

Anti-diabetic, anti-cancer potential and anti HIV of Bitter Gourd (*Momordica charantia*) Extract: A Mini Review

ABSTRACT

Aims:

To review the antidiabetic properties, pharmacological characteristics, and phytochemical research on *Momordica charantia* (bitter gourd) and assess its potential as a therapeutic agent for diabetes and cancer prevention.

Study Design:

Review of existing literature and research studies, including pre-clinical trials and animal and in vitro studies.

Methodology:

Analysis of traditional uses, pharmacological data, and phytochemical research on *M. Charantia*. Evaluation of anti-diabetic and anti-HIV properties based on available studies.

Results:

- *M. Charantia* has shown anti-diabetic and hypoglycemic effects in pre-clinical studies.
- Limited and unreliable clinical data due to poor research design and inadequate statistical power.
- Recent studies indicate potential anti-tumor, anti-diabetic, and anti-HIV properties.
- Plant extract components have demonstrated effectiveness in cancer prevention through immune function enhancement, induction of cell death, and inhibition of cancer-related processes.

Conclusion:

M. Charantia holds promise as a therapeutic agent for diabetes management and cancer prevention. However, there is a need for better-designed clinical trials to confirm its efficacy and establish reliable clinical evidence.

Keywords: *Momordica charantia*, Antidiabetic properties, Traditional medicine, Cancer prevention.

1. INTRODUCTION

M. Charantia, commonly referred to as bitter melon, is a flowering vine in the Cucurbitaceae family. This tropical plant is widely grown for its highly bitter fruits, which are used in cooking and as a home remedy for diabetes, in Asia, India, East Africa, and South America. It is a perennial climber that reaches a maximum height of five meters. It bears oblong fruits with a rough surface. Bitter melon is a valuable vegetable and medicinal plant that, because of its nutrient-dense composition of beneficial compounds, shows great promise in treating diabetes. Its exceptional adaptability in treating a wide range of medical conditions is attributed to the presence of bioactive chemicals, vitamins, minerals, and antioxidants. Bitter melon fruit is packed with important vitamins like vitamin C, vitamin A, vitamin E, vitamin B1, B2, B3, and vitamin B9 (folate) [1]–[6]. It also has caloric values of 213.26, 241.66, and 176.61 Kcal/100g in its leaf, fruit, and seed [7]. In addition, the fruit is a great source of essential minerals like potassium, calcium, zinc, magnesium, phosphorus, iron, and dietary fiber. Various studies, including our own, have found that bitter melon contains over 30 Natural Products that have medicinal uses, such as proteins, peptides, and small compounds. Some of these compounds have shown promise as antitumor, anti-diabetic, and anti-HIV agents [6], [8], [9].

2. MEDICINAL APPLICATION OF *M. CHARANTIA*

Bitter melon has a wide range of potential benefits, including anti-cancer, anti-inflammatory, cholesterol-lowering, and anti-viral properties. Its bioactive components such as triterpenoids, phenolic acids, flavonoids, lectins, and proteins have shown anti-cancer activity with few side effects.

The phenolic compounds found in bitter melon may have antioxidant and anti-mutagenic properties, while its components have been used to treat Microbial infections, menstrual problems, Hyperlipidemia and Digestive disorders. Bitter melon is also effective in treating malaria due to its anti-helminthic properties.

However, it should be avoided by pregnant women due to its abortifacient agent, and its seed extracts have anti-spermatogenic effects. It provides protection to pancreatic B-cells by down-regulating/lowering down MAPKS and NF-KB in MJNCNs cells and is used as a broad-spectrum anti-bacterial agent against various bacteria, including E. coli, Salmonella, Staphylococcus aureus, Pseudomonas, and Streptobacillus [7], [10], [11], [11], [12]. Administering it orally can stimulate the endocrine pancreatic β -cells to secrete insulin, and feeding the alcoholic extract of it can lead to a clear enhancement in the Islet's of Langerhan's. The extract of bitter melon demonstrated antitumor effects in mice, and in vitro studies showed that it inhibited cell proliferation in breast cancer (MDA-MB-231, MCF-7) and colon cancer cell lines (BxPC-3, MiaPaCa-2, and AsPC-1)[1], [4], [6], [13], [14].

In athymic nude mice, the in vivo study on pancreatic cancer xenograft volume by Kaur et al.[5] showed a noteworthy decrease in MiaPaca-2 tumor weight without any concomitant damage.

Momordica Charantia lectin (MCL) has been shown to inhibit the viability of NPC cell lines CNE-1 and CNE-2, as well as to cause autophagy, apoptosis, and cell cycle arrest. It also suppresses the growth of HepG2 and PLC/PRF/5 hepatocellular carcinoma (HCC) cell lines, as shown by MTT analysis and an in-vitro colony formation experiment. Like MCL, MAP308 (Momordica Antiviral Protein) is a single-chain RIP that has been demonstrated to stop the growth of cancer cells, trigger apoptosis, and stop the cell cycle. Additionally, it has been discovered that MAP308 reduces histone deacetylase (HDAC), which is known to interact with oncogenic fusion proteins, while increasing histone acetylation and inhibiting HepG2 proliferation. Like MAP308, α - and β -momorcharin exhibit anti-tumor action [11], [13], [15]. Both α -MMC and MCP30 were reported to promote apoptosis and cell cycle arrest in NPC and prostate cancer cell lines, respectively, when isolated from bitter melon as MAP308. The NPC cell lines CNE-1 and HONE-1 were the only ones that α -MMC selectively killed, while non-cancerous altered human nasopharyngeal epithelial NP69 cells were barely affected. It demonstrated encouraging anti-tumor characteristics in hypoxic areas, which are linked to metastasis and treatment resistance. While Western blot analysis demonstrated activation of caspase-8, -9, and -3 in a time and dose-dependent manner leading to cell cycle arrest in the G0/G1 phase, Annexin V/PI staining confirmed that α -MMC induced apoptosis in CNE-2 and HONE1 cells. HONE1 cells showed very little caspase activation; instead, these cells were stopped in the S-phase upon. MCP30 was found to induce apoptosis in prostate cancer cell lines PC-3, LNCaP, and PIN, without any cytotoxic effect on non-cancerous prostate cell lines RWIPE-1.

FACS and Western blot analysis verified the induction of apoptosis and cell cycle arrest, which resulted in the suppression of tumor development. Type 1 RIPs, type 2 RIPs, lectin, and RNase from bitter melon may be used as therapeutic agents to treat cancer. Components of bitter melon lower Cyclin B1 and Cyclin D1 levels while raising p21 levels, which causes cell cycle arrest. Numerous bacteria, including Salmonella typhi, Bacillus subtilis, Escherichia coli, Staphylococcus aureus, and Klebsiella pneumonia, were efficiently stopped from growing by the ethanol extract of **M. charantia** leaves.

In experiments on animals, bitter melon extract demonstrated hypoglycemic action by inhibiting the liver's fructose-1,6-bisphosphatase and glucose-6-phosphatase enzymes while also enhancing insulin sensitivity, glucose tolerance, and insulin signaling. Purified lectins momordin and agglutinin reduced Ehrlichascites tumor without generating animal toxicity at an LD50 of 5 mg/kg of body weight. The extract also boosted NK cell activity without any cytotoxic impact. Furthermore, kuguacin-J isolated from the leaves demonstrated cytotoxicity and drug susceptibility in ovarian and cervical cancer cells [7][13][6].

3. EFFECTS OF **M. CHARANTIA** EXTRACTS ON DIFFERENT DISEASES

3.1. Effect of **M. Charantia** on Diabetes

In many developing countries, Herbal treatments has been normally used to control diabetes. Among the plants that have undergone thorough research for their potential in treating diabetes is **M. Charantia**. This plant has a long history of traditional use, which has been validated by the evidence from modern science, making it one of the most promising natural remedies for diabetes. A study of the traditional use of **M. Charantia** in India revealed that it is one of the most effective plants for lowering blood glucose levels in diabetic patients. The different extracts and chemical components from the Bitter gourd may elicit effect of Hypoglycemia via several mechanisms, That includes encouraging the use of glucose by skeletal muscle and the peripheral nervous system, suppresses

adipocyte differentiation and intestinal glucose uptake while reducing gluconeogenic enzymes, stimulating the HMP¹⁴ pathway's key enzyme, and protecting islet β -cells and their functions [6][1], [4], [7], [16]–[18].

3.2. M. Charantia's Anti-inflammatory and anti-oxidant properties

The ongoing low-grade inflammation caused by lifestyle and diet choices can have an impact on both the immune system and gut bacteria. The relationship between different dietary components and their ability to reduce inflammation is not fully understood, but some components may help in preventing chronic inflammation and assisting in treatment. *M. Charantia* has been researched for its potential in treating conditions such as T2DM, dyslipidemia, obesity, and cancer, showing promising results in lowering blood sugar and cholesterol levels. However, more clinical trials are needed to confirm these findings. Chronic inflammation plays a role in the development of many diseases, and oxidative stress is closely linked to this process, with both factors influencing each other [6][9], [19].

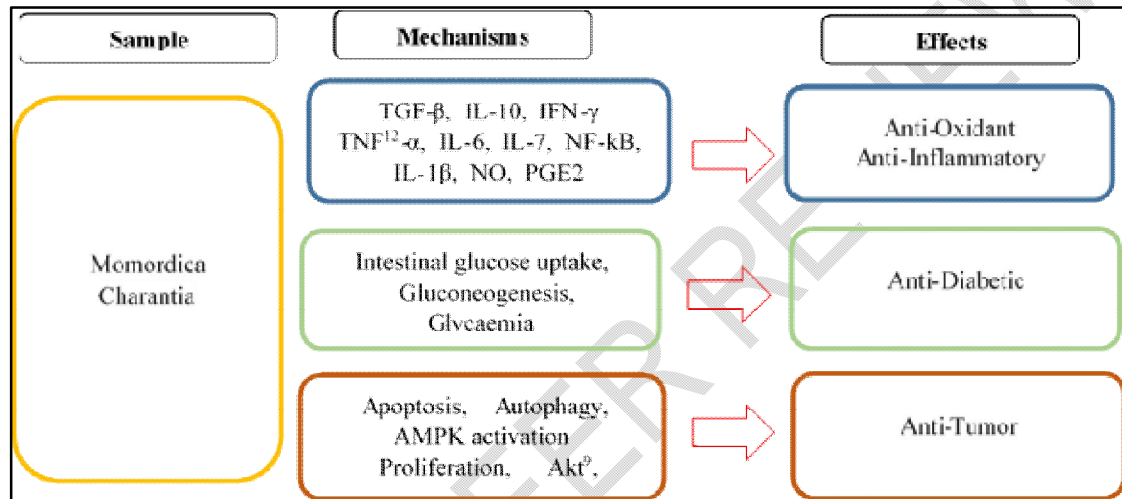


Figure 1 The Pharmacological actions of *M. Charantia*

3.3. Anti-HIV & Anti-tumor effect of *M. Charantia*

The plant protein MAP30, extracted from bitter melon (*MomordicaCharantia*), has antiviral and anti-tumor properties, acting against multiple stages of the HIV life cycle and inhibiting viral integrase and ribosome activity. The MAP30 gene has been cloned and expressed, and this study aims to characterize the recombinant MAP30 (re-MAP30) and assess its activities against HIV and tumors. In this report, we demonstrate that re-MAP30 has the same inhibitory effect on HIV-1 and some human tumors as the natural form of MAP30 (nMAP30). To evaluate the anti-HIV activity, we measured the formation of quantitative focal syncytia on CEM-ss cell monolayers, expression of the viral core protein p24, and the reverse transcriptase activity associated with the virus in H9 cells that were infected with HIV-1. Metabolic labeling of protein synthesis in tumor cells was used to measure the anti-tumor activity. Re-MAP30 did not exhibit any appreciable harm to either the uninfected viral target cells or normal human cells within the measured dose range. In terms of cell-free ribosome inactivation, prevention of viral DNA integration, and topological inactivation of viral DNA, recombinant MAP30 (re-MAP30) demonstrates the same actions as natural MAP30 (nMAP30). A significant amount of homogenous material is made available by the cloning and production of the gene encoding the physiologically active re-MAP30 gene, enabling the conduct of clinical research and structure-function analyses on this novel antiviral and antitumor drug [11], [11], [13], [15], [20], [21].

3.4. Cancer-Preventive Effects of Bitter Melon

Clinical studies on the effects of bitter melon extract and its active ingredients on cancer are currently lacking. However, laboratory studies have been conducted on cancer cell lines as well as preliminary animals models/patterns, while preventive studies have been conducted on various animal models of cancer including the Stomach, Liver, Prostate, Head and Neck, Blood, Breast, Colon, and Skin Cancers. Crude extracts of *M. Charantia* prepared using water, ethanol, or methanol

have been used in these studies. In vitro and in vivo therapeutic investigations on a variety of cancer types, including head and neck, brain, breast, colon, ovarian, pancreatic, kidney, liver, lung, and cervical cancer in women, have also employed crude extracts or isolated compounds. The findings on the effects of *M. Charantia* on cancer chemopreventive measures and treatments are concluded in Table 1 and Figure 2 and are mentioned below [9][4], [6], [14].

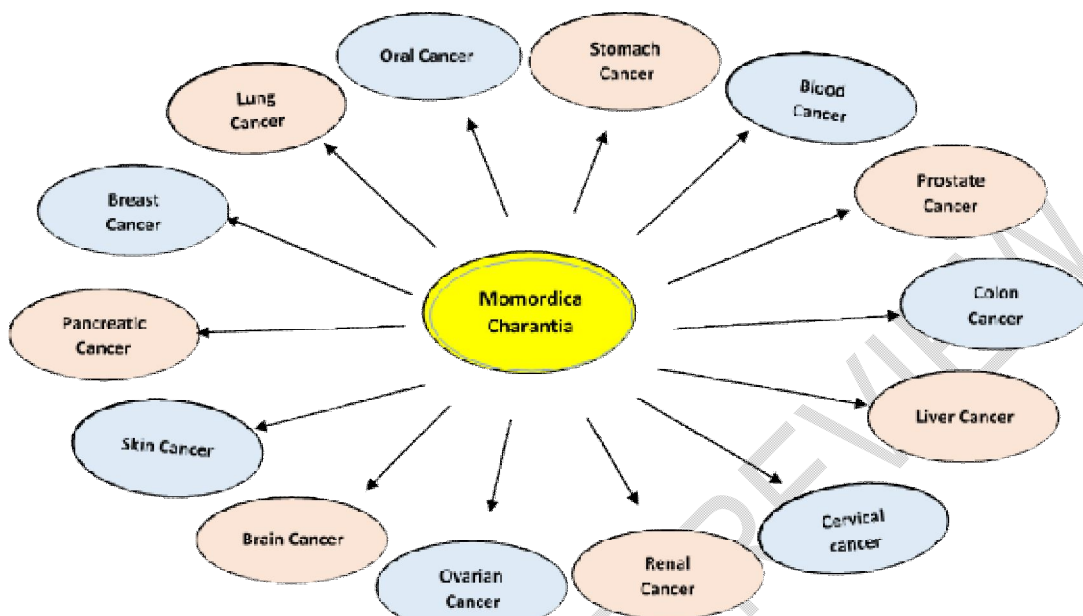


Figure 2 Cancer types that *M. Charantia* prevent's.

3.4.1. Blood Cancer

In a study conducted on mice, it was initially observed that the ammonium acetate precipitates of bitter melon water extract had a cancer-preventive effect as they prevented tumor formation and boosted immune function. Nonetheless, when tested on normal human peripheral blood lymphocytes, the crude extract exhibited minimal impact in contrast to the lymphocytes obtained from individuals with acute or chronic leukemia. In the same way, the 30kD Momordica antiviral protein (MAP30) found in bitter melon effectively suppressed the growth and triggered programmed cell death (apoptosis) in the HL-60 cell line of human acute myeloid leukemia (AML), as well as in THP-1 cells and AML cells from patients, with the degree of response being reliant on both the dosage and duration of exposure. Furthermore, it was discovered that certain seed extract-derived fractions, such as Mc-1, Mc-2, Mc-3, and Mc-2Ac, improved the leukemia cell line HL60's differentiation in a dose-dependent way. Another study found that a significant constituent of the seeds, 15,16-dihydroxy α -eleostearic acid, caused HL60 cells to undergo programmed cell death, or apoptosis. Peripheral blood mononuclear cells were not significantly affected by the α -eleostearic acid that was isolated from the seeds using ethanol, however it was demonstrated to suppress the proliferation of leukemia cell lines ED and Su9T01 [6][6], [11], [22].

3.4.2. Breast Cancer

Studies were conducted both as a preventive measure and as a therapeutic approach on models of breast cancer. The aqueous extract derived from the fruit demonstrated a time and dose-dependent inhibition of proliferation and stimulation of programmed cell death (apoptosis) in MCF-7 and MDA-MB-231 breast cancer cells, with cell viability reduced by 80%. Even after five days of treatment, the extract had no negative effects on primary mammary epithelial cells (HMEC). Similar to the effects of the water extract, the extract's component MAP30 efficiently suppressed MDA-MB-231 cells in both in vitro and in vivo tests using SCID mice. A 0.5% concentration of the water extract, given consistently to drinking water-fed SHN virgin mice, inhibited the growth of mammary tumors without any documented adverse effects. Ingestion of the extract at a concentration of 30% v/v by drinking water inhibited tumor growth, activated autophagy, and reduced cholesterol esterification in animal models

of breast cancer cells 4T1 and E0771 as well as in a xenograft model of human breast cancer cell MDA-MB-231. particularly bitter melon [6][15].

3.4.3. Colon Cancer

In male F344 rats, the inclusion of *M. Charantia's* seed oil in their meals resulted in a dose-dependent decrease in the incidence and multiplicity of colon cancer induced by azoxymethane (AOM). The free fatty acid and 9-cis, 11-trans, 13-trans-conjugated linolenic acid, which were extracted from *M. Charantia's* seed oil, reduced the vitality of Caco-2 cells. Moreover, the water extract of its seed, which has an ethanol to water ratio of 1:1, had the strongest antileukemic effects on 116 cells from a human colon carcinoma. Furthermore, it was shown that the whole fruit's methanol extract promoted autophagy and inhibited the proliferation of HT-29 and SW480 cells as well as the development of colonies and spheres. On the other hand, compared to the extract from the entire skin, the extract from the entire fruit had a stronger effect on the cell lines. Both extracts had no cytotoxic/ antileukemic effects on fibroblasts in non-cancerous human foreskin (HFF). Additionally, researchers found that the extract enhanced the sensitivity of colon cancer cells to doxorubicin. The compound in the methanol extract that inhibits P-glycoprotein in human epithelial colorectal adenocarcinoma cells Caco2 was discovered by Konishi et al. Furthermore, α -eleostearic acid was shown to limit the growth of HT29 colon cancer cells [6][4], [22].

3.4.4. Gastric Cancer

Swiss albino mice were subjected to the administration of fruit extract (at concentrations of 2.5% and 5%) for both short and long term periods, resulting in the inhibition of forestomach carcinogenesis induced by benzo(a)pyrene [B(a)P]. The preventive effects were observed to be more effective with long-term treatment. The leaf's methanol extract showed promising therapeutic effects on AGS gastric adenocarcinoma cells, while bitter melon protein compounds (Fractioned I–III) were also successfully extracted through high-speed counter-current chromatography. These compounds were found to inhibit the growth of the human gastric cancer cell line SGC-7901, with Fraction II demonstrating the most potent anticancer activity [6][2].

3.4.5. Throat and Head Cancer

This group includes cancers affecting various areas such as the mouth, tongue, nasal passages, sinuses, glands, throat, and voice box. Studies have shown that bitter melon extract has potential anti-cancer properties, specifically in Cal27, JHU029, and JHU022 cells. The extract is believed to inhibit cell growth, promote cell death, block c-Met signaling, and reduce metabolism. When given orally to mice, the extract led to reduced cell growth, cell death, and inhibited tumor growth. It also decreased the presence of certain immune cells within tumors and spleens. Continuous oral administration of the extract prevented the development of tongue cancer in mice, modulating various biological processes. Additionally, a component of bitter melon called alpha-momorcharin was found to be effective against nasopharyngeal carcinoma cells while sparing healthy cells [6].

3.4.6. Liver Cancer

By affecting the expression of genes linked to angiogenesis, proliferation, metastasis, and apoptosis, a 40 mg/kg dose of methanol extract was given both before and after the onset of carcinogenesis, effectively preventing the development of hepatocellular carcinoma induced by di-ethylnitrosamine (DENa) and carbon tetrachloride (CCl₄). Additionally, HepG2 cells treated with a 5% v/v fruit extract for 48 hours showed a significant reduction in cell viability (63%) as a result of the suppression of hepatic triglyceride synthesis and apolipoprotein B release. Both α -MMC and MAP30 seeds showed cytotoxic effects on HepG2 cells. MAP30 seed also prevented the formation of HepG2 cell xenograft tumors in nude mice without causing any negative side effects. The anti-fibrosis and anti-cancer properties of a number of compounds were assessed against the human hepatoma cells HepG2 and Hep3B. These compounds included furfurylpyrrolidone, goyaglycoside-I, charantagenin-F, and other [6][23].

3.4.7. Lung Cancer

Water or methanol extraction of the bitter melon plant leaf exhibits dose-dependent cytotoxic effects on lung adenocarcinoma cells CL1 and non-small cell lung cells A549. On the other hand, lung WI-38 cells and normal human embryonic kidney HEK293 cells were less susceptible to these effects. In A549 cells, both α -MMC and MAP30 inhibited proliferation, and led to cell cycle arrest in the S-phase and apoptosis, with the degree of effect being dependent on both the dose and duration of exposure. The effects of MAP30 were more potent than those of α -MMC on these cells [6][21].

3.4.8. Pancreatic Cancer

It was found that a fruit's water extract may decrease the proliferation of human pancreatic cancer cells, such as BxPC-3, MiaPaCa-2, AsPC-1, and Capan-2, and induce apoptosis. Additionally, it hindered the proliferation of gemcitabine-resistant AsPC-1 cells and induced autophagy, with the outcomes being influenced by dosage and duration of treatment. The extract also targeted pancreatic cancer stem cell (CSC) populations expressing CD44+/CD24+/EpCAM and markers like SOX2, OCT4, NANOG, and CD44, both in lab settings and in animal studies. Furthermore, it boosted sensitivity to gemcitabine, decreased tumor volume, and hampered the activity of glucose transporter GLUT121 and lactate transporter MCT4 in a xenograft model [6][5], [7], [12], [15], [16], [24].

3.4.9. Cancer of Prostate Gland

By disrupting the progression and proliferation of the cell cycle, the oral treatment of *M. Charantia* extract was able to prevent the formation of prostatic intraepithelial neoplasia in TRAMP11 animals. In the meantime, mice's incidence of PC3 cell xenograft tumors was inhibited by a 1% and 5% ethanol extract of bitter melon leaves added to their food, all without having an unfavorable effect on their body weight. In fact, the same extract reduced PLS10 cell-mediated metastasis and raised the survival rate of the mice when injected into the food at dosages of 0.1% and 1%. In lab tests, bitter melon extract was found to have a negligible impact on primary prostate epithelial cells but to cause over 90% of cell death in PC3 and LNCaP cells.

Furthermore, it was found that whole fruit water extract can induce G2-M phase cell cycle arrest and growth inhibition in vitro of rat prostatic cancer cells. Similarly, in both in vitro and in vivo settings, bitter melon leaf ethanol extract inhibited the growth of prostate cancer. In human prostatic intraepithelial neoplasia (PIN) cells, PC-3 cells, and LNCaP cells, it was discovered that another bitter melon compound, MAP30, at concentrations ranging from 1–20 μ g/mL, inhibited cell proliferation and induced apoptosis in a dose-dependent manner without harming normal prostate cells (RWPE-1). Furthermore, PC-3 xenograft tumor growth in nude mice was successfully inhibited by intraperitoneal treatment of MAP30 [6].

3.4.10. Skin Cancer

Fruit extract was given orally to mice, which avoided carcinogen-induced skin carcinogenesis, enhanced survival rates, decreased lipid peroxidation, and activated liver enzymes like catalase, glutathione-S-transferase, and glutathione peroxidase. It also assisted in lessening lymphocyte DNA damage. Given as a pre-treatment or as a continuous local application at doses of 500 and 1000 mg/kg body weight, the methanol extract from the fruit and leaf significantly reduced the formation of skin papillomas induced by dimethylbenz[a]anthracene (DMBA)/croton oil, prevented the formation of micronuclei and chromosomal aberrations, and increased the survival rates in Swiss albino mice. It was discovered that two cucurbitane-type triterpene glycoside chemicals isolated from the fruit might stop mice's skin from becoming cancerous when exposed to DMBA and peroxy nitrite. Fruit and leaf extracts in 50% methanol at doses of 500 and 1000 mg/kg body weight decreased the growth of xenograft tumors in mice and improved survival rates in a melanoma treatment model. Additional research on these substances is required [6][4], [6], [9], [22].

Table 1. *M. Charantia's* functions in the therapy and prevention of cancer [6]

| S. No. | Oncology Model | M. charantia Essences / Constituents | Precautionary & Beneficial effects |
|--------|----------------|--------------------------------------|------------------------------------|
|--------|----------------|--------------------------------------|------------------------------------|

| | | | |
|----|---------------------|---|--|
| 1 | Gastric Organ | Fruit extract, leaf methanol extract, and fractionated proteins I-III were among the samples tested. | The substance exhibited anti-carcinogenic properties in human gastric cancer cell lines and effectively prevented benzo (a) pyrene [B(a)P]-induced forestomach papillomagenesis in mice models. |
| 2 | Mammary Gland | The fruit's aqueous extract, dried extract, and isolated chemicals including 3 β ,7 β ,25-trihydroxycucurbita-5,23 (E)-dien-19-al (TCD), eleostearic acid, RNase MC2, and MAP30 are the components of interest. | Inhibiting glioma cell expansion, migration, and invasion while simultaneously promoting apoptosis. It was found to have the power to stop oral cancer cells from growing and metabolising while also inducing apoptosis in these cells. |
| 3 | Craniofacial region | Water extract of fruit. | Also, it resulted in the regression of 4NQO-induced mice tongue carcinogenesis as well as syngeneic and xenograft tumours of oral cancer. |
| 4 | Cerebral Organ | MAP30, momorcharin α and β , charantagenins D and E, sterol, 7-oxo-stigmasta-5, and 25-diene-3-O- β -d-glucopyranoside were among the constituents. | By promoting apoptosis, it prevented the proliferation, migration, and invasion of glioma cells. |
| 5 | Respiratory Organ | The leaf has been processed into a water extract and a methanol extract, and these extracts contain components such as MAP30 and α -MMC2. | It impeded the proliferation, migration, and invasion of human lung cancer cells, and triggered cell cycle arrest and apoptosis within these cells. |
| 6 | Prostatic gland | The seeds contain Kuguacin-J as well as a 30 kDa protein known as MCP30 | It prevented the growth of both xenograft tumours and spontaneous tumours in TRAMP mice. It also inhibited the proliferation, advancement of the cell cycle, and metastasis of prostate cancer cells. |
| 7 | Large Bowel | The fruit has been processed into a methanol extract, and there are also extracts and oils derived from the seeds. These extracts and oils contain α -eleostearic acid, MAP30, and various cucurbitane-type triterpene glycosides that have been isolated. | In addition to inducing cell cycle arrest, apoptosis, and autophagy and decreasing colon cancer cell growth, it also increased doxorubicin sensitivity and blocked cancer stem cells. Also, it shielded F344 rats from developing colon cancer that was brought on by azoxymethane (AOM). |
| 8 | Renal Organ : | The fruit has been processed into a water extract as well as a methanol extract. | Adrenocortical carcinoma cells' growth and steroidogenesis was inhibited, and it induced apoptosis inside these cells. |
| 9 | Circulatory Fluid | There are extracts derived from the seeds and the fruit, specifically a seed extract and a water extract of the fruit. These extracts contain components such as MAP30 and α -eleostearic acid. | Several leukaemia cell types, including HL-60, THP-1, HL60 ED, Su9T01, HUT-102, and Jurkat, were able to have their growth suppressed by this chemical, which also promoted apoptosis. Also, it reduced tumour development in mice and increased their survival rates while boosting immunological function. |
| 10 | Cervix uteri | There is an extract derived from the leaves as well as a component known as kuguacin-J. | Inhibiting vinblastine and paclitaxel resistance in KB-V1 human cervical cancer cell line. |

| | | | |
|----|------------------|--|--|
| 11 | Ovarium | There is a water extract derived from the fruit as well as a component known as kuguacin J. | Both in vitro and in vivo models of human ovarian cancer exhibited a reduction in growth, an increase in apoptosis, and an improvement in cisplatin sensitivity. |
| 12 | Pancreatic Gland | There is a water extract derived from the fruit as well as an extract derived from the leaves. | It prevented the growth and metabolism of cancer cells and induced apoptosis in xenograft tumours as well as cancer cells. |
| 13 | Hepatic Organ | There is an extract containing karaviloside III, as well as isolated compounds such as MAP30, RNase MC2, and lectin. | It inhibited the growth of human and murine liver cancer cells as well as xenograft tumours in nude mice. Moreover, it stopped the liver carcinogenesis in rats caused by DENA1/CCI43. |

4. MOLECULAR AND GENETIC ANALYSIS OF *MOMORDICA CHARANTIA*

The interaction of several bioactive components in *M. Charantia* is what gives it, its anticancer properties. The stage of carcinogenesis at which crude extract of Bitter Gourd or pure components are provided affects both their ability to prevent and treat cancer. Yet, it has been discovered that the molecular pathways behind both prevention and treatment are similar. Few in vivo studies have been undertaken, and the majority of research on the molecular pathways behind *M. Charantia's* anticancer properties has utilised cancer cell line models grown in vitro. Figure-3 depicts a summary of the molecular processes of *M. Charantia's* anticancer capabilities[9][8].

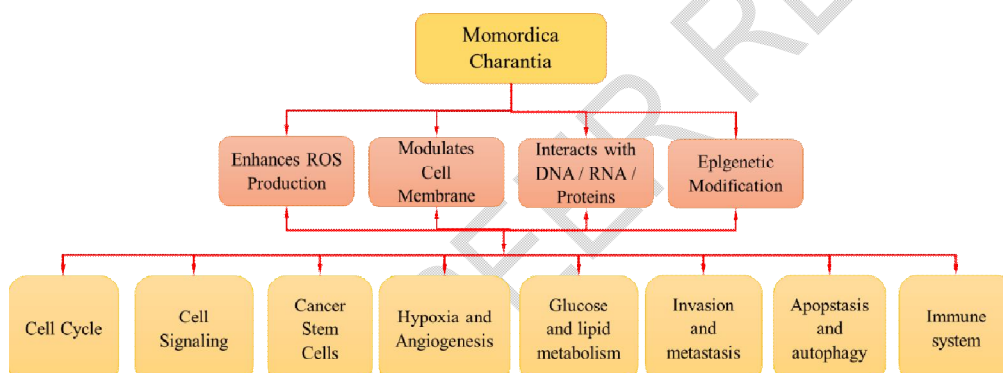


Figure 3M. *Charantia* molecular processes for treating and preventing cancer. Blunt arrows represent inhibition, while sharp arrows represent activation/induction.

In terms of genetic analysis, a dendrogram based on a cluster analysis of 51 bitter gourd accessions based on 10 quantitative features (UPGMA) was produced using the unweighted pair group approach with arithmetic mean. A Bayesian-based approach was used to analyze the population structure of the 51 bitter gourd accessions into six primary groups, which were clustered togetherPDMGy-201. A gynoeocious line, stood out from the other three monoecious genotypes in cluster I. With varied K values ranging from 3 to 51, the Bayesian-based approach predicted membership fractions for the 51 accessions. The structural method's log-likelihood analysis revealed that 3 (K=3) was the ideal value. Likewise, it was discovered that K's greatest ad hoc measure is 3. The 51 bitter gourd accessions may be divided into three subgroups, according to the findings of the K approach. Subgroups were created for admixtures that had a likelihood of less than 60% based on membership fraction. Based on a clustering analysis using the UPGMA method, which produced results that were comparable to those of the structure study, the accessions were divided into three groups. The 51 bitter gourd accessions were classified into three groups through UPGMA cluster analysis. Group I included four small-fruited bitter gourd accessions from central and eastern India. Group II was the most genetically diverse, consisting of 35 medium-sized fruited accessions from various origins, including exotic lines. Group III contained 11 long and extra-long fruited accessions. Among the accessions, Sel-25 was identified as the most genetically diverse. The analysis revealed four distinct groups within the accessions, each with its own unique characteristics. The PCA plot showed significant variability among the 51 accessions, with a total of 27.47% explained by the three axes analyzed [8].

5. FINDING AND DISCUSSION

The utilization of *M. charantia* as medicine is a major focus in the fields of diabetes and nutrition. For many years, it has been used as a dietary supplement and ethnomedicine for treating conditions and symptoms associated with diabetes. It is known for its diverse range of medicinal properties that can be used to treat numerous diseases. This is explained by the plant's over 225 therapeutic components, each of which has the ability to operate alone or in concert to produce a variety of therapeutic effects. More specifically, only some *M. Charantia* extracts—such as charantin, insulin-like peptide, and alkaloid-like extracts—have hypoglycemic effects when it comes to diabetes. These extracts regulate and treat diabetes mellitus through a variety of methods. Type 1 and type 2 RIPs, lectin, RNase, and other possible therapeutic agents for the treatment of cancer are found in the bitter melon plant. Numerous cancer cells undergo apoptosis when exposed to these drugs, and the apoptotic pathways involved have been extensively researched. These bitter melon proteins may have an effect on other malignancies, according to future study. Numerous non-proteinaceous small compounds with significant biological properties can be found in bitter melon.

Studies have shown that bitter melon may be effective in inhibiting the growth, survival, and spread of cancer cells across various cancer types, without harming normal cells. Before moving to clinical trials, more research is needed to explore the potential benefits of the key components in bitter melon. With its rich nutrients and bioactive compounds like triterpenoids, triterpene glycoside, phenolic acids, and more, bitter melon has the ability to influence multiple cellular processes that could prevent and treat cancer. While it has the potential to enhance cancer prevention and be a complement to traditional cancer treatment, further research is required to fully understand its mechanisms and potential for interventional therapies.

The wide range of factors that can affect the preparation and potency of bitter melon can lead to conflicting results in research, making it challenging to determine the optimal dosage for effectiveness and safety. It is important to be cautious when combining bitter melon with other medications for lowering blood glucose levels, as there may be additional effects. This study examined the potential of specific bitter melon varieties for yield and early maturity based on ten key characteristics. The diverse genetic variations identified in this research will be valuable in future breeding efforts to increase bitter melon productivity. The study also revealed a strong genetic foundation in the existing germplasm of bitter melon, which can be utilized for various breeding strategies aimed at enhancing the crop.

To advance research on *Momordicacharantia*, addressing the existing challenges of limited and inconsistent clinical data is paramount. Future studies should prioritize well-designed, large-scale human clinical trials with adequate statistical rigor to accurately assess its antidiabetic and anticancer effects. These trials should focus on identifying the mechanisms of action, optimizing dosages, and evaluating long-term safety and effectiveness. Further phytochemical research is essential to isolate and understand the active compounds, complemented by detailed pharmacokinetic and pharmacodynamic studies. Collaborative efforts across disciplines, incorporating modern biotechnology and genomics with traditional medicine, will help validate *M. Charantia's* therapeutic potential. Standardizing cultivation, extraction, and preparation methods will ensure consistent and reliable clinical results, paving the way for its integration into mainstream medical practice.

6. CONCLUSION

Bitter melon, also known as *Momordicacharantia*, is a plant with significant medicinal properties, traditionally used for managing diabetes and cancer. It contains compounds with hypoglycemic and anticancer effects that may enhance conventional cancer treatments. However, more research is required to identify the active components and establish the optimal dosage for both efficacy and safety. Caution is advised when using bitter melon alongside other blood glucose-lowering agents. Furthermore, genetically diverse strains have been identified, which could be used in breeding programs to improve the productivity of *M. Charantia*, making it a valuable option for agricultural development. Further research should focus on well-designed, large-scale clinical trials to confirm the therapeutic benefits of *M. Charantia* and establish standardized guidelines for its use. Detailed studies on its pharmacokinetics and pharmacodynamics are necessary to understand its mechanisms of action and optimize dosages. Collaborative research, integrating modern biotechnology and traditional medicine, will be crucial in validating and expanding its medicinal applications. Additionally, standardizing the cultivation, extraction, and preparation methods will ensure consistent and reliable

results. Exploring the genetic diversity of *M. Charantia* can lead to the development of improved varieties with enhanced medicinal properties and agricultural potential.

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

References

1. M. Thakur and R. K. Sharma, "bitter gourd: health properties and value addition at farm scale a," *Kisaan E- Patrika*, vol. 1, no. 2, p. 2016, 2016. Available: www.marumegh.com.
2. M. B. Krawinkel and G. B. Keding, "Bitter gourd (*Momordica charantia*): A dietary approach to hyperglycemia," *Nutr. Rev.*, vol. 64, no. 7, pp. 331–337, 2006, doi: 10.1301/nr.2006.jul.331-337.
3. L. T. Yoshime, I. L. P. de Melo, J. A. G. Sattler, E. B. T. de Carvalho, and J. Mancini-Filho, "Bitter gourd (*Momordica charantia* L.) seed oil as a naturally rich source of bioactive compounds for nutraceutical purposes," *Nutrire*, vol. 41, no. 1, pp. 1–7, 2016, doi: 10.1186/s41110-016-0013-y.
4. D. Kwatra *et al.*, "Methanolic extracts of bitter melon inhibit colon cancer stem cells by affecting energy homeostasis and autophagy," *Evidence-based Complement. Altern. Med.*, vol. 2013, 2013, doi: 10.1155/2013/702869.
5. M. Kaur *et al.*, "Bitter melon juice activates cellular energy sensor AMP-activated protein kinase causing apoptotic death of human pancreatic carcinoma cells," *Carcinogenesis*, vol. 34, no. 7, pp. 1585–1592, 2013, doi: 10.1093/carcin/bgt081.
6. S. Sur and R. B. Ray, "Bitter melon (*Momordica charantia*), a nutraceutical approach for cancer prevention and therapy," *Cancers (Basel)*, vol. 12, no. 8, pp. 1–22, 2020, doi: 10.3390/cancers12082064.
7. B. Joseph and D. Jini, "Antidiabetic effects of *Momordica charantia* (bitter melon) and its medicinal potency," *Asian Pacific J. Trop. Dis.*, vol. 3, no. 2, pp. 93–102, 2013, doi: 10.1016/S2222-1808(13)60052-3.
8. A. Alhariri *et al.*, "Analysis of genetic diversity and population structure in bitter gourd (*Momordica charantia* L.) using morphological and SSR markers," *Plants*, vol. 10, no. 9, pp. 1–17, 2021, doi: 10.3390/plants10091860.
9. M. Bortolotti, D. Mercatelli, and L. Polito, "Momordica charantia, a nutraceutical approach for inflammatory related diseases," *Front. Pharmacol.*, vol. 10, no. MAY, pp. 1–9, 2019, doi: 10.3389/fphar.2019.00486.
10. A. J. John, R. Cherian, H. S. Subhash, and A. M. Cherian, "Evaluation of the efficacy of bitter gourd (*Momordica charantia*) as an oral hypoglycemic agent - A randomized controlled clinical trial [3]," *Indian J. Physiol. Pharmacol.*, vol. 47, no. 3, pp. 363–365, 2003.
11. A. Upadhyay, P. Agrahari, and D. K. Singh, "A review on salient pharmacological features of *Momordica charantia*," *Int. J. Pharmacol.*, vol. 11, no. 5, pp. 405–413, 2015, doi: 10.3923/ijp.2015.405.413.
12. A. M. L. Dans *et al.*, "The effect of *Momordica charantia* capsule preparation on glycemic control in Type 2 Diabetes Mellitus needs further studies," *J. Clin. Epidemiol.*, vol. 60, no. 6, pp. 554–559, 2007, doi: 10.1016/j.jclinepi.2006.07.009.
13. E. F. Fang, L. Froetscher, M. Scheibye-Knudsen, V. A. Bohr, J. H. Wong, and T. B. Ng, "Emerging Antitumor Activities of the Bitter Melon (*Momordica charantia*)," *Curr. Protein Pept. Sci.*, vol. 20, no. 3, pp. 296–301, 2018, doi: 10.2174/1389203719666180622095800.
14. E. F. Fang, C. Z. Y. Zhang, J. H. Wong, J. Y. Shen, C. H. Li, and T. B. Ng, "The MAP30 protein from bitter gourd (*Momordica charantia*) seeds promotes apoptosis in liver cancer cells in vitro and in vivo," *Cancer Lett.*, vol. 324, no. 1, pp. 66–74, 2012, doi: 10.1016/j.canlet.2012.05.005.
15. S. F. Oyelere *et al.*, "A detailed review on the phytochemical profiles and anti-diabetic mechanisms of *Momordica charantia*," *Heliyon*, vol. 8, no. 4, p. e09253, 2022, doi: 10.1016/j.heliyon.2022.e09253.

16. D. Sathishsekar and S. Subramanian, "Antioxidant properties of Momordica Charantia (bitter gourd) seeds on Streptozotocin induced diabetic rats," *Asia Pac. J. Clin. Nutr.*, vol. 14, no. 2, pp. 153–158, 2005.
17. L. Leung, R. Birtwhistle, J. Kotecha, S. Hannah, and S. Cuthbertson, "Anti-diabetic and hypoglycaemic effects of Momordica charantia (bitter melon): A mini review," *Br. J. Nutr.*, vol. 102, no. 12, pp. 1703–1708, 2009, doi: 10.1017/S0007114509992054.
18. R. Y. Yang *et al.*, "Better bitter gourd: A food-based approach to manage type 2 diabetes and promote health in developing countries," *Acta Hort.*, vol. 1106, no. December, pp. 161–167, 2015, doi: 10.17660/ActaHortic.2015.1106.25.
19. A. Ganesan, S. Natesan, P. G. Perumal, R. Vellayutham, K. Manickam, and N. Ramasamy, "Anxiolytic, antidepressant and anti-inflammatory activities of methanol extract of Momordica charantia Linn leaves (Cucurbitaceae)," *Iran. J. Pharmacol. Ther.*, vol. 7, no. 1, pp. 43–47, 2008.
20. P. L. H. Sylvia Lee-Huang", "Anti-HIV and anti-tumor activities of recombinant MAP30 from bitter melon," *Gene*, vol. 161, pp. 151–156, 1995.
21. J. Pitipanapong, S. Chitprasert, M. Goto, W. Jiratchariyakul, M. Sasaki, and A. Shotipruk, "New approach for extraction of charantin from Momordica charantia with pressurized liquid extraction," *Sep. Purif. Technol.*, vol. 52, no. 3, pp. 416–422, 2007, doi: 10.1016/j.seppur.2005.11.037.
22. A. Angadi, Y. H. Kumar, and S. Ahmed, "Medicinal and nutritional importance of bitter melon (Momordica charantia L): A review article," ~ 297 ~ *J. Pharmacogn. Phytochem.*, vol. 3, pp. 297–300, 2018.
23. H. Sciences, "Revised FSSAI annual of Methods of Analysis of Foods-reg," *FSSAI*, vol. 4, no. 1, pp. 1–23, 2016.
24. F. E. Pehlivan, "Bitter Melon: A Multifunctional Medicinal Plant with Powerful Bioactive Compounds," *Intech*, pp. 225–240, 2016, [Online]. Available: <https://www.intechopen.com/books/advanced-biometric-technologies/liveness-detection-in-biometrics>.

Abbreviations

| | |
|-------------------------------|---|
| DENA ¹ | Diethylnitrosamine |
| MMC ² | Momorcharin |
| CCL ₄ ³ | Carbonatetrachloride |
| DMBA ⁴ | 7,12-Dimethylbenz(a)anthracene |
| ROS ⁵ | Reactive Oxygen Species |
| 4NQO ⁶ | 4-Nitroquinoline 1-oxide |
| AMPK ⁷ | 5'-AMP-Activated Protein Kinase |
| MAP30 ⁸ | Momordica Antiviral Protein 30kD |
| AKT ⁹ | AKT Serine/Threonine Kinase |
| ERK ¹⁰ | Extracellular signal-regulation kinase |
| TRAMP ¹¹ | Transgenic Adenocarcinoma of the mouse Prostate |
| TNF ¹² | Tumor Necrosis Factor |
| GLUT ¹³ | Glucose Transporter |
| HMP ¹⁴ | Hexos Monophosphate Shunt |