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Momordica charantia L.: Unlocking its Potential as a Nutritional Food Through Ethnomedicinal and Pharmacological Properties

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ABSTRACT

The plant known as *Momordica charantia* L. or bitter melon, has been cultivated for centuries due to its recognized pharmacological and nutritional properties. This plant, belonging to the Cucurbitaceae family, contains a diverse range of bioactive compounds, some of which exhibit potent biological effects. As a result, bitter melon has been utilized in traditional medicine around the world, primarily for managing diabetes, as well as addressing conditions such as cancer and inflammation-related diseases. Many studies have demonstrated the effectiveness of bitter melon extracts in lowering blood sugar levels in people with type 2 diabetes. However, most of the research that is currently available on bitter melon's bioactive components has utilized solely animal models and cell lines. Therefore, extensive clinical trials have been required to determine the effectiveness as well as safety of bitter melon in patients as the actual impact on human health has yet to be conclusively established. Moreover, both animal as well as laboratory research have revealed that under certain circumstances, bitter melon may cause toxic or negative effects. Thus, this review endeavour aims to furnish a comprehensive account of the ethnomedicinal, nutritional and pharmacological properties and potential adverse effects associated with bitter melon.

KEYWORDS

Momordica charantia L., bitter melon, momordicin, phagocytosis, AIDS, type 2 diabetes mellitus

INTRODUCTION

Humans have traditionally relied on nature to fulfil their needs for food, medicine and shelter. In this way, plants contribute significantly to the world's food and medicinal resources[1]. The World Health Organization (WHO) states that populations benefit from a variety of valuable plant resources for food, medicine and timber. This is true for *Momordica charantia* (Fig. 1) as well as its leaves and stems are reported to have therapeutic characteristics[2]. The Cucurbitaceae family, which includes about 800 tropical and subtropical species, includes this evanescent plant. The family has been divided into two subfamilies: Zanonidoids and Cucurbits, with squash belonging to the latter[3]. The *Momordica* genus, which includes over 600 species, has been identified in tropical regions and is well-known for its therapeutic and nutritional properties. Among these species, *Momordica balsamina* L., *Momordica cochinchinensis* Spreng., as well as *Momordica charantia* L. are noteworthy, but *Momordica charantia* is the most widely cultivated. The Cucurbitaceae family comprises 119 genera, including *Gurania* Cogn. (75 species), *Sicyos* L. (50 species), *Momordica* (45 species), *Cayaponia* Manso (45 species) and *Cucumis* L. (32 species).

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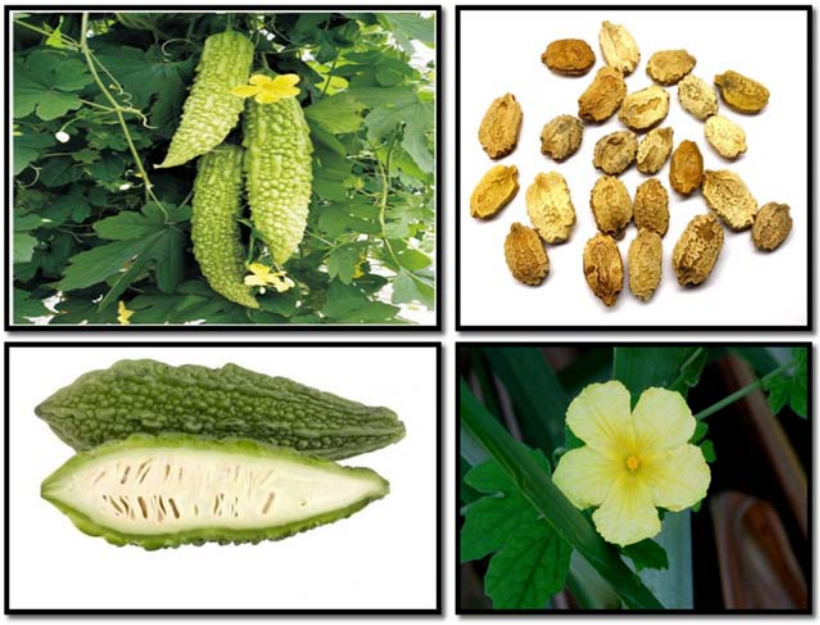

Fig. 1: Different parts of *Momordica charantia* L. (Source: Google)

Among all the species of the *Momordica* genus, *Momordica charantia and Momordica balsamina* are the ones that can be found in intertropical zones around the world[4]. Frequently addressed as "bitter melon" or else "bitter gourd", these plants have a bitter taste in all their parts. There are currently 12 documented species in Asia as well as 47 in Africa. While all Asian species are dioecious, 24 African species are dioecious and 23 are monoecious and all of these species have unisexual flowers. These plants are creeping, but they can also climb with the help of established support. Compared to other species in the same family, they prefer less acidic soils while growing best in soils with a pH of 6.5-6.8. The seeds will not germinate if the substrate temperature is below 10°C, but they will germinate within 5 to 8 days if the temperature is between 25-30°C. To ensure good fruit maturity and preservation, the plant must be well-supplied with phosphorus and potassium[5]. Despite the bitter gourd's nutritional benefits and medicinal qualities, its consumption has grown dramatically throughout Asia, East Africa, as well as South America. According to the WHO[6], 80% of the developing country's people depend on conventional medicine, predominantly utilizing plant extracts to fulfil their primary healthcare requirements[7]. The plant is widely used in traditional medicine and to some extent in human food[8]. According to some researchers, ethnobotanical knowledge of plant resources is crucial for the proper preservation of these natural resources[9]. Similarly, *Momordica charantia* displays numerous biological activities, suggesting that it could serve as a natural option to enhance the management of various diseases and function as a bio-herbicide[10]. The main objective of this review is to explore the bioactive constituents and ethnomedicinal properties of various anatomical structures of *Momordica charantia*, with particular emphasis on its anti-diabetic and anti-carcinogenic attributes, aiming to elucidate the therapeutic applications of *Momordica charantia* and provide substantive references for its development as a multifunctional nutraceutical and pharmaceutical agent.

Methodology: The current evaluation was put together with the assistance of numerous relevant literary works which are widely accessible on the internet through resources like Google Scholar, PubMed, Web of Science, NCBI, Scopus and many more. The data collection and analysis were conducted between May and July, 2024.

Origin of *Momordica charantia*: Tropical plants like *Momordica charantia* are indigenous to the Old World and can be found in the Caribbean, South America, Africa and Asia. It is extensively grown in China, India, Southeast Asia and East Africa and grows well in tropical regions such as the Amazon, Asia,

East Africa, as well as the Caribbean. *Momordica charantia* is not only used for food but also in traditional pharmacopoeia by various populations around the world. This important commercial vegetable is particularly significant in countries like India, Vietnam, Thailand, Malaysia, the Philippines and South China[11].

Morphology of *Momordica charantia*: The *Momordica charantia* is an annual herbaceous plant that can grow up to 5 m tall. It has thin, greenish herbaceous stems with simple, grooved tendrils. The leaves are membranous, alternate and simple, resembling those of vine leaves. They have a hairy, mucorinated surface, a toothed edge and a pubescent lobed base. The blade has a broadly oval-reniform or orbicular outline measuring between 2.5 and 12.5 cm, with a deeply palmate-lobed cordate base. The flowers are small, diclinous and pale yellow or whitish. They have a diurnal anthesis and are carried by frail peduncles, with the flowering time occurring around 55 to 60 days[12]. Male flowers have three stamens, while female flowers have a three-lobed stigma and an inferior ovary. Fruit formation occurs through cross-pollination and sometimes with self-fertilization. The fruits are pendulous berries, largely ovoid and equipped with an attenuated ellipse beak. When fully ripe, its dimensions are approximately 2 to 7 cm in length and 1.5 to 2 cm in width. The mature fruit is usually orange in colour with a reddish, slimy pulp surrounding the seeds. They are decorated with approximately 8 longitudinal rows of subconical tubercles and numerous smaller tubercles in the intervals. They often open into 3 valves, revealing the seeds surrounded by a viscous red pulp[13]. However, some cultivars have a smooth or spiny surface and rounded protuberances with rows in the form of 8 to 10 longitudinal ribs. Other cultivars have completely thorny fruits without longitudinal ribs. Some varieties of *Momordica charantia* can be differentiated based on fruit morphology or characteristics, but genetic data are scarce, making it difficult to estimate genetic diversity correctly. In addition, categorizations based on genetic distances and fruit characteristics continue to be conducted, which enables the classification of specific plants as the same variety. As a result, the variety of fruits were discovered that have an elliptical, oblong or ovoid shape. Additionally, varieties with smooth or rough fruits can also be found. Productivity and fruit length are also factors that contribute to identifying varieties. The seeds are encased in a reddish pulp and are consumed by animals in general and birds in particular. They are oblong, measuring approximately 10 mm and are flattened in shape, with a whitish or brownish colour. The integuments are sculpted with fluted edges and some cultivars are completely spiny and ribless, with a light brown or sometimes blackish colouring. However, in India, the seeds of cultivars have a narrower morphology with pointed ends as well as a surface coated with triangular "teeth" with dark brown colouration[14].

Nutritional value of *Momordica charantia*: According to nutritional research, this plant has a lot of proteins, vitamins, carbohydrates, minerals, as well as fibres along it has the optimal nutritional value among cucurbits. Fruits are made up of 93.2% water, 18.02% protein, as well as 0.76% lipids by dried weight, respectively[15,16]. Vitamins C, A, as well as P, along with thiamine, riboflavin, niacin and minerals, are abundant in green fruits[17]. Additionally, seeds of *Momordica charantia* can be an excellent source of lipids, including conjugated linolenic acid, which makes up 63-68% of the weight as eleostearic acid and polyunsaturated fatty acids, which make up almost 45% of the weight[18]. Monoterpenes, phenylpropanoids and sesquiterpenes can all be found in the essential oil that was extracted from the seeds. Phenolic compounds are also widely distributed throughout the pericarp, aril, stem and leaves of the plant. These compounds have the ability to prevent oxidative damage by directly interacting with reactive oxygen species as well as stimulating endogenous defense systems[19].

Chemical constituents of *Momordica charantia*: The plant *Momordica charantia*, commonly referred to as bitter melon, is a plant that contains a diverse array of bioactive chemical constituents (Table 1). These consist of phenolic acids, flavonoids, essential oils, triterpene glycosides, fatty acids, saponins, cucurbitan-type triterpenoids, as well as a variety of proteins with different characteristics and roles. It's

Table 1: Major bioactive compounds and their functions found in *Momordica charantia*

Bioactive compounds	Distribution	Functions
Lipids	Seeds	Antitumour
	Flesh	Antioxidant
Sterols	Pericarp	Antimicrobial
	Fruit	
Saponins	Fruit	Hypolipidmic
	Root	Antiviral
	Seed	Antihyperglycemic
Phenolics	Seed	Immune enhancement
	Pericarp	Antioxidant
	Fruit	Anti-inflammation
Terpenoids	Stem	Hypoglycaemic
	Leaf	Cancer chemoprevention
	Fruit	Antidiabetic
		Antioxidant
		Anticancer
Peptides and proteins	Seed	Antimicrobial
		Superoxide dismutase
		Polynucleotide adenosine glycosidase (PAG)
		Phospholipase
		RNA N-glycosidase
		DNase-like
		Immune suppression
		Anti-tumour
Polysaccharides	Various parts of the plant	Antidiabetic
		Immune enhancement
		Antioxidant
		Antitumour
		Neuroprotective
Glycosides	Fruit	Lower blood glucose levels increase glucose metabolism and decrease gluconeogenesis

crucial to remember that these phytochemical components are present in different amounts and are not evenly distributed throughout the entire plant[20]. For instance, bioactive compounds such as charantin, momordicin, momordine and momordicosides G, I and K are found in all parts of the plant, while momordenol, momordicilin, cucurbitin and cucurbitacin are specifically extracted from the leaves[21]. The fruits of *Momordica charantia* include polypeptides, carbohydrates, lipids, saponins, proteins, flavonoids, sterols, triterpenoids, as well as alkaloids; fruit cultivated in Asia contains higher concentrations of these compounds. Additionally, not only do *Momordica charantia's* leaves as well as fruits contain a wide range of bioactive substances, but immature fruits specifically boast cucurbitan-type triterpenoids, flavonoids, saponins, along phenolic compounds. It's worth noting that the bitterness of the fruit is attributed to the presence of triterpenoid compounds and their glycosides[22].

Ethnomedicinal uses of *Momordica charantia*: The *Momordica charantia,* a plant native to tropical and subtropical areas, is occasionally referred to as the bitter gourd or else bitter melon. It belongs to the family Cucurbitaceae. Rich in nutritional as well as nutraceutical components, phytochemicals found in *Momordica* species' fruits and leaves may offer a number of health benefits. The plant has been widely employed in conventional as well as folk medicine for a variety of medical conditions, such as the management of bacterial and viral infections, obesity, cancer, Type 2 Diabetes Mellitus (T2DM), hypertension and even Acquired Immune Deficiency Syndrome (AIDS)[23,24]. Bitter melon, also referred to as karela, has been utilized in Ayurveda medicine for centuries. Its pharmacological qualities are ascribed to several parts of the plant, including the leaves, roots, seeds, as well as especially the unripe fruits[25]. Due to its laxative, anti-helminthic, along diuretic properties, the juice finds application in the treatment of several disorders, chronic fever, including joint pain, jaundice and illnesses of the liver or else digestive

system. Additionally, burns, boils, rashes and chronic skin conditions are treated locally utilizing it. For the treatment of T2DM, consuming whole plants is recommended[19]. In traditional Turkish medicine, the oil derived from ripe bitter melon fruit macerated in warm olive oil is combined with honey and used to prevent as well as treat gastric ulcers[26]. The fruit, seeds and leaf juice of the bitter melon are mostly used in African traditional medicine to cure skin diseases (roots), syphilis, menorrhea, fever, inflammation and worm infection. Leaf decoction is employed to treat type 2 diabetes; fruits and leaves are used to heal burns, ulcers and jaundice among other liver diseases. Additionally, *Momordica* preparations are given for treating gonorrhoea, chicken pox, malaria, measles, as well as scabies. It is utilized to treat diabetes in the Caribbean as a fruit juice or leaf decoction. Additionally, malaria, dysentery infections, high blood pressure, womb, as well as worm infections are treated with the leaf decoction. Leaf baths are utilized in the treatment of rheumatism[20].

Pharmacological properties: The different parts of *Momordica charantia* exhibit several ethnopharmacological effects such as immunomodulatory, antioxidant and antiviral activities.

Antidiabetic activity: *Momordica charantia* extracts can be used to treat all types of diabetes, according to researchers. The extracts have demonstrated potent antidiabetic activity on both animal and human cells in the laboratory. Specifically, oral treatment of the aqueous extract of *Momordica charantia* fruit has been demonstrated to stimulate the production of insulin from β cells in isolated Islets of Langerhans from hyperglycemic obese mice along with significantly lower blood sugar levels in diabetic rats produced by streptozotocin. Additionally, the extracts have been found to promote cell renewal in diabetic rats and to aid in the healing and recovery of damaged cells. Other studies have also shown that the P-polypeptide isolated from bitter gourd fruits has hypoglycemic activity similar to insulin[27]. *Momordica charantia* extracts may have an antidiabetic effect because of their capacity to raise serum protein levels and improve peripheral glucose consumption, which in turn increases insulin secretion[28].

Antioxidant activity: Vietnamese and Indian researchers have reported on the *Momordica charantia* fruit's antioxidant activities under *in vitro* and *in vivo* conditions on animal cells. These activities are attributed to the phytochemical compound's polysaccharides, saponins and flavonoids found in the fruit's pulp and seeds. Hepatic marker alterations in rats with ammonium chloride-induced hyperammonaemia suggest that the extract may also be useful in maintaining the cellular integrity of liver tissue. The median effective concentration (CEM50) of this extract is 2.22 mg/mL, which is a measure of the concentration needed to induce a response halfway between the baseline and maximum effect after a certain period of exposure[29].

Anti-cancer activity: The development and spread of certain cancer forms have been related to chronic inflammation. Researchers have identified two main pathways through which inflammation can contribute to cancer development. Tumor-extrinsic inflammation, the first pathway, is caused by a variety of factors, including exposure to environmental contaminants, bacterial as well as viral infections, along with lifestyle choices. This pathway, which is controlled by the innate immune system, includes transcription factors like NF-κB and STAT3 along with the generation of major inflammatory cytokines including TNF-α, IL-1, as well as IL-6. Tumor-intrinsic inflammation is the second pathway, which is brought on by neoplastic alterations that invite immune cells into the tumor microenvironment and produce inflammatory mediators. This pathway contributes to the development of an inflammatory milieu that promotes various steps of progression of cancer. Common characteristics of both pathways include the activation of transcription factors like NF-κB as well as STAT3 and the generation of primary inflammatory cytokines[10]. Preventing or reversing inflammation has become an essential strategy for managing the progression of cancer, given the importance of inflammatory alterations in various types of cancer. A number of phytochemicals, such as extracts from *Momordica charantia*, have shown promising potential as adjuvants in traditional

anticancer therapy because they can stop the progression of cancer[30]. Many studies assessing the effectiveness of *Momordica charantia* extracts or purified components against different tumour-derived cells have suggested that dietary consumption of *Momordica charantia* could help reduce the risk of several cancers. However, the primary purpose of these investigations into *Momordica charantia* extracts has been their potential employment as chemo-preventive agents. The majority of studies have reported anti-proliferative and immunomodulatory effects[31]. The ability of *Momordica charantia* extracts to modulate several dysregulated signalling pathways in various cancer types is thought to be responsible for their anti-cancer properties. These pathways include the MAPK pathway, the Akt/mTOR/p70S6K pathway via AMPK activation, the Wnt/β-catenin signalling pathway, as well as the modulation of cell cycle proteins, which in turn induces cell cycle arrest, apoptosis or other pathways leading to the death of the cell. Three *Momordica charantia* cucurbitane type triterpene glycosides have recently been revealed to have substantial anti-tumor effects in hepatic carcinoma-derived cell lines[32]. The anti-inflammatory properties of the extract of *Momordica charantia*, which have been shown to influence several inflammatory-related signalling pathways, might be a major factor in its effectiveness as a tumor-prevention agent[33]. Further research is required to determine the potential use of *Momordica charantia* extracts as nutraceuticals in the treatment of cancer, despite the fact that anti-cancer activity has been shown in cancer cell lines in xenografted mice. Some *Momordica charantia* proteins belonging to the RIP family have demonstrated significant anti-tumour activity[34]. These proteins have been utilized to produce anti-cancer drugs, especially in the form of immunoconjugates or ITs, which selectively deliver toxic proteins to malignant cells. Cell translation is strongly inhibited by these proteins[35]. Despite the lack of clinical evidence supporting the anti-tumor activity of *Momordica charantia* components in people, the literature that is currently available points to a very likely protective role for *Momordica charantia* throughout the development of tumor cells as well as when the tumor progresses. Components of *Momordica charantia* can inhibit oxidative stress, which can favour the first neoplastic transformation. Furthermore, *Momordica charantia* components have the ability to influence chronic inflammation, which is responsible for tumor invasion of surrounding normal tissues and angiogenesis during tumor progression, hence enabling them to exert their anti-tumour effect.

Antimicrobial activity: The antimicrobial activity of the pulp extract of *Momordica charantia* is extensive, as evidenced by its effectiveness against a range of microorganisms, including *Escherichia coli*, *Staphylococcus*, *Pseudomonas*, *Salmonella* and *Streptobacillus*. Furthermore, when mixed with immature fruits of *Momordica charantia*, methanolic leaf extracts demonstrated robust antibacterial activity, particularly against *Escherichia coli* and *Staphylococcus aureus*[36].

Antiviral activity: The stems as well as leaves of *Momordica charantia* exhibit an extremely effective inhibition of specific viruses, including HSV-1 and SINV. Many of the compounds that have been extracted from the plant and shown to have antiviral activity are proteins and steroids[37]. Moreover, studies have revealed that proteins from *Momordica charantia* can inhibit the activity of HIV by suppressing the core protein's (p24) expression of the virus, while also reversing the activity of the enzyme viral transcriptase-associated virus (HIV-RT), with a minimal impact on the cellular synthesis of DNA or proteins of other cell types. The ethanol extracts of *Momordica charantia* have also shown a direct protective effect against Coxsackie virus (CVB3)[38].

Anti-inflammatory activity: Certain studies suggest that *Momordica charantia* possesses anti-inflammatory and immunomodulatory effects. Administration of 2% as well as 5% *Momordica charantia* dry powder orally was found to significantly reduce the infiltration of macrophages in the BAT (brown adipose tissues) along with epididymal adipose tissues of rats fed a high-fat diet, which consequently led to the negative regulation of pro-inflammatory cytokine monocytes, specifically TNF-1 and IL-6[39]. Moreover, more research showed that extracts from *Momordica charantia* vegetative parts and immature fruit can reduce oxidative stress in the brain caused by a high-fat diet and regulate levels of neuroinflammatory markers (TNF-, IL-16, IL-22 and IL-17R)[40].

Immunomodulatory activity: According to earlier research, *Momordica charantia* leaf methanolic extract has a remarkable ability to increase phagocytic activity in *in vivo* studies. These extracts' polysaccharides have been demonstrated to suppress lymphocyte activity or change the kinetics of immune response measures, among other immunomodulatory functions. These substances notably suppress the mitogenic reactions of mouse spleen cells to lipopolysaccharides, sometimes referred to as lipoglycans or endotoxins and concanavalin A, a glycoprotein of the lectin family, which causes T4 lymphocytes to secrete pro-inflammatory cytokines. Additionally, momordicin has been shown to activate and promote the proliferation of B lymphocytes by inducing the activity of immunoglobulins. Furthermore, after 96 hrs of co-culture, these polysaccharide substances cause the spleen cells to release a significant amount of immunoglobulin M (IgM)[41].

Side effects of *Momordica charantia*: The ethanolic *Momordica charantia* seeds extract has been found to induce significant histological changes in the testicular cells and reproductive organs of albino mice, leading to infertility. However, it is thought that the leaf aqueous extracts lower progesterone and estrogen plasma levels, suggesting that they may affect reproductive hormones. This suggests that alpha momorcharin (α-MMC) present in the leaves could potentially lead to early abortion in pregnant rats. Additionally, beta momorcharin (β-MMC) has shown contrasting effects by influencing embryo adhesion and implantation. Additionally, it has been discovered that several *Momordica charantia* components have inhibitory effects on the gastrointestinal nematodes that cause chronic infections. Momordin, extracted from the leaves and fruits, has been observed to exhibit hypotensive effects on rats with a history of severe hypertension[42].

CONCLUSION

This study has highlighted the ethnomedicinal knowledge and biological properties of *Momordica charantia*, a climbing plant cultivated in subtropical as well as tropical regions. The plant has been employed in traditional Asian medicines for various disease treatments, as well as its main constituents are responsible for its pharmacological activities, including antidiabetic, anticancer and antimicrobial properties. The review of the traditional uses and medicinal properties of *Momordica charantia* provides valuable insights into its potential as a natural remedy for various diseases. The future scope of this research includes further investigation of the pharmacological activities of *Momordica charantia* as well as its potential as a natural remedy for several diseases. Additionally, the study of the molecular mechanisms underlying its biological properties may provide insights into its therapeutic potential. The development of new formulations and delivery systems for *Momordica charantia* may also enhance its efficacy and safety as a natural remedy.

SIGNIFICANCE STATEMENT

Bitter gourd, with its pharmacological, nutritional and ethnomedicinal properties, remains underutilized due to its bitter taste. This review illustrates the functional benefits of the fruit and other plant parts and how emerging technologies like nanoencapsulation and green extraction methods enhance its potential as a functional food, emphasizing the need for value addition. *Momordica charantia* is highlighted as a promising therapeutic plant for treating various diseases, being an accessible and affordable phytochemical rich in nutrients. This review supports the nutritional, pharmacological and ethnomedicinal significance of *Momordica charantia*, providing a basis for its application in food and medicine and with further research, it is expected to see broader use in the food, pharmaceutical and medical sectors.

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