in human breast cancer by suppressing TNBC cell growth\textsuperscript{120}. Considering the performed in vitro and in vivo studies, it is thought that consumption of \textit{M. charantia} supplement may help reduce the risk of cancer.

Other biological activities
It has been reported that \textit{M. charantia} polysaccharides have a neuroprotective effect that can reduce neuronal death caused by thrombin in primary hippocampal neurons\textsuperscript{121,122}. The hepatoprotective effect of \textit{M. charantia} water soluble polysaccharides has been investigated on the CCl4 liver damaged mouse model, and it has been shown that plant water soluble polysaccharides can reduce mouse serum ALT damage to 10.6% and AST damage to 30.7%\textsuperscript{104}. In another study, the effects of pectic polysaccharide supplement isolated from \textit{M. charantia} against female reproductive toxicity and infertility triggered by sodium arsenite in Wistar rats were investigated. Pectic polysaccharide has been reported to significantly reduce ovarian and uterine lipid peroxidation and the formation of reactive oxygen species from sodium arsenite by regulating superoxide dismutase, catalase and glutathione peroxidase activities. It has been noted that pectic polysaccharide therapy reduces sodium arsenite toxicity by modulating S-adenosine methionine pool components such as B12, folate and homocysteine. Thus, a successful fertility was reported in rats receiving supplements instead of infertile conditions\textsuperscript{123}. MAP30 isolated from \textit{M. charantia} has been reported to inhibit the HIV viral integrase and cause irreversible relaxation of superhelix viral nucleic acids. These changes caused by the MAP30 protein have been reported to prevent viruses from integrating themselves into host cell genomes\textsuperscript{29}.

TOXICITY
Although there have been many studies on \textit{M. charantia}, strong enough, randomized, placebo-controlled clinical trials are needed to properly determine safety and effectiveness before being routinely recommended. It is likely to cause additional side effects, especially when taken with other glucose-lowering agents. There are no other data on pediatric dosages. Convulsions and hypoglycemic coma were observed in two children, whose glycemia decreased strongly 1-2 hours after \textit{M. charantia} tea was given on an empty stomach\textsuperscript{124}. It has been reported as the most serious side effect known to humans. Other known side effects of \textit{M. charantia} are the reduction of fertility in mice, an increase in γ-glutamyltransferase and alkaline phosphatase levels and headaches in...
animals receiving oral juice and seed extract. It has been reported that favism disease caused by glucose-6 phosphate dehydrogenase enzyme deficiency may develop after consumption of *M. charantia*. The disease is defined by other symptoms such as hemolytic anemia, headache, stomach pain, and coma. It was determined that this was due to the glycosidic compound named “vicin” in the composition of *M. charantia*. It has been reported that the fertility rate of mice fed with *M. charantia* juice supplement decreased. It has been reported that particular attention should be paid to the use of plants in pregnant women, since the proteins in the composition of *M. charantia* significantly reduce fertility in animal models and pose a risk of losing the baby. It has been reported that spermatogenesis is inhibited in dogs fed with *M. charantia* fruit extract. In the study performed with MAP30 protein isolated from *M. charantia*, it was stated that human sperm was not affected.

In diabetic animal models, it was reported that hepatotoxicity symptoms were not observed based on histological and biochemical observations after treatment with *M. charantia*. Even if histopathological changes do not occur in animals with liver disease, caution should be exercised as transaminase increase is reported.

Many in vitro and in vivo studies have been conducted in which the beneficial effect of *M. charantia* on the heart has been reported. In a study conducted to investigate the potential developmental toxicity on fetal heart development using zebrafish (Danio rerio) embryos, seed extract was reported to be lethal with LD₅₀ values. In addition, multiple anomalies were detected in zebrafish embryos at these concentrations. In the same study, it has been reported that the fruit extract can be used safely without harming zebrafish embryos at a concentration of 200 μg/mL. However, it has been reported that severe cardiac hypertrophy develops in embryos treated with fruit extract over time and the cardiac myoblast specification process is impaired in zebrafish embryos. It was emphasized that the supplement should be used with caution to prevent possible damage to the development of the fetus in pregnant diabetic patients due to the teratogenicity of the seed extract and fruit extract cardiac toxicity.

A case of acute interstitial nephritis has been reported in a man with type 2 diabetes and hypertension using the hyponidd drug containing *M. charantia*. Anuria was defined in 2-3 days following edema and urinary reduction in the patient who took one tablet daily for a week. Kidney toxicity has been reported in mice treated with *M. charantia* for more than a week. It has been reported that *M. charantia* seeds and the outer shell contain lectin, which inhibits protein synthesis in the intestinal wall, but this is not related to clinical signs or symptoms in humans.

*M. charantia* can cause additional side effects when taken with blood sugar lowering agents. It has been observed that glucose-lowering effects are enhanced in rats supplemented with sulfonylurea tolbutamide together with *M. charantia* juice. Additional glucose-lowering effects were observed in 8 of 9 patients who took *M. charantia* juice or fruit powder with sulfonylurea. In a woman with type 2 diabetes, it has been reported that the use of *M. charantia* and garlic supplements containing sulfonylurea chlorpropamide and curry caused additional glucose-lowering effects.

Safety data are derived from animal models rather than clinical studies. Clinical findings indicating that long-term use of *M. charantia* at high doses may cause kidney conditions should be tested by better organized clinical trials. In a meta-analysis study, it was reported that better structured studies are needed by emphasizing the scarcity of clinical data. People who report allergies to other herbs from the Cucurbitaceae family should avoid the use of *M. charantia*.

**CONCLUSION**

It is known that the majority of the world population prefer traditional folk medicine products to industrial products. One of the main reason for the increased interest in herbal medicinal products is that natural products will be considered less toxic, but this is often a false perception. In health problems, many components...
of vegetable origin obtained from natural products have the potential to act as supplements, alone or in mixtures. Due to the synergistic effect, many active compounds may have therapeutic potential much higher than the effects they can give alone when given as a herbal preparation. 

*M. charantia* plant is a natural product known to be used for many years in the treatment of type 2 diabetes. There are many scientific studies supporting the anti-inflammatory and antioxidant properties of the plant, and it is a strong candidate that can clearly contribute to reducing the consumption of plant glycemia as well as reducing analgesic drug consumption in infectious diseases. There are also studies showing its effectiveness in the treatment of obesity, wound healing and supporting the immune system. Many in vitro and in vivo studies have been conducted on the investigation of the anticancer activity of *M. charantia*. The ability of *M. charantia* bioactive components to modulate a variety of cell cycle regulating proteins located in different signal paths has been clearly demonstrated in studies showing anticancer activity. The plant is known to play a vital role in cancer development and progression in cell signaling cascades. The *M. charantia* plant remains popular in the discovery of natural products, with its ability to suppress tumors by targeting multiple oncogenic signaling pathways. More studies are needed where *M. charantia* extracts or bioactive chemicals isolated from the plant are combined with chemotherapeutic drugs to see if they increase drug effectiveness or reduce side effects. There is also a gap in the field of clinical testing of all activities. Few clinical studies on *M. charantia* focused only on the effects on type 2 diabetes and were performed on a small number of subjects. Better clinical studies are needed on hyperglycemic efficacy. In addition, plant efficacy should be verified by increasing in vitro, in vivo and well-organized clinical trials in other areas where its use has traditionally been reported. It is known that the use of *M. charantia* herb together with the drugs used in the treatment of diabetes causes rapid decreases in blood sugar. Better safety studies are needed to perform the safety tests of the plant, to clarify the side effects and to adjust the doses in a controlled manner.

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