

Medicinal and health-promoting properties of Bitter gourd (*Momordica charantia*) and its extracts

Abstract

Numerous documented researches have been conducted to evaluate the potential of using different plants and herbs as traditional medicines. Bitter gourd (*Momordica charantia*) is an agricultural commodity belonging to the plant kingdom and family Cucurbitaceae. Besides having a higher content of calcium and iron, this plant also possesses considerable numbers of vitamins such as B₁, B₂, B₃, and C. These are great sources of some biologically active compounds such as momordicin I, II, and cucurbitacin B. The salutary perceptions have been also emphasized as they are useful in protecting from cardiovascular conditions such as atherosclerosis thereby, regulating the blood cholesterol level in the body. Bitter gourd entire fruit, seeds, and leaves help lower the fat accumulation and also control the impaired antioxidant status. Though this plant could facilitate the balance effect of anti-HIV drugs, the contents of ration amino sugar variate by declined and inclined, observed in lungs, heart, liver, and spleen during diabetes.

Key Words: *Bitter gourd, medicinal usage, curing potential*

1. Introduction

Traditionally, herbs and natural substances in plants are utilized for medicinal purposes because of having higher contents of plant-based antioxidant compounds.

Recent pharmacological research has explained that the bitter melon due to its health benefits and functional activities considered a “medicine food homology” plant [1][2]. Plants have a high ability to produce aromatic substances in aerobic cellular conditions through the interaction of oxygen with polyphenols. Mostly, these interactions played an important role in producing immunity against molecular and herbivores [1,3]. The production of organic matter such as DNA, proteins, carbohydrates, and lipids is damaged by reactive oxygen species (ROS). Various compounds are present in ROS such as hydrogen peroxide, superoxide (O_2^-), and hydroxyl (OH) radicals. The harmful reactions caused by ROS can be controlled by enzymatic and non-enzymatic antioxidants, eradicating pro-oxidants and scavenging free radicals [4]. Several synthetic antioxidants including Butylated hydroxytoluene (BHT) and BHA (hydroxyanisole), are usually used in many foods but have some negative influence on the body. Moreover, it has been proposed that intake of antioxidant-enriched remarkably reduces the disease's attack.

Bitter melon is a vegetable also termed as balsam pear or Karela, (*Momordica charantia*; *Cucurbitaceae* family) originated in sub-tropical and tropical areas of South America and Asia (Fig.1). The literal meaning of *Momordica* is “to bite” presenting the leaf edges taste in bitterness after chewing a fruiting part. The bitter melon is green colored, having a cucumber-resembling shape in resemblance to cucumber, and it changes color to orange-yellow upon ripening [5,6]. Besides having several gastric and therapeutic benefits, the bitter melon is also considered to have beneficial impacts on various spleen and liver diseases including gout, rheumatism, and blood purification. Sun et al. [7] found that bitter melon contained a significant level of hypoglycemic influence.

This study also identified several health-beneficial pharmacological properties of bitter gourd, including antibiotics, antiviral, antibacterial, anti-tumor, etc. [7].

Botanical Classification

Kingdom: *Plantae*
 Division: *Magnoliophyta*
 Class : *Magnoliopsida*
 Order: *Viales*
 Family: *Cucurbitaceae*
 Genus: *Momordica*
 Species: *Charantia*



Bitter gourd

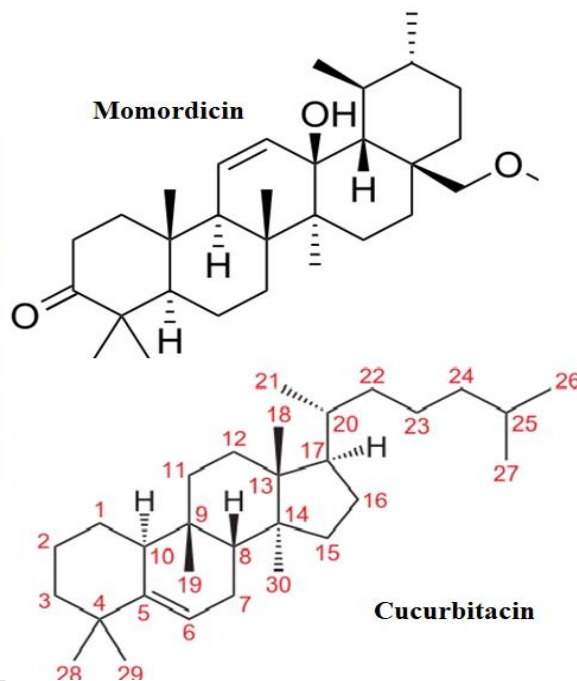


Fig. 1 Bitter gourd botanical classification and its structure a) Momordicin b) Cucurbitacin

Bitter gourd provides a variety of amino acids including glutamine, valine, arginine, lysine, leucine, alanine, asparagines, tryptophan, histidine, threonine, methionine (Table.3). It has been reported that intake of bitter gourd in different forms are beneficial to reduce blood glucose level. It contains a large number of hypoglycemic compounds such as charantin, olanolic acid 3-O-monodesmoside, and polysaccharides. Previous studies showed that bitter gourd contained several health-beneficial compounds, including carbohydrates, lipids, proteins, saponins, flavonoids, triterpenoids, and alkaloids (Table. 1) [8,9]. The biochemical (ascorbic acid), flavonoids, and bioactive compounds are present in good amounts and considered major sources of antioxidants in bitter gourd [10]. Polysaccharides which account for almost 2.6–3.5g per 100 g of bitter

gourd, are considered the major bioactive compounds in bitter gourd, therefore, have attained much consideration due to their numerous bioactivities such as antidiabetic, immune-regulation, antioxidant, antimicrobial and antitumor activities (Fig.2) [11–13]. Several polysaccharides with different structural behaviors were extracted from bitter gourd [14].

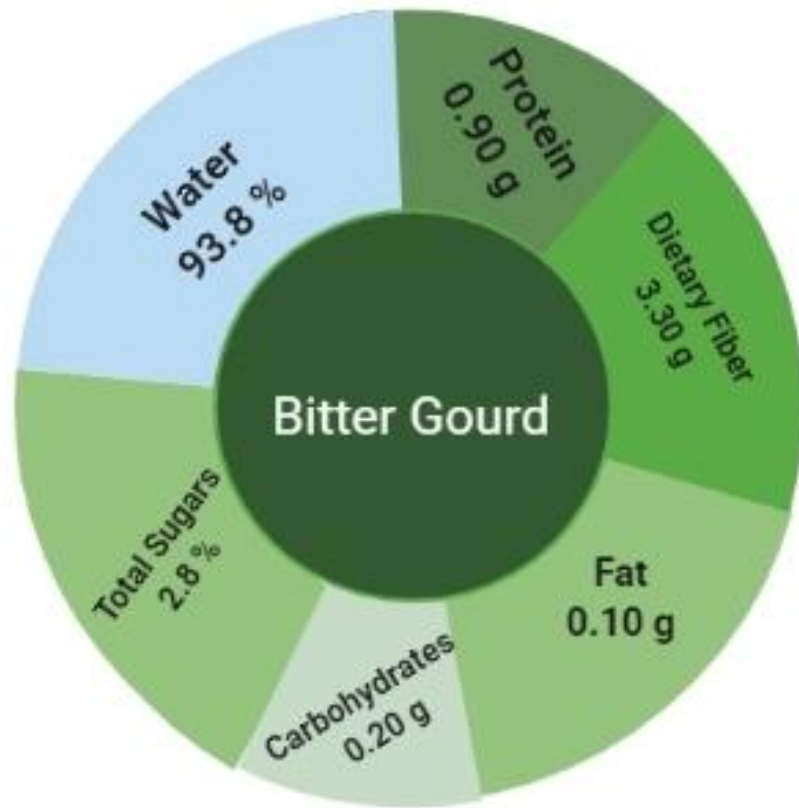


Fig.2 Nutritional Composition of bitter gourd (adopted from[8]).

Previous studies proved that the consumption of saponin-free methanolic extract remarkably reduced the glucose content in normal and insulin-dependent diabetes (IDDM) [15]. It also contains insulin-substitute compounds polypeptide P, which can be useful for diabetic patients [16]. Previously researchers showed the anti-diabetic

characteristics of bitter gourd after feeding animals with bitter gourd[17–19]. In the present review, we have elucidated the possible medicinal potential of bitter gourd (Fig.3), and its extract against several diseases (Table.2). The health-promoting benefits of bitter gourd from previous studies were also shown in this study. Moreover, the mechanism behind the effectiveness of bitter gourd against diseases was also explained in our current review.

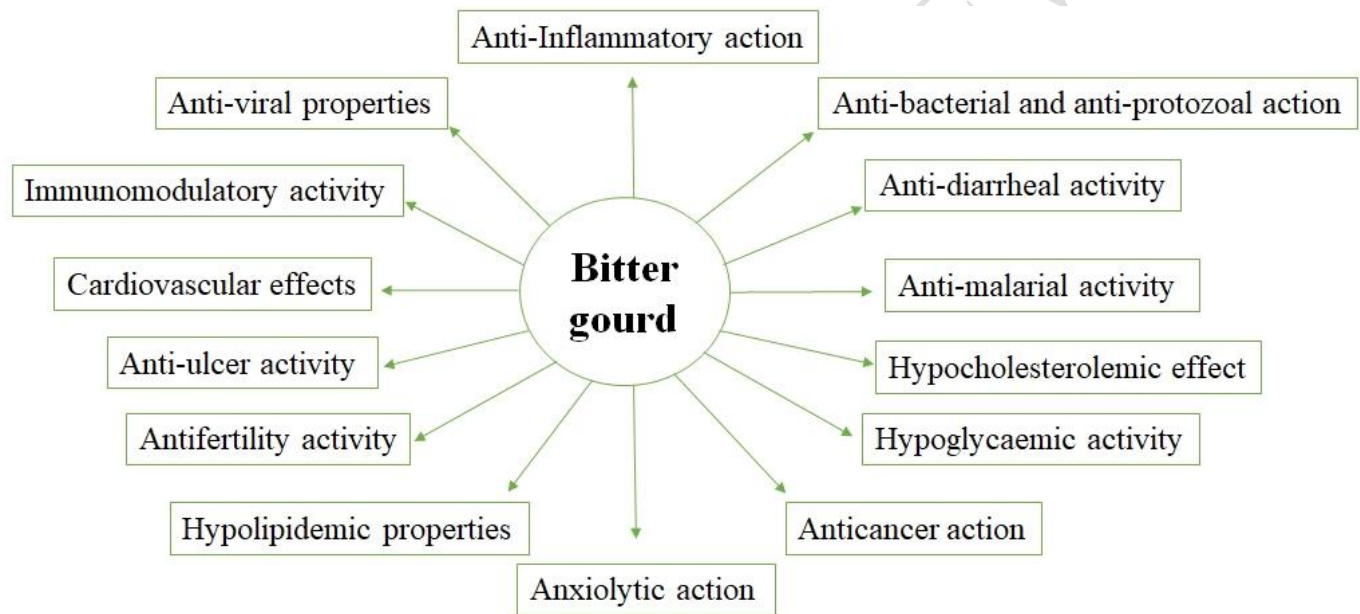


Fig. 3. Medicinal properties illustration of bitter gourd.

2. Biological active substances in bitter gourd

The availability of various biologically active compounds in bitter gourd could enhance its potential use in food to intake several health-promoting substances such as momordicin I and II and cucurbitacin B. However, bitter gourd comprises numerous bioactive glycosides along with other terpenoid compounds. There are various chemical compounds such as cytotoxic (ribosome-inactivating), momordin, and momorcharin found in bitter gourd that are utilized for medicinal purposes. Cucurbitacin is a class of

biochemical compounds that are found in plants of the family of Cucurbitaceae. It is cytotoxic and poisonous for some animals and bitter taste for humans.

2.1. Medicinal perspectives of bitter gourd

The presence of bioactive molecules in bitter melon as a natural product can delay the aging process. Several phytochemical constituents as functional ingredients were found in bitter melon for example tannins, alkaloids, flavonoids, glycosides, phenolic, and terpenoids. A variety of saponins were found in the plant of *Momordica charantia* including karavilagenin momordin, momordicin, kuguacin, karaviloside, and momordicoside [20]. In another research, the lifespan of obese rats fed on bitter melon increased significantly in contrast to controlled rats [21]. Because of the functional ingredients, bitter gourd has numerous pharmacological properties, including antifungal [12], antioxidant [22], anti-diabetic[23], anti-obesity, hypotensive, stomachic, and blood cholesterol-lowering effects, and anticancer properties [24]. Diabetes mellitus and accompanying problems were a correct instance of lifestyle interrelated ailments. The inactive routine increased the consumption of alimentary energy, and obesity was among the numerous reasons for diabetes mellitus and metabolic syndrome [25]. The medications which are used for diabetes mellitus management have various side effects, therefore, there is a need to substitute these medications. Hence, the bitter gourd having several health benefits can be a potential candidate to improve the diabetic situation, thereby, lowering the burden on anti-diabetic medicines [26].

2.1.1 Bitter gourd helps in the prevention of Malaria

Conventionally, bitter melon was used to treat in Asia and other regions. However, its leaves were also used to make tea in Panama and Colombia, while it was

cooked with garlic and onion in Guyana. The mixture of garlic, onion, and bitter gourd leaves is known as corilla, which has been used for the prevention of malaria. In-vitro studies proved that bitter melon species hold anti-malarial activity while unclear concerning in-vivo results [5]. Previous studies found that the leave extract of this plant excellent fight against the bacterial and viral attacks by improvising antibodies of *S. typhi* infected mouse, decreasing infection proportion in blood. Traditionally, this plant is effective against different viral diseases (chickenpox and measles). The extraction with ethanol from bitter melon leaves and stems prevents viral attacks of HSV-1 and SINV [7].

2.1.2 Anti-hyperlipidemic activities of Bitter gourd

The anti-hyperlipidemic effect has been significantly observed by the utilization of *Momordica charantia*. In recent times, it has been described that an altered mechanism of bitter melon could repair the impaired beta cells consequently aggregating the insulin level and its sensitivity [27]. It hinders glucose absorption by constraining the functionality of glucosidase hence also arouses the release and production of adiponectin and thyroid hormones. Bitter melon improves the action of adenosine-5-monophosphate kinase that is associated with uptake of glucose level and proclamation of fat (fatty tissues), hence, triggering the reduction of weight [28]. Another research also showed that significant reduction in blood lipid levels of diabetic rats treated with extract of *Momordica charantia*. Triglycerides (hepatic production) also cause the hyperlipidemic influence of HIV-1-protease inhibitors, which are having lipoprotein instead of lipoprotein clearance[29].

2.1.3 Bitter gourd against HIV diseases

Bitter gourd possesses a lot of potential proteins incorporated in lectin, type I RIP, type II RIP, and ribonuclease which have strong positive impacts against HIV and tumors. Proteins class lectins or glycoproteins binding properties with erythrocyte-agglutinating and carbohydrate are useful as anti-HIV and antitumor agents [30]. In vivo studies reported that bitter melon seeds were helpful in cardioprotection by down-regulating of NF- κ B inflammatory process. Another characteristic of non-protein binding with insulin is due to presence of lectin in bitter melon. Lectin affects peripheral tissues and brain appetite signals and promotes the hypoglycemic effect of blood glucose. The hypoglycemic properties in bitter melon developed because of the stimulation of lectin with the bitter melon ingestion[31]. While in vitro studies showed that two compounds known as α -eleostearic acid in seeds and 15,16-dihydroxy- α -eleostearic acid in fruit were observed to stimulate apoptosis of leukemia cells. Chong et al. [32] found another disease prevention in the rat colon disease with the help of 0.01% bitter melon oil (0.006% as α -eleostearic acid) presence in the diet [32].

Bitter gourd (*Momordica charantia*) has been traditionally used to treat various diseases, while some wild species of bitter gourd such as *Momordica charantia* Linn. var. *abbreviata* ser. (WBG), are more potent in disease prevention. Moreover, only limited bio-physiological impacts were observed in WBG. Similarly, the bitter gourd was also found to have remarkably anti-inflammatory impacts by decreasing prostaglandin E2 (PGE2), interleukin (IL)-7 and tumor necrosis aspect and intensifications conversion growth attribute and IL-10 secretion in RAW 264.7 macrophages, Caco-2 cells, and

THP- 1 cell [19,33]. The feeding of the fruiting part of the bitter gourd significantly improved the T helper 2 hormonal responses and T helper 1 cellular immunity [34].

Currently, the chemical compounds showed significantly resolved health issues in the presence of phytochemicals in bitter gourd. It has been reported that Charantins comprising steroidal-saponins were abundantly present, indicating the hypoglycemic and anti-hyperglycemic activity [35]. Furthermore, several phenolic compounds including gallic acid, gentisic acid (2,5-dihydroxyl benzoic acid), and catechins are presented in bitter gourd. Cyclooxygenase-2 (COX-2) mRNA expression was also found to be successfully inhibited after bitter gourd treatment due to enhancing the anti-inflammation property of gentisic acid which is a metabolite of salicylic acid and PGE2 [36,37].

2.1.4. Role of bitter Gourd against diabetic disease

Diabetes is a health issue caused by the consumption of high levels of carbohydrates, fat, and protein, and can be addressed by delaying digestion and expanding fasting and postprandial glucose levels. Sathishsekar et al. [38] found a decrease in the diabetes level after feeding rodents with bitter gourd. Oral feeding of around 150 mg/kg for 30 days duration demonstrated a significant decrease in fasting blood glucose level, hepatic and renal thiobarbituric corrosive responsive substances, and hydro-peroxides. The treatment likewise brought about a critical expansion in diminished glutathione, catalase, superoxide dismutase, glutathione-s-transferase, and glutathione peroxidase in the liver and kidney of diabetic rodents. This study showed that seeds of *Momordica charantia* may adequately standardize the disabled cell reinforcement status in streptozotocin-instigated diabetes. This feeding caused the quick defensive impacts

against lipid peroxidation by searching for free extremists thereby decreasing the danger of diabetic inconveniences [38].

Zimmet et al. [39] found that diabetes is an illness of extraordinary worry to a large population around the world and is known for its difficulties in incorporating diabetic neuropathy, nephropathy, and retinopathy. During diabetic nephropathy, stromal cell layer thickening is known to happen in the kidney. The cell layer thickening during nephropathy caused the establishment of heparin sulfate a sulfated proteoglycan, laminin a high-atomic weight glycoprotein, and Type IV collagen a perplexing glycoprotein. These are interlinked in a fine design for typical filtration to occur during diabetes, thereby, lessening the content of heparin and sulphate, and laminin, which is also associated with the expansion of type IV collagen, consequently influencing the pore size to cause kidney harm. Modifications in the stromal cell layer in various tissues during diabetes are of major concern and would require an immediate examination. Besides insulin or medicine, diet is also a major element to consider while the management of diabetes [40].

Spent turmeric is a side-effect of curcumin processing, which stays after curcumin was extracted from turmeric. The spent turmeric is rich in dietary filaments and contains both soluble and insoluble dietary strands. Dietary filaments are grounded to assume useful parts against different illnesses such as diabetes, colon malignant growth, coronary illness, and so on [41]. They are consumed as a source of insoluble lattice to slower down the ingestion of glucose, therefore, enhancing gastrointestinal health. Conversion of complex dietary fiber to short-chain fatty acids could increase their health beneficial properties. The body weight diminished significantly in diabetic rodents, but loads of

spleen and heart did not have any significant changes. The unpleasant gourd and spent turmeric were found to be beneficial in controlling diabetics' conditions and these symptoms[42].

Fukami et al. [43] found that total sugar contents could damage the liver, spleen, and mind. Uronic corrosive substance in liver, spleen, and mind could also diminish, while minimal increment was seen in testis. Amino sugar contents also diminished the liver, spleen, lungs, and heart health during diabetes. The decline in sulfation of glycol-conjugates was also seen in diabetic patients which was enhanced by harsh gourd and spent turmeric, apart from the cerebrum. Protein contents were observed to diminish in the liver, while an increment was seen in the brain organ. The examinations showed the adjustment in glycol digestion during diabetes and enhancement to various degrees by taking care of severe gourd and spent turmeric for rodents.

Fukami et al. [43] found that diabetes influenced a significant number of the metabolic occasions prompting the underlying changes inside the cells and their vascular framework, therefore prompting long haul confusions of diabetes. Diabetic nephropathy is one of the main sources of end-stage renal turmoil (ESRD) and records huge mortality in diabetic patients. Structural changes in diabetic nephropathy in Type 1 diabetic patients are very transcendent with the thickening of the glomerular cellar layer (GBM) and mesangial extension. During diabetes, serious super underlying and practical adjustments in the GBM might be due to significant physiological changes causing end-stage renal turmoil. The overwhelming macromolecules associated with the design of GBM are glycoconjugates compounds such as fibronectin, heparan sulfate, and laminin, type IV collagen. These are connected to frame a boundary to charged particles, thereby,

going about an obvious organic channel. Analysis of GBM during diabetes has shown the decline and under sulfation of heparan sulfate (HS) [a significant glycosaminoglycan consists of a dynamically sulfated disaccharide rehash with a uronic corrosive (glucuronic or iduronic corrosive) and glucosamine] which fills in as charge specific obstruction in the filtration of macromolecules. These progressions are typically connected with upgraded penetrability to macromolecules prompting ESRD.

2.1.5. Role of bitter gourd in preventing diabetes mellitus type II

Jayasooriya et al. [44] studied the therapeutic utilization of bitter gourd against diabetes and found that the bitter gourd and its extracts could display a powerful hypoglycemic action in normoglycemic and streptozotocin-prompted diabetic rodents. The westernization of dietary propensities observed in Japan has caused an increase in infection risks such as fatty liver, diabetes, and hyperlipidemia. Therefore, there is an enhanced interest in seeing plant-based substitutes improve such conditions. Habicht et al.[45] found that the diverse bioactive mixtures are associated with the hypoglycemic impact of bitter gourd extracts. Moreover, lipids and saponins were helpful for diabetic patients. The white bitter gourd has lower saponin fixation, thereby could be having less compelling. Absolute lipids and fatty corrosive synthesis appear to rely more upon the development of the natural products rather than the contrasts between assortments. Consequently, green bitter gourd at a young maturity level that is tenderly handled can be considered for the anticipation and treatment of diabetes mellitus. Moghadasian and Frohlich. [46] studied that bitter melon had specific parts which could improve the lipid problems including fatty liver and hyperlipidemia. Currently, very few detailed studies

are available explaining the dietary impact of bitter gourd on serum and liver lipids, but several studies found the positive impact of bitter gourd on type II diabetes mellitus.

2.1.6. Role of bitter gourd in preventing renal failure

Traditionally, plants have been an excellent source of medication, and several plants extract have been utilized to control Diabetes Mellitus in numerous nations. Among these plants, the varieties having dietary filaments were considered major food parts to administer to diabetic patients. Bitter gourd was considered one of the major medicinal plants against diabetes. Harsh gourd (*Momordica charantia* LINN.) from Cucurbitaceae family is generally a devoured vegetable in India, and its products are widely utilized in fables medication in the administration of various infections including diabetes [47]. There is an incredible need to recognize treatments that could help in curing end-stage renal disease. Moreover, the best remedy for diabetes might also be to permit the patient to stay safe from the side effects, as well as health conditions with normal metabolic state and to get away from long haul intricacies.

2.1.7. Role of bitter gourd in lowering liver cholesterols

Gamarallage et al. [48] observed that Koimidori is the best bitter melon assortment regarding its capability to bring down the hepatic fatty substance fixation; the subsequent investigation was also performed to discover the dynamic component(s) by fractionation of its powder with natural solvents such as methanol and n-hexane. The impacts on reducing serum and liver fatty substances showed that liver fatty substances focused in rodents could be taken care of in diets containing 1% methanol and 3% Koimidori powder. These two different parts extricated by n-hexane and $\text{CH}_3)_2\text{CO}$, or the lingering division could expand the hepatic fatty oil levels. Along these lines, the

powerful dynamic component(s) of Koimidori could bring down the liver's fatty substances due to bitter melon extract. One more fascinating perception in this analysis was that the methanol portion can effectively bring down the liver cholesterol. As free cholesterol stays unaltered, these impacts are to some degree because of the diminished collection of cholesterol esters. Therefore, this proposes that some useful components in the methanol part of Koimidori could bring down the fatty substance just like cholesterol in the liver.

2.1.8. Role of bitter gourd against cancer

Worldwide, the second leading cause of death is cancer. To cure this disease many products of dietary plants show promising anticancer effects. Among those, Bitter melon or bitter gourd is used as folk medicine and considered a rich source of many bioactive compounds such as phenolic acids, lectins triterpenoids, triterpene glycoside, etc., which show major anticancerous activities without significant negative effects[49].

Alam et al. [50] found that the fatty corrosive arranged from BGO rich in 9c, 11t, 13t-CLN displayed huge apoptosis in Caco-2 cells via the reduction of Bcl-2 proteins which are an apoptosis silencer. The 9c, 11t, 13t-CLN decontaminated from BGOFFA additionally surprisingly decreased the cell feasibility and prompted the apoptosis reactions in Caco-2 cells (information not shown). These outcomes demonstrated that the impact of BGO is mostly dependent on the apoptosis prompted by 9c, 11t,13t-CLN. Moreover, 9c,11t-CLA didn't influence the cell reasonability nor the apoptosis of Caco-2 cells in the current review, albeit 9c,11t-CLA has been accounted for to restrain cell multiplication or incite apoptosis in colon malignant growth cell lines [50].

Girnun et al. [51] reported that the apoptosis and anti-proliferative actions of BGOFFA rich in 9c, 11t,13t-CLN were significantly higher than that of 9c,11t-CLA in Caco-2 cells. The GADD45 and p53 played a significant role in the development of hindrances and apoptosis acceptance in many kinds of malignant growth cells, therefore, PPARg has been considered beneficial in forestalling disease [51].

Kohno et al.[52] also reported overexpression of PPARg proteins in rats administered with BGO compounds. PPARg ligands such as 15d-prostaglandin (PG) J2 and troglitazone were reported to influence the growth inhibition and caused the apoptosis in cancer cells. Furthermore, PPARg protein ligands inhibited the development of ACF, which are the main putative precursor lesions for colonic adenocarcinoma, which could be influenced by the treatment with azoxymethane (AOM) and dextran sodium sulfate in rats. They also found that BGO-FFA could improve themRNA and PPARg protein levels in Caco-2 cells. Kohno et. [52] also found that the improvement of expression (PPARg) by BGO-FFA may be beneficial in preventing carcinogenesis of the colon.

Tsuzuki et al. [53] have found that 9c,11t,13t-CLN caused apoptosis in the cells (DLD-1) through the peroxidation of lipids. Though, it was not mentioned whether lipid peroxidation and signaling (GADD45, p53, and PPARg) reactions occurred during apoptosis or through multiple signaling pathways. Further research is needed to assess the apoptosis induction mechanisms in Caco-2 cells by purifying 9c,11t,13t-CLN as well as BGO-FFA [53].

3. Conclusion

Modern lifestyle is a major reason for unhealthiness and could be a major cause of diseases such as diabetes, cancer, HIV, etc. Consumption of plant-based natural resources could enhance immunity against diseases. Undoubtedly bitterness and phytochemicals presented in bitter gourd (*Momordica charantia*) have significant positive effects in curing diseases against inflammation and diabetic patient. This improvement might be due to the slower release of glucose in the gastrointestinal tract and the production of short-chain fatty acids from the fiber compounds through colon microbes. This review provides comprehensive information concerning medicinal plant potential in human life. This review never draws borderlines of bitter gourd usage but also delivers desirable future studies to describe clinical effects on human consumption.

Ethical approval

Ethics approval was not required for this research.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. Naqvi, S. A. R.; Ali, S.; Sherazi, T. A.; Haq, A.-U.; Saeed, M.; Sulman, M.; Rizwan, M.; Alkahtani, S.; Abdel-Daim, M. M. Antioxidant, antibacterial, and anticancer activities of bitter gourd fruit extracts at three different cultivation stages. *J. Chem.* **2020**, 2020.
2. Yan, J.-K.; Yu, Y.-B.; Wang, C.; Cai, W.-D.; Wu, L.-X.; Yang, Y.; Zhang, H.-N. Production, physicochemical characteristics, and in vitro biological activities of polysaccharides obtained from fresh bitter gourd (*Momordica charantia* L.) via

- room temperature extraction techniques. *Food Chem.* **2021**, 337, 127798, doi:10.1016/j.foodchem.2020.127798.
3. Gowri, S. S.; Vasantha, K. Phytochemical screening and antibacterial activity of *Syzygium cumini* (L.)(Myrtaceae) leaves extracts. *Int J Pharm Tech Res* **2010**, 2, 1569–1573.
 4. Ogunlana, O. E.; Ogunlana, O. O. In vitro assessment of the free radical scavenging activity of *Psidium guajava*. *Res. J. Agric. Biol. Sci.* **2008**, 4, 666–671.
 5. Saeed, F.; Afzaal, M.; Niaz, B.; Arshad, M. U.; Tufail, T.; Hussain, M. B.; Javed, A. Bitter melon (*Momordica charantia*): a natural healthy vegetable. *Int. J. Food Prop.* **2018**, 21, 1270–1290.
 6. Vijayalakshmi, B.; Salimath, P. V Effect of bitter gourd and spent turmeric on glycoconjugate metabolism in streptozotocin-induced diabetic rats. *J. Diabetes Complications* **2009**, 23, 71–76.
 7. Sun, L.; Zhang, X.; Dong, L.; Zhang, C.; Guo, P.; Wu, C. The triterpenoids of the bitter gourd (*Momordica Charantia*) and their pharmacological activities: A review. *J. Food Compos. Anal.* **2021**, 96, 103726, doi:10.1016/j.jfca.2020.103726.
 8. Krishnendu, J. R.; Nandini, P. V Nutritional composition of bitter gourd types (*Momordica charantia* L.). *Int. J. Adv. Eng. Res. Sci.* **2016**, 3, 236876.
 9. Jia, S.; Shen, M.; Zhang, F.; Xie, J. Recent advances in *Momordica charantia*: functional components and biological activities. *Int. J. Mol. Sci.* **2017**, 18, 2555.
 10. Kumari, P.; Verma, R. B.; Nayik, G. A.; Solankey, S. S. Antioxidant potential and health benefits of Bitter gourd (*Momordica charantia* L.). *J. Postharvest Technol.*

2017, 5, 1–8.

11. Raish, M. Momordica charantia polysaccharides ameliorate oxidative stress, hyperlipidemia, inflammation, and apoptosis during myocardial infarction by inhibiting the NF- κ B signaling pathway. *Int. J. Biol. Macromol.* **2017**, 97, 544–551.
12. Zhang, B.; Xie, C.; Wei, Y.; Li, J.; Yang, X. Purification and characterisation of an antifungal protein, MCha-Pr, from the intercellular fluid of bitter gourd (*Momordica charantia*) leaves. *Protein Expr. Purif.* **2015**, 107, 43–49.
13. Tan, H.-F.; Gan, C.-Y. Polysaccharide with antioxidant, α -amylase inhibitory and ACE inhibitory activities from *Momordica charantia*. *Int. J. Biol. Macromol.* **2016**, 85, 487–496.
14. Zhang, F.; Lin, L.; Xie, J. A mini-review of chemical and biological properties of polysaccharides from *Momordica charantia*. *Int. J. Biol. Macromol.* **2016**, 92, 246–253.
15. Sorifa, A. M. Nutritional compositions, health promoting phytochemicals and value added products of bitter gourd: a review. *Int. Food Res. J.* **2018**, 25.
16. Kobori, M.; Ohnishi-Kameyama, M.; Akimoto, Y.; Yukizaki, C.; Yoshida, M. α -Eleostearic acid and its dihydroxy derivative are major apoptosis-inducing components of bitter gourd. *J. Agric. Food Chem.* **2008**, 56, 10515–10520.
17. Saeed, F.; Arshad, M. S.; Nadeem, M. T.; Arshad, M. U. Hypoglycemic and hypolipidemic effects of different parts and formulations of bitter gourd (*Momordica Charantia*). *Lipids Health Dis.* **2017**, 16, 1–11.

18. Shih, C.-C.; Lin, C.-H.; Lin, W.-L.; Wu, J.-B. Momordica charantia extract on insulin resistance and the skeletal muscle GLUT4 protein in fructose-fed rats. *J. Ethnopharmacol.* **2009**, *123*, 82–90.
19. Krawinkel, M. B.; Keding, G. B. Bitter gourd (*Momordica charantia*): a dietary approach to hyperglycemia. *Nutr. Rev.* **2006**, *64*, 331–337.
20. Poolperm, S.; Jiraungkoorskul, W. An update review on the anthelmintic activity of bitter gourd, *Momordica charantia*. *Pharmacogn. Rev.* **2017**, *11*, 31.
21. Preuss, H. G.; Echard, B.; Clouatre, D.; Bagchi, D.; Perricone, N. V Niacin-bound chromium increases life span in Zucker Fatty Rats. *J. Inorg. Biochem.* **2011**, *105*, 1344–1349.
22. Güdr, A. Influence of total anthocyanins from bitter melon (*Momordica charantia* Linn.) as antidiabetic and radical scavenging agents. *Iran. J. Pharm. Res. IJPR* **2016**, *15*, 301.
23. Jiang, B.; Ji, M.; Liu, W.; Chen, L.; Cai, Z.; Zhao, Y.; Bi, X. Antidiabetic activities of a cucurbitane-type triterpenoid compound from *Momordica charantia* in alloxan-induced diabetic mice. *Mol. Med. Rep.* **2016**, *14*, 4865–4872.
24. Naz, R.; Anjum, F. M.; Butt, M. S. Dietary supplementation of bitter gourd reduces the risk of hypercholesterolemia in cholesterol fed sprague dawley rats. *Pak. J. Pharm. Sci.* **2016**, *29*.
25. Zhu, Y.; Bai, J.; Zhang, Y.; Xiao, X.; Dong, Y. Effects of bitter melon (*Momordica charantia* L.) on the gut microbiota in high fat diet and low dose streptozocin-induced rats. *Int. J. Food Sci. Nutr.* **2016**, *67*, 686–695.

26. Babish, J. G.; Pacioretty, L. M.; Bland, J. S.; Minich, D. M.; Hu, J.; Tripp, M. L. Antidiabetic screening of commercial botanical products in 3T3-L1 adipocytes and db/db mice. *J. Med. Food* **2010**, *13*, 535–547.
27. Chaturvedi, P. Antidiabetic potentials of *Momordica charantia*: multiple mechanisms behind the effects. *J. Med. Food* **2012**, *15*, 101–107.
28. Yang, S. J.; Choi, J. M.; Park, S. E.; Rhee, E. J.; Lee, W. Y.; Oh, K. W.; Park, S. W.; Park, C.-Y. Preventive effects of bitter melon (*Momordica charantia*) against insulin resistance and diabetes are associated with the inhibition of NF- κ B and JNK pathways in high-fat-fed OLETF rats. *J. Nutr. Biochem.* **2015**, *26*, 234–240.
29. Bai, J.; Zhu, Y.; Dong, Y. Response of gut microbiota and inflammatory status to bitter melon (*Momordica charantia* L.) in high fat diet induced obese rats. *J. Ethnopharmacol.* **2016**, *194*, 717–726.
30. Fang, E.; Ng, T. Bitter gourd (*Momordica charantia*) is a cornucopia of health: a review of its credited antidiabetic, anti-HIV, and antitumor properties. *Curr. Mol. Med.* **2011**, *11*, 417–436.
31. Gadang, V.; Gilbert, W.; Hettiarachchy, N.; Horax, R.; Katwa, L.; Devareddy, L. Dietary bitter melon seed increases peroxisome proliferator-activated receptor- γ gene expression in adipose tissue, down-regulates the nuclear factor- κ B expression, and alleviates the symptoms associated with metabolic syndrome. *J. Med. Food* **2011**, *14*, 86–93.
32. Lii, C.-K.; Chen, H.-W.; Yun, W.-T.; Liu, K.-L. Suppressive effects of wild bitter gourd (*Momordica charantia* Linn. var. *abbreviata* ser.) fruit extracts on

- inflammatory responses in RAW 264.7 macrophages. *J. Ethnopharmacol.* **2009**, *122*, 227–233.
33. Harinantenaina, L.; Tanaka, M.; Takaoka, S.; Oda, M.; Mogami, O.; Uchida, M.; Asakawa, Y. Momordica charantia constituents and antidiabetic screening of the isolated major compounds. *Chem. Pharm. Bull.* **2006**, *54*, 1017–1021.
34. Ike, K.; Uchida, Y.; Nakamura, T.; Imai, S. Induction of interferon-gamma (IFN- γ) and T helper 1 (Th1) immune response by bitter melon extract. *J. Vet. Med. Sci.* **2005**, *67*, 521–524.
35. Horax, R.; Hettiarachchy, N.; Islam, S. Total phenolic contents and phenolic acid constituents in 4 varieties of bitter melons (*Momordica charantia*) and antioxidant activities of their extracts. *J. Food Sci.* **2005**, *70*, C275–C280.
36. Manabe, M.; Takenaka, R.; Nakasa, T.; Okinaka, O. Induction of anti-inflammatory responses by dietary *Momordica charantia* L.(bitter melon). *Biosci. Biotechnol. Biochem.* **2003**, *67*, 2512–2517.
37. Kobori, M.; Amemiya, J.; Sakai, M.; SHIRAKI, M.; Sugishita, H.; Sakaue, N.; Hoshi, Y.; Yukizaki, C. Bitter melon induces apoptosis in HL60 human leukemia cells and suppresses the production of inflammatory cytokine in RAW264. 7 macrophage like cells. *日本食品科学工学会誌* **2006**, *53*, 408–415.
38. Sathishsekar, D.; Subramanian, S. Antioxidant properties of *Momordica Charantia* (bitter melon) seeds on Streptozotocin induced diabetic rats. *Asia Pac. J. Clin. Nutr.* **2005**, *14*, 153.
39. Zimmet, P.; Alberti, K.; Shaw, J. Global and societal implications of the diabetes

- epidemic. *Nature* **2001**, *414*, 782–787.
40. Gilbertson, H. R.; Brand-Miller, J. C.; Thorburn, A. W.; Evans, S.; Chondros, P.; Werther, G. A. The effect of flexible low glycemic index dietary advice versus measured carbohydrate exchange diets on glycemic control in children with type 1 diabetes. *Diabetes Care* **2001**, *24*, 1137–1143.
41. Moos, P. J.; Edes, K.; Mullally, J. E.; Fitzpatrick, F. A. Curcumin impairs tumor suppressor p53 function in colon cancer cells. *Carcinogenesis* **2004**, *25*, 1611–1617.
42. Gururaj, A. E.; Belakavadi, M.; Salimath, B. P. Antiangiogenic effects of butyric acid involve inhibition of VEGF/KDR gene expression and endothelial cell proliferation. *Mol. Cell. Biochem.* **2003**, *243*, 107–112.
43. Fukami, K. E. I.; Ueda, S.; Yamagishi, S.-I.; Kato, S.; Inagaki, Y.; Takeuchi, M.; Motomiya, Y.; Bucala, R.; Iida, S.; Tamaki, K. AGEs activate mesangial TGF- β -Smad signaling via an angiotensin II type I receptor interaction. *Kidney Int.* **2004**, *66*, 2137–2147.
44. Jayasooriya, A. P.; Sakono, M.; Yukizaki, C.; Kawano, M.; Yamamoto, K.; Fukuda, N. Effects of *Momordica charantia* powder on serum glucose levels and various lipid parameters in rats fed with cholesterol-free and cholesterol-enriched diets. *J. Ethnopharmacol.* **2000**, *72*, 331–336.
45. Habicht, S. D.; Kind, V.; Rudloff, S.; Borsch, C.; Mueller, A. S.; Pallauf, J.; Yang, R.; Krawinkel, M. B. Quantification of antidiabetic extracts and compounds in bitter gourd varieties. *Food Chem.* **2011**, *126*, 172–176.

46. Whittaker, M. H.; Frankos, V. H.; Wolterbeek, A. M. P.; Waalkens-Berendsen, D. H. Effects of dietary phytosterols on cholesterol metabolism and atherosclerosis: clinical and experimental evidence. *Am. J. Med.* **2000**, *109*, 600–601.
47. Kumar, G. S.; Shetty, A. K.; Salimath, P. V Modulatory effect of bitter gourd (*Momordica charantia* LINN.) on alterations in kidney heparan sulfate in streptozotocin-induced diabetic rats. *J. Ethnopharmacol.* **2008**, *115*, 276–283.
48. Senanayake, G. V. K.; Maruyama, M.; Shibuya, K.; Sakono, M.; Fukuda, N.; Morishita, T.; Yukizaki, C.; Kawano, M.; Ohta, H. The effects of bitter melon (*Momordica charantia*) on serum and liver triglyceride levels in rats. *J. Ethnopharmacol.* **2004**, *91*, 257–262.
49. Sur, S.; Ray, R. B. Bitter Melon (*Momordica Charantia*), a Nutraceutical Approach for Cancer Prevention and Therapy. *Cancers (Basel)*. **2020**, *12*, doi:10.3390/cancers12082064.
50. Alam, M.; Ali, S.; Mohammad, T.; Hasan, G. M.; Yadav, D. K.; Hassan, M. B Cell Lymphoma 2: A Potential Therapeutic Target for Cancer Therapy. *Int. J. Mol. Sci.* **2021**, *22*, 10442.
51. Girnun, G. D.; Smith, W. M.; Drori, S.; Sarraf, P.; Mueller, E.; Eng, C.; Nambiar, P.; Rosenberg, D. W.; Bronson, R. T.; Edelman, W. APC-dependent suppression of colon carcinogenesis by PPAR γ . *Proc. Natl. Acad. Sci.* **2002**, *99*, 13771–13776.
52. Kohno, H.; Yasui, Y.; Suzuki, R.; Hosokawa, M.; Miyashita, K.; Tanaka, T. Dietary seed oil rich in conjugated linolenic acid from bitter melon inhibits azoxymethane-induced rat colon carcinogenesis through elevation of colonic

- PPAR γ expression and alteration of lipid composition. *Int. J. Cancer* **2004**, *110*, 896–901.
53. Tsuzuki, T.; Tokuyama, Y.; Igarashi, M.; Miyazawa, T. Tumor growth suppression by α -eleostearic acid, a linolenic acid isomer with a conjugated triene system, via lipid peroxidation. *Carcinogenesis* **2004**, *25*, 1417–1425.
54. Nerurkar, P. V.; Lee, Y. K.; Linden, E. H.; Lim, S.; Pearson, L.; Frank, J.; Nerurkar, V. R. Lipid lowering effects of Momordica charantia (Bitter Melon) in HIV-1-protease inhibitor-treated human hepatoma cells, HepG2. *Br. J. Pharmacol.* **2006**, *148*, 1156.
55. Negi, G.; Kumar, A.; S Sharma, S. Nrf2 and NF- κ B modulation by sulforaphane counteracts multiple manifestations of diabetic neuropathy in rats and high glucose-induced changes. *Curr. Neurovasc. Res.* **2011**, *8*, 294–304.
56. Senanayake, G. V. K.; Banigesh, A.; Wu, L.; Lee, P.; Juurlink, B. H. J. The dietary phase 2 protein inducer sulforaphane can normalize the kidney epigenome and improve blood pressure in hypertensive rats. *Am. J. Hypertens.* **2012**, *25*, 229–235.
57. Palombo, J. D.; Ganguly, A.; Bistrrian, B. R.; Menard, M. P. The antiproliferative effects of biologically active isomers of conjugated linoleic acid on human colorectal and prostatic cancer cells. *Cancer Lett.* **2002**, *177*, 163–172.
58. Kimura, Y.; Akihisa, T.; Yuasa, N.; Ukiya, M.; Suzuki, T.; Toriyama, M.; Motohashi, S.; Tokuda, H. Cucurbitane-Type Triterpenoids from the Fruit of Momordica charantia. *J. Nat. Prod.* **2005**, *68*, 807–809.

Table 1: Estimated Minerals and Vitamins contents in bitter gourd

Minerals	Value mg/100g	Reference
Calcium (Ca)	84	
Magnesium (Mg)	85	
Phosphorus (P)	99	
Potassium (K)	608	
Sodium (Na)	11	[8]
Zinc (Zn)	0.30	
Manganese (Mn)	0.53	
Selenium (Se)	0.9	
Iron (Fe)	2.04	
Vitamins	Value mg/100g	

Vitamin C*	88	
Thiamin	0.181	
Riboflavin	0.326	[8]
Niacin	1.110	
Pantothenic acid	0.063	
Vitamin B-6	0.806	
Folate (µg)	128	

* total ascorbic acid

Table 2: Over-view of diseases prevention by Bitter gourd

Diseases	Model	Reference
HIV	Human study	[54]
	Rat study	[31]
	Rat study	[32]
Diabetic	Human case study	[40]
	Rat study	[38]
	Rat study	[42]
	Rat study	[6]
	Human case study	[43]
Renal failure	Human case study	[55]
Mellitus type II	Rat study	[44]
	Rat study	[46]

	Rat study	[45]
Liver Cholesterols	Rat study	[56]
	Rat study	[57]
	Rat study	[51]
Cancer	Rat study	[52]
	Rat study	[53]
	Rat study	[58]

Table 3. Quantification of amino acid in immature and mature seeds of bitter gourd (adopted by Sorifa. [15])

Amino Acids	Immature Seed	Mature Seed
Arg	48.8	80.8
His	70.2	40.9
Met	26.3	23.6
Ala	49.8	46.7
Val	42.8	36.7

Cys	21.3	16.5
Asx	91.3	16.5
Thr	24.9	17.4
Glx	95.9	124
Tyr	56.5	44.7
Lys	107	98.7

***Quantity in mg/100g**

UNDER PEER REVIEW