Bitter gourd an exceptional crop: A review focuses on nutraceutical and pharmaceutical properties

Divyanandan Vatas and Sonia Morya

Abstract
The aim of this paper is to review the nutraceutical and pharmaceutical properties of the bitter gourd. There are many health benefits of bitter gourd especially for diabetic patients as it has hypoglycemic effect due to the lectin present in it which binds with 2 insulin receptors acting as insulin, which naturally results in the lowering of the blood glucose levels and losing the appetite. The oligosaccharides present in bitter gourd can boost our immunity naturally which helps our body to stay healthy and lowers the risk of various diseases. Its anti-inflammatory properties can heal the wounds and cuts more easily. Bitter gourd is also taken as a therapeutic remedy for cancer, as it is having anti-tumor or anti-cancer properties but further studies are yet to be done to prove. Due to its anti-viral properties, its juice can be consumed during a viral fever or contagious disease, also the protein found in bitter gourd can inhibit the HIV activity and depresses the expansion of viral core protein while having less effect on cellular DNA. Due to its anti-microbial property, it can be used prevent any infectious area like cuts or burns, usually the paste of bitter gourd is applied on the affected area. Bitter gourd has also shown major antioxidant activity which is good for one’s health as these antioxidants helps us to remove the free radicals present in our body which can cause various diseases and can lower our immunity.

Keywords: Nutraceutical, pharmaceutical, anti-diabetic, anti-cancerous, anti-viral, anti-inflammatory

1. Introduction
Bitter gourd is also known as *Momordica charantia* L., an exceedingly nutritive climber belonging to Cucurbitaceae family, is broadly used as highly nutritive vegetable and traditional medicine in all over the world. *M. charantia*, also called as bitter gourd, is dispersed in tropical and subtropical areas of Asia, Africa, South America, the Caribbean, and portions of the Amazon Basin (Li et al. 2020) [1]. The fruit, and it’s all parts, are bitter in taste produced by non-toxic cucurbitane glycosides, which includes momordicoside K, momordicoside L, momordicine I, and momordicine II. Containing many medicinal properties, including anti-diabetic, hypcholesterolemic, hypotriglyceridemic, anti-tumor, hypotensive, immunostimulant, anti-viral, anti-inflammatory, antioxidant, anti-leukemic, anti-bacterial, anthelmintic, anti-mutagenic, anti-ulcer, and insecticidal properties has verified in different parts of bitter gourd (Li et al. 2020) [1]. The medicinal worth of bitter gourd has been informed from ancient eras for the cure of sicknesses like toothache, diarrhea, pimples and diabetes. The advantageous effects of bitter gourd crude extract or isolated composites that are related with depressing diabetes and lipidemia, anti-bacterial, antifungal and anti-HIV actions. The molecular mechanisms of cancer inhibition and treatment by bitter gourd (Sur et al. 2020) [2]. The uses of pharmaceutical and fragrant herbs in traditional conducts dates posterior to very old ages. There are several traditional and herbal pharmaceutical products which are being opted as additions for the management of many diseases (Aydın et al. 2020) [3]. Utmost recognized drug active bodies are the molecules that have been isolated from the natural goods and have been verified for effectiveness. The usage of the molecules isolated from the plants as the medication dates back to the 1800s. The huge majority of drugs permitted up to 1990 are the molecules with the natural goods or products (Aydın et al. 2020) [3]. Into the bargain, the combination of several active substances acquired by the withdrawal of the natural products with different solvents can display a synergistic effect and react far more efficiently to the traditional treatment than a particular chemical molecule will illustrate. Hence, extraction, refinement and efficient studies of the natural yields in the area of traditional medication is the area that has always been discovered from the ancient eras till at present deprived of dropping its significance (Aydın et al. 2020) [3]. Evidence-based assessment of the efficiency and the safety of constituents isolated from the medicinal and pharmaceutical plants
is vital for traditional medicine to be grounded on the safe fundamentals. For the decisive harmless claims of herbal supplements, it is essential to perform the experimentations to determine the efficiency of natural products that are generally known in the traditional treatment within the vitro, vivo and pharmaceutical studies (Aydın et al. 2020) [3]. Bitter gourd comprises a group of biologically active plants chemicals containing triterpenes, proteins, steroids, alkaloids, saponins, flavonoids and acids due to which a plant holds anti-fungal, anti-bacterial, anti-parasitic, anti-viral, anti-fertility, anti-tumorous, hypoglycemic and anti-carcinogenic properties. Fruits are used as traditional prescription to cure many diseases like, rheumatism, gout, worms, colic, sickness of liver and spleen. It has also shown its usefulness in the treatment of cancer and diabetes (Banerjee et al. 2019) [4]. The partitions of bitter gourd extract have reportedly shown numerous nutraceutical activities, comprising hypoglycemic, anti-bacterial, anti-viral, cytotoxic, triglyceride-lowering and anti-inflammatory activities. The extracts of bitter gourd triggered peroxisome proliferator-activated receptor α, and have anti-inflammatory, and antioxidant activities. Bitter gourd vegetation is rich in case of minerals such as Cu, Fe, Mg, Zn, and Ca. Several fatty acids like lauric, myristic, palmitic, stearic, and linolaic acids are also existent (Banerjee et al. 2019) [4].

2. Traditional use of bitter gourd
Bitter gourd has been used in numerous Asian traditional medicine or pharmaceutical systems for an extended time, as valuable for the prevention and treatment of many illnesses. Fruits of bitter gourd are used for the treatment of asthma, ulcers, constipation, fever, diabetes, cough, gout, helminthiases, inflammation, leprosy, skin diseases, burns and wounds. It shows hypoglycemic properties in both animals and as well as human studies. The juice of the leaves of bitter gourd is used for the treatment of piles, cleanse blood and also used in liver recompenses, dyspepsia, jaundice and cholera (Banerjee et al. 2019) [4].

2.1 Regular use of bitter gourd to control diabetics
Bitter gourd juice
Bitter gourd’s leaves are cleaned and washed then chopped. 6 tablespoons of the finely chopped leaf is added in 2 glasses of water. This blend must be stewed for around 15 minutes in an open pan or pot. Then it is endorsed to cool. The recommended dose is 1/3rd cup of the juice thrice a day. This method is much effective in the treatment of the diabetes type 2 (Kumar, 2010; Banerjee et al. 2019) [4, 5].

3. Various biological activities of bitter gourd
3.1 Anti-diabetic
The lectin present in the bitter gourd has insulin-like action, which is due to its property of linking together with 2 insulin receptors. This lectin compound helps in the lowering of blood glucose levels by performing on peripheral tissues and due to its similar to insulin's properties in the brain, suppressing the hunger or craving (Joseph, 2013) [6]. This lectin compound is the main provider to the hypoglycemic effect that progresses after eating bitter gourd and it might be a good option for managing the adult-onset diabetes. This Lectin binding is non-protein definite, and this is probably why bitter gourd has been accredited with the immunostimulatory action, by connecting receptors that control the immune system, therefore stimulating the said receptors (Joseph, 2013; Banerjee et al. 2019) [4, 6]. The consequence of bitter gourd on streptozotocin-induced diabetic rats with specific highlighting on kidney heparin sulfate (HS) was studied. That study presented an incomplete setback of all the diabetes persuaded effects by bitter gourd. The upsurge in the components of glycol-conjugates throughout diabetes was considerably diminished by the consumption of the bitter gourd (Banerjee et al. 2019) [4]. Diabetes related advancement in the actions of enzymes taking part in the synthesis and degradation of glycosaminoglycans (GAGs) were expressively dropped by bitter gourd supplementation. GAGs configuration shown that the decrease in the amino sugar, and uronic acid contents during diabetes and bitter gourd consumption was effectual in contradicting this reduction. The reduction in the sulfate content in the GAGs throughout diabetes was also improved by the consumption of the bitter gourd which also showed the valuable role of the bitter gourd in adjusting of the glyco-conjugate and heparin sulfate related kidney difficulties during the diabetes hence extending late complications of the diabetes (Banerjee et al. 2019) [4].

3.2 Hypoglycemic activity
There are abundant in vitro, in vivo and a small number of medical studies that are supporting the usage or consumption of the bitter gourd as in a total fruit, excerpt or dehydrated powder, which be able to lower blood sugar levels. In approving or admiring with these studies, it is also communal to use the bitter gourd as a substitute to drop the blood sugar or glucose levels in the management of type 2 diabetes. In the constituent analysis of bitter gourd extract, it has been revealed that the compounds presenting structural resemblances to the animal insulin are accountable for the hypoglycemic effect (Xu et al. 2015) [7]. In over-all, it has been recommended that the bitter gourd polysaccharides devise a major effect on hypoglycaemia. Polysaccharides have been described to have protecting and reparing effects on pancreatic islet tissue and the capability to diminish blood sugar. Polysaccharides are believed to show the anti-hyperglycemic activities by refining glucose tolerance, glucose intestinal immersion, or refining glucose breakdown or metabolism (Xu et al. 2015) [7].

Into the bargain, a blend of polypeptides called ‘polypeptide p’ isolated from the seeds and 2 steroid glycosides stated as ‘charantin’ are additional chemical molecules described to have hypoglycemic properties. Bitter gourd’s juice or aqueous extract has been conveyed to be a nontoxic substitute for depressing the blood sugar levels (Aydin et al. 2020) [3]. Glucosaminoglycans extracted from plant, fruits and vegetables, have been believed to have advantageous effects on diabetes breakdown or metabolism. It also has been stated that the blend of extreme molecular mass alkali polysaccharides pulled out from the bitter gourd polysaccharides has the greatest anti-hyperglycemic effect and can decrease the blood sugar levels over increased insulin discharge from the Beta cells (Aydin et al. 2020) [3].
bitter gourd could upsurge the endothelium-derived calming factor production in the cell propagation, the improvement of the inflammatory and immune reaction, and inspires the splenocytes and thymocytes (Panda et al. 2015) [8]. In immune-inhibited mice from cyclophosphamide, it has been described that the unit clearance index, manufacture of serum hemolysis, spleen index, thymus index and natural eradicator cell cytotoxicity can be enlarged to the normal control levels with the help of the bitter gourd polysaccharides. It has been conveyed that the juices or aqueous extract of the bitter gourd can upsurge the phagocytic index and the ratio of adhesion of great doses of neutrophils to nylon buffers amplified to significantly larger when compared to usual or standard control animals (Panda et al. 2015) [8].

3.4 Anti-inflammatory activity
It is recognized that the oxidative stress and inflammation trigger each other and oxidative stress plays an important role in chronic infectious diseases. The advantageous properties of the bitter gourd seem to be due to anti-inflammatory and antioxidant activities. Bitter gourd displays anti-inflammatory effects by acting on numerous significant signal pathways that are involved in the inflammation (Biswas, 2016) [9]. Momordicoside G is one of the bioactive constituents of the bitter gourd, that has been stated to contribute to the restoration of lung damages. The anti-inflammatory properties of the bitter gourd, a novel bioactive peptide isolated from bitter gourd seed, have been assessed and stated to have an anti-inflammatory result by dropping the production of intracellular responsive oxygen species (Biswas, 2016) [9]. The wound-healing action of the olive oil macerate of bitter gourd was inspected in the linear incision and circular excision wound models. It has been renowned that bitter gourd oil displays healing activity in incision and excision wound models and also shows around 31.3% of anti-inflammatory activity (Jones et al. 2018) [10]. Experimental records have revealed that the bitter gourd has wound-healing and anti-inflammatory effects. It is also well-known that bitter gourd shows a role in the wound healing via increasing oxygenation via rushing the production of growing aspects, confirming the propagation of fibroblast cells and hastening capillary flow or circulation (Jones et al. 2018) [10]. The antioxidant and antimicrobial properties of phytochemicals present in the plant mass are believed to play an important role in quickening the wound healing procedure. Bitter gourd supplements are believed to play an important role in decreasing inflammation, chubbiness and insulin resistance in overweight by regulating the serum levels of cytokines. Bitter gourd’s powdered supplements have been stated to diminish systemic inflammation (Jones et al. 2018) [10]. In a medical study, done by applying bitter gourd to thirty-eight patients with the primary knee osteoarthritis and dummy (placebo) supplementation to thirty-seven patients up to three months. The effect of bitter gourd on decreasing the pain in patients with the primary knee osteoarthritis was assessed (May et al. 2018) [11]. After the three months of the programme, the bitter gourd cluster can be seen with considerably decrease in their body-weight, body mass index (BMI) and blood sugar while fasting, and noteworthy enhancements in knees osteoarthritis stood observed. The study disclosed that the bitter gourd can be proposed for a substitute for dropping the requirement of analgesic drug intake by decreasing the pain and enhancing the indicators in diseased people (May et al. 2018) [11].

3.5 Antioxidant activity
The antioxidant activity of bitter gourd polysaccharides has been broadly studied and have been revealed to unveil substantial antioxidant activity. Although polysaccharides are described to be the key foundation of the antioxidant activity, it has also been renowned that uronic acid and proteins can reinforce the antioxidant activity (Tan & Gan 2016) [12]. It has been stated that pectin polysaccharide that is isolated from the bitter gourd has a major effect on the elimination of hydroxyl radicals liable on the amount and could inhibit the lipid peroxidation (Tan & Gan 2016) [12]. The hydroxyl and superoxide radical hunting abilities of the three hydrophilic polysaccharide parts that are isolated from the bitter gourd have been assessed, all of which have exposed to have an influential hydroxyl radical hunting and weak superoxide radical hunting effects (Wang et al. 2016) [13]. Sulfated alteration of bitter gourd polysaccharides has conveyed to display improved antioxidant activity in vitro. In addition, it has also been presented that the polysaccharides can result in enhanced antioxidant activity by cumulating the water solubility by some chemical alteration (Wang et al. 2016) [13]. It has been distinguished that the treatment or the management of neuroblastoma cells with the bitter gourd extract can decrease the cytotoxic oxidative stress from peroxide (H2O2) by growing the intra-cellular cleansing action. Triterpene glycosides isolated from the fruits and the stems of bitter gourd have also described to meaningfully hinder xanthine oxidase activity (Kim et al. 2018) [14]. Triterpenoids isolated commencing bitter gourd bulks presented an inhibitory effect on the cleansing activities and the xanthine oxidase activity. The antioxidant composites in the bitter gourd seed powders have been described to prevent lipid peroxidation by representing latent usual antioxidant activity. The antioxidant activity of bitter gourd in contradiction of oxidative harm initiated by peroxynitritis has been assessed in vitro and has been undoubtedly presented to contribute to enhancement (Kim et al. 2018) [14].

3.6 Anti-tumor/anti-cancer activity
Bitter gourd extract has described to have a promising potential as an adjuvant in traditional anti-cancer rehabilitations. The usefulness of bitter gourd extracts and constituents isolated from the bitter gourd counter to diverse tumor cells was calculated (Salehi et al. 2018) [15]. Anti-proliferative and immune-modulatory effects have been described in most studies. Bitter gourd has been publicized to temper proteins linked with diverse cancer pathways. The cell sequence is stopped by inflection of the indication path and cell cycle proteins, and an antitumor effect is revealed by persuading the apoptosis or additional cell demise pathways (Salehi et al. 2018) [15]. Bitter gourd polysaccharides have been stated to hinder propagation of humanoid leukemia cell line K562. Sulfate alteration of bitter gourd extract has been displayed to expressively prevent the development of HepG2 and Hela cells, and it has been conveyed that sulfated alteration could increase the anti-tumor activity (Farooqi et al. 2018) [16]. 3-triterpene glycosides isolated from the bitter gourd have been stated to display the major antitumor activity in cell lines consequential from liver carcinoma. Specifying the effect of bitter gourd extracts on several inflammatory-related signalling passageways, it is believed to be an important part as an anti-tumor agent (Farooqi et al. 2018) [16].
The usefulness of bitter gourd liquid counter to PanC pancreatic cancer cells has been established in vitro. Autophagy inhibitors expressively inhibit the cell death of cancer cells (Yue et al. 2019) [17]. Bitter gourd juice has been stated to cause the cell death by triggering the autophagic alleyway in medically-affected pancreatic cancer (AsPC-1) cells. In an additional study, assessing the effect of bitter gourd juice on aiming pancreatic cancer-related cancer stem cells (PanC-CSCs), it was conveyed that the supplement might cause a reduction in the expression of genetic material and the proteins which plays a role in the restoration and reproduction of PanC-CSC (Yue et al. 2019) [17]. Nine compounds containing 3 cucurbitan-type triterpen glycosides extracted from the young fruit of bitter gourd, antihepatic fibrosis activity counter to murine hepatic stellate cells (t-HSC/Ci-6) and It was examined for antihepatoma activity counter to two kinds of liver cancer cell line (HepG2 and Hep3B) (Dhar et al. 2018) [18]. Karavilosid III has been stated to cause the reserve of the t-HSC/Ci-6 cell line and display cytotoxicity activity counter to the Hep3B and Hep2B cell lines. It has also been advanced as a chemotherapy agent for the cure of liver fibrosis or carcinoma. MAP30 has been described to have in vitro antineoplastic effects (Dhar et al. 2018) [18]. These effects are believed to be due to the capability to decrease the expansion of growth aspect receptors devoted to the breast factor, such as the transmutran tyrosine kinase receptor programmed by the HER2 oncogene. It was resolute in vivo that the tumor development in S180 sarcoma and H22 liver tumor was considerably inhibited by bitter gourd polysaccharides (Dhar et al. 2018) [18].

3.7 Anti-viral activity

Ethanol extracts from the leaves and shoots of bitter gourd greatly hinder HSV-1 and SINV viruses and study also proposes that the antiviral activity imitates an adjacent necessity on photosensitizers rather than momordinic I or II. A variability of composites extracted from bitter gourd having antiviral activity, a lot of them are proteins and steroids (Upadhyay et al. 2015) [19]. Kugucin C and Kugucin E extracted from the rootstock of bitter gourd presented reasonable anti-HIV-1 activity with EC50 values of 8.45 and 25.62 g/mL, while utilizing minimal cytotoxicity on non-infected C8166 cells (IC50 > 200 g/mL). MAP30 is the focal constituent of antiviral activity in vitro; it selectively executes lymphocytes and macrophage infected by HIV, hinders HIV-1 virus DNA duplication in monocytes, while using minimal cytotoxicity on non-infected cells (Upadhyay et al. 2015) [19]. Likewise, study also establish that MAP30 of bitter gourd proteins can hinder HIV activity, slow down the expression of the virus essential protein p24 and viral-associated reverse transcriptase (HIV-RT), while having a little effect on cellular DNA or protein synthesis in H9 cells. MRK29, as lectin extracted from the bitter gourd, was establishing to act over hang-up of viral reverse transcriptase. Momordinic had straight protecting effect on Coxsackie virus (CVB3)-infected myocardioyte, and depressed the RNA transcription and conversion of CVB3 in myocardial cells (Upadhyay et al. 2015) [19].

3.8 Anti-microbial activity

Essential fats of bitter gourd seeds have substantial inhibitory effect on S. aureus, even though having not as much of impact on E. coli and C. alibicans (Wang et al. 2016; Jia et al. 2017) [13, 20]. The aqueous extract from bitter gourd seed unveiled substantial antimicrobial activity counter to numerous bacteria in the succeeding ascending order, P. multocida, S. typhi S. epidermidis and L. bulgaricus (Wang et al. 2016) [13]. As for the ethanoic extract, the order was S. aureus, M. luteus, E. coli, S. epidermidis and L. bulgaricus, while n-hexane and petroleum ether excerpts were in effect counter to S. aureus. Bitter gourd pulp excerpt has been established to have wide-spectrum antimicrobial activity, the similar as the hydrophilic leaf excerpts, which displayed antibacterial actions against E. coli, Staphylococcus, Pseudomonas, Salmonella and Streptobacillus (Wang et al. 2016; Jia et al. 2017) [13, 20]. This may be recognized to 5-a-stigmasta-7, 25-dien-3-b-ol, elasterol and lanosterol. Ethanol excerpt of bitter gourd leaves display reserve on B. cereus and S. aureus. The ethanol portion has no seeming effect on E. coli, which was compared with the dealing of the ethyl acetate excerpts (Wang et al. 2016) [13]. Methanolic extract from bitter gourd leaves displayed the robust antibacterial activity between a number of carbon-based solvent extract, with a substantial hindering effect on E. coli and S. aureus (Jia et al. 2017) [20].

3.9 Wound healing activity

A sequence of irregularities such as diminished immune reaction and neovascularization, growth factor insufficiencies and diminished synthesis of collagen are related with the diabetes and to the hindered wound healing (Hussan et al. 2014) [22]. Treatment with bitter gourd extract or fruit palm, cream or lotion can considerably improve the wound closing down process in the diabetic patients, and upregulate the TGF-expression in the injury or lesion tissue, which plays a significant part in modifiable cell growth and distinction. For the normal investigational animals, methanol withdrawals also had a comparable effectiveness and considerably compact wound area and less time period of epithelialization (Hussan et al. 2014) [22].

4. Toxicity and side effects

Even though the whole plant is fundamentally harmless to human physique underneath usual conditions, it might persuade adversative reactions according to various acceptances, treating methods, physical variances and other circumstances (Adewale et al. 2014) [23]. There have been rumors of toxicity ever since 1960s, mostly comprising severe toxicity, long-lasting toxicity and reproductive toxicity. Periodic consumption of bitter gourd leaves was used to inhibit childbirth in India. The ethanolic excerpt of bitter gourd Linn kernels have shown a larger influence on spermatogenesis and persuaded histological variations in reproductive organs of the subject (Adewale et al. 2014) [23]. Associated investigation is generally about the toxicity of hypodermic injection and information on oral toxicity are quite rare. Scientific studies established that high-dose consumption (comparable to 250-500 gm) of the bitter gourd fruit initiated stomach ache and diarrhea in diabetes (Temitope & Lekan 2014; Jia et al. 2017) [20, 24]. Furthermore, the aqueous excerpt was testified to considerably reduction in the hemoglobin concentration of test subjects. Bitter gourd lectin is having a cytotoxic effect, which expressively hindered DNA and protein synthesis in human outlying blood lymphocytes of normal or leukaemic cells. At the cellular level, 500 to 600 mcg/mL of total phenolic extract (TPE) was also described to be toxic to keratinocytes and fibroblasts in vitro (Temitope & Lekan 2014; Jia et al. 2017) [20, 24].
5. Future prospects
Regardless of the widespread bitter gourd practice in quite a lot of traditional medication, primarily for type 2 diabetes, there are reasonably limited data from medical trials and a little published studies registered a limited number of patients, for these causes, secure data are more frequently consequent from animal models. At hand, there are too some studies displaying its efficiency in the treatment of chubbiness, wound or injury restorative and backing up the immune system. Various in vitro and in vivo studies have been directed on the examination of the anticancer activity of bitter gourd. The capability of bitter gourd bioactive constituents to temper a variety of cell cycle adaptable proteins situated in various signal paths has been noticeably established in studies presenting anticancer activity. Due to this shortage of standardization in medical studies, it still denotes a restriction in the acknowledgement of the therapeutic worth of bitter gourd by a share of the scientific community. A latest meta-analysis underlined the scarcity of data from medical trials and the need for more organized and well-conducted studies.

6. Conclusion
It is recognized that the mainstream of the world population favours traditional informal medicine produces to industrialized products. One of the core aim for the better interest in herbal pharmaceutical products is that natural products will be deliberated as less toxic. In various health difficulties, many constituents of vegetable derivation obtained from natural produces have the prospective to act as supplements, only or in combinations. Due to the synergistic effect, various active composites could have the therapeutic benefits considerably advanced than the effects they be able to give unaided when given as herbal preparation. Bitter gourd vegetable is a natural produce recognized to be used for numerous years in the management of type 2 diabetes. Enhanced medical studies are desirable on hyperglycemic efficiency, but the practice of bitter gourd ought to be careful as it can cause the hypoglycaemia in the patients of diabetes which can be serious. So one should be taking it in small amounts when necessary. In addition, its efficacy would be confirmed by the increasing in vitro, in vivo and well organized medical trials in the regions where its practice has traditionally been testified. Use of the bitter gourd in foods and pharmaceuticals field are still in the preliminary processing phases. The health profits are still far away from being entirely utilized. Due to its many health purposes, the bitter gourd can be consumed in lowering blood glucose, in tumor therapy and other traits of medical applications with wide prospects underneath the foundation of certifying safety. It is recognized that the use of bitter gourd along with the medications used in the management of diabetes can cause a quick fall in blood sugar level. Superior safety studies are required to accomplish the safety trials of the bitter gourd, to make clear the side effects and to regulate the amounts in an orderly manner.

7. Reference


