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POSITIVE IMPACT OF BITTER GOURD ON DIABETIC PATIENTS- A REVIEW

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Abstract: *Momordica charantia*, often called as bitter gourd has traditionally been used to treat diabetes and its consequences in Ayurvedic and Chinese medicine. Bitter gourd is generally ignored owing to its bitter taste even though it is good supply of quite a few nutrients. *M. charantia* is one of the most promising herbs for diabetes today, with both traditional use and contemporary scientific evidence of its therapeutic function. According to several published clinical studies, bitter melon extract from the fruit, seeds, and leaves contains many bioactive components that have hypoglycemic effect in both diabetic animals and people. It has many bioactive compounds such as gallic acid, chlorogenic acid, polysaccharides, antioxidants, catechins, charatine, alkaloids, quinine, flavonoids, triterpenoids etc., additionally a good source of minerals and vitamins. Several medicinal effects of bitter gourd have been considered such as antidiabetic, anti-mutagenic, antioxidant, anti-lipolytic, analgesic, hypoglycemic, anti-viral and immunomodulatory. The current review aims to emphasize the antidiabetic activity of *M. charantia*, its bioactive compounds and clinical trials to clarify its potential therapeutic effects on diabetes.

Index Terms **– Antidiabetic, Bioactive Compounds, Charatin, Bitter Gourd, *Momordica Charantia.***

1. INTRODUCTION

Diabetes mellitus is a highly prevalent metabolic dysfunction affecting the human population worldwide which is defined by hyperglycemia and caused by insulin impairment. Chronic hyperglycemia, a typical side effect of unchecked diabetes, damages, impairs, and eventually destroys several organs, including the kidneys, eyes, nerves, heart, and blood vessels. Diabetes can be classified into two types as - type-1 diabetes and type-2 diabetes.

Type-1 diabetes also known as insulin dependent diabetes, is characterized by inadequate insulin production and necessitates daily insulin treatment. This occurs as a result of cellular-mediated autoimmune destruction of pancreatic beta cells. Type-2 diabetes also known as non-insulin dependent diabetes, is brought on by the body's inefficient use of the hormone insulin. Type-II diabetes is frequently caused by a combination of risk factors, including genetics, obesity, poor food, insufficient exercise, ageing, hypertension, and others [Newman et al, 1987, kaprio et al, 1992]. There is a different type of diabetes that has been identified as gestational diabetes, which typically develops during pregnancy and is caused by glucose intolerance. Although this is a short-term ailment but it may carry a long-term risk of diabetes [Bellamy et al, 2009].

World Health Organization estimates that 422 million persons worldwide have diabetes, as of 2014. It resulted in 1.5 million deaths in 2012, type II diabetes being the main cause of death for most people. Additionally, type II diabetes was once only seen in adults, but it is now found in kids also (WHO. Global report on diabetes, 2016).

There are various medicinal plants and their products that are important for treating various diseases of mankind. For so many years, these plants and plant extracts are being used to cure diabetes. According to WHO, there are 21000 plants listed which have been used for so long to treat many diseases in the World (Joseph and Jini, 2013).

Bitter gourd (karela) having botanical name *Momordica Charantia* is also known as balsam pear is a very crucial plant for the treatment of diabetes (Joseph and Jini, 2013). Bitter melon is a sophisticated plant remedy whose history of usage as a meal and a medicine is remarkably long. several plants are used as both food and medicine. Typically, these plants are nutritious, tonic, and supporting nature. Although they are efficient, they rarely produce substantial hypoglycemic effects or adverse effects on the reproductive system because it is frequently eaten as food, bitter melon is unique and has also been used for a long time to treat ailments like diabetes, regulating the menstrual cycle, treating infertility, and causing abortions, in addition to treating infections, psoriasis, and meningitis. The numerous uses of the plant are only now being fully explored by modern science, and there is still a lot we do not know about it (Kathy et al, 2005). It is being used since ages in local population of India, Asia, South America, East Africa (Joseph, Jini, 2013 and Gupta et al, 2011). It is grown in equatorial and semi tropical belt (Cicek, 2022 and Shubha et al, 2018). It was first grown in India and then ultimately taken to China in the 14th century (Abo et al, 2008). Bitter gourd has been used since long as a conventional medicine, used for the cure of laxative, stomachic, anthelmintic, and more importantly for the treatment of diabetes and its complications. It has antidiabetic properties (Shubha et al, 2018) and is very beneficial for blood glucose level maintenance and lipid concentration (Cicek, 2022).

According to some researchers it has been proved that bitter gourd has some insulin like properties which gives positive result in lowering blood glucose and urine glucose level (Janagal et al, 2018). It is found to prevent cholesterol (Saeed et al, 2018), prevent cancer (Bai et al, 2016), prevents dementia (Joshi et al, 2017), prevents oxidation and inflammation (Bortolotti et al, 2019). Bitter melon has long been used as an indigenous medicine for treating tumors, bronchial asthma, pore and skin problems, stomach problems and hypertension (Shubha et al, 2018). There are many bioactive compounds present in bitter gourd which has primary and secondary metabolites. Primary metabolites such as protein, chlorophyll, and sugar whereas secondary metabolites contain carotenoids, alkaloids, phenolics, cucurbitane, saponins and triterpoids etc. (Gayathry and John, 2022). Secondary metabolites are accountable for nourishing food properties, it hardly contributes to dietary cost but are very good for the body (Daniel et al, 2014).

2. Cultivation of bitter gourd

All around the world, karela is a climber that is both annual and perennial, grown 1500 meters above sea level. It is grown from April to July, during the warmest season, by scattering seeds in a hole. A half-inch gap is used to sow the seeds by providing manures and using a meter distance. Exactly one plant is retained and once or twice a day, plant seedlings are watered. plants start to bloom after 30-35 days of germination. After blossoming for 15-20 days, fruits are ready for harvest (Gupta et al, 2011).

3. Nutritional attributes

Bitter gourd is generally ignored owing to its bitter taste even though it is good supply of quite a few nutrients (Gayathry and John, 2022). It has more nutrition than other cucurbits (Miniraj et al, 1993) namely squash, pumpkin, cucumber, and zucchini (krawinkel & Keding, 2006). It is considered a suitable source of proteins, minerals, vitamins, and carbohydrates, (Yawalkar, 1980). It has vitamins such as vitamin A, vitamin E, Thiamine, Riboflavin, Niacin, folate, and vitamin C. Likewise, it has many minerals such as potassium, iron, calcium, magnesium, phosphorus, and zinc. It also has a good amount of fiber (Gayathry and John, 2022).

4. Nutritional Composition of Bitter Gourd

Nutritional composition of *M. Charantia* taken from Gayathry and John, 2022 and Sorifa, 2018 is given below in Table 1:

Table 1: Nutritional Composition of Bitter Gourd

PARAMETERS	AMOUNT
Protein(g)	0.90
Fat(g)	0.10
Carbohydrate(g)	0.20
Dietary fiber(g)	3.30
Total sugars (%)	2.8
Chlorophyll(mg)	10.9
Thiamine(mg)	0.05
Riboflavin	0.03
Niacin	0.40
Phosphorus(mg)	69.0
Calcium	20.0
Potassium	26.0
Iron	0.9
Sodium	3.0
Zinc	0.1
Water (%)	83.2-92.4
Lipids (%)	0.1-1
Vitamin A as carotenoid	210-220 IU

5. Health effects of bitter gourd- According to (Thakur and Sharma, 2016) bitter gourd shows several effects on health such as:

a. Bitter gourd helps increase the uptake of glucose by maintaining blood sugar levels.

b. The antioxidants properties of tetraterpenoids shield people from cancer agents and decrease the risk of coronary heart diseases.

c. Consumption of bitter gourd more than required can cause reduction in sperm count.

d. Bitter gourd is found to prevent microbial infections, cancer, and tumor growth.

e. Leaves of bitter gourd along with tulsi leaves are used for the cure of respiration related problems such as asthma, common cold, bronchitis etc.

f. Juice of bitter gourd is consumed by the patients of ringworm, rabies, and psoriasis.

g. It is being used since long as a purifier of blood because of its bitter tonic properties.

6.Antidiabetic effects of bitter gourd

Diabetes has traditionally been treated with a variety of herbal medicines in Asia and other underdeveloped nations (Malviya et al, 2010, Jarald et al, 2008, Chauhan et al, 2010, & Singh et al, 2011). One plant that has undergone extensive research for the treatment of diabetes is *M. charantia* (Hasan et al, 2012). *M. charantia* is one of the most promising herbs for diabetes today, with both traditional use and contemporary scientific evidence of its therapeutic function (Cefalu et al, 2008 & Leung et al, 2010). According to research on *M. charantia's* traditional applications in India, this is one of the most significant plants for decreasing blood glucose levels in diabetic patients (Paul et al, 2010).

7. Bioactive compounds in bitter gourd

Scientists are becoming more curious in researching bitter melon's bioactive chemicals and their effects on the body due to the wide range of medical issues that it can treat. However, as numerous studies have shown, a lot of focus has been placed on anti-diabetic substances and their hypoglycemic properties [Islam et al, 2011, Hazarika et al, 2012]. According to several published clinical studies, bitter melon extract from the fruit, seeds, and leaves contains many bioactive components that have hypoglycemic effect in both diabetic animals and people [Wehash et al, 2012, Fuangchana et al, 2011]. Charantin, polypeptide-p, and Vicine are three of the main chemicals isolated from bitter melon and acknowledged as hypoglycemic agents [Joseph and Jini, 2013].

7.1 Charantin

Charantin is a characteristic cucurbitane-type triterpenoid found in *M. charantia* that has anti-diabetic properties [Krawinkel et al 2006, Patel et al, 2010]. Pitiphanpong et al shown that charantin can be utilized to treat diabetes and may be able to substitute medication. It is a compound blend of two chemicals, sitosteryl glucoside and stigmasteryl glucoside [Pitiphanpong et al, 2007]. Chen et al. extracted 14 cucurbitane triterpenoids, kuguacins, from the vines and leaves of M. charantia, including two pentanorcucurbitacins, one octanorcucurbitacin, and two trinorcucurbitacins, as well as six recognized analogues [Chen et al, 2009]. Charantin was extracted and quantified from bitter melon fruit using a high-performance thin layer chromatographic method [Thomas et al, 2012].

According to studies, the substance is more efficacious than the oral hypoglycemic drug tolbutamide [Cousens et al, 2008]. Two charantin aglycones were extracted and identified as sitosterol and stigmastadienol glycosides in a study; however, when examined individually for their hypoglycemic effects in vivo, these two elements did not generate any significant changes in blood glucose levels [Harinantenaina et al, 2006]. This suggests that charantin may contain other components that have yet to be identified and are responsible for the hypoglycemic activity found in diabetics (Joseph and Jini, 2013).

7.2 Polypeptide-p

Polypeptide-p, often known as p-insulin, is an insulin-like hypoglycemic protein that has been shown in gerbils, langurs, and humans to lower blood glucose levels when delivered subcutaneously [Tayyab et al, 2012]. Because p-insulin resembles human insulin's activity in the body, it can be used as a plant-based insulin alternative in people with type 1 diabetes [Paul et al, 2012]. Wang et al. recently cloned and expressed the 498 bp gene sequence coding for the *M. charantia* polypeptide p gene, as well as showed that the recombinant polypeptide has a hypoglycemic effect in alloxan-induced diabetic mice [Wang et al, 2011]. Oral injection of bitter melon seed extract exhibits hypoglycemic effects in streptozotocin (STZ) induced type 1 diabetic mice [Wehash et al, 2012]. This shows that molecules other than p-insulin found in bitter melon seeds may be effective in the treatment of type 1 diabetes [Joseph and Jini, 2013].

7.3 Vicine

The other significant component identified from bitter melon seeds is vicine, a glycol alkaloid [Haixia et al, 2004]. Intraperitoneal injection of this pyrimidine nucleoside has been found to induce hypoglycemia in non-diabetic fasting rats [Ham et al, 2009]. However, vicine, which is contained in fava beans, has been demonstrated to cause favism, an acute condition characterized by hemolytic anemia, in people who have a hereditary lack of the enzyme glucose-6-phosphatedehydrogenase [Basch et al, 2003]. Although there have been no cases of favism caused by bitter melon, anyone who are vulnerable to the disease should avoid eating it. More research is needed to ensure the safety and efficacy of utilizing vicine to treat hyperglycemia [Joseph and Jini, 2013].

8. Clinical studies of bitter gourd

There are numerous studies on the impact of bitter melon on the diabetes. Typically, the design of these investigations is superior than the medical research. However, there are some issues with the animal research as well (Kathy et al, 2005).

Additionally prepared bitter melon was used in the pharmacologic experiments and administered in various ways, this reflects the fact that bitter melon was traditionally used as a diabetes treatment in a variety of methods. Some civilizations smashed the fruit and filtered to create juice. Fruit occasionally was boiled and consumed. The fruit is chopped and steeped in many cultures. sometimes with chilly or decocted water, sometimes with or without seeds. In certain cultures, the whole plant was consumed as food. Making definitive claims about the melon study is difficult, its optimum form, dosage, and mode of action. However, regardless of the dosage form, most of the study tended to corroborate accepted wisdom regarding the use of bitter melon to treat diabetes (Kathy et al, 2005).

These research on animals have indicated that bitter melon in numerous ways prevents the body from absorbing glucose and encourages glucose utilization. An insulin-like polypeptide found in the liver promotes pancreatic beta-cell formation and insulin secretion (Chen et al, 2003 and Basch et al, 2003). There has not been any evidence of a rise in insulin levels in the blood, and it is still not understood how exactly bitter melon lowers blood sugar. Overall, the observations made historically, in clinical research, and in animal experiments strongly imply that bitter melon has a role to play in the treatment of diabetes (Kathy et al,2005).

Yet another benefit of melon is that it may lessen diabetes problems. Diabetes is connected to permanent functional and structural alterations in the blood vessels, nerves, kidneys, and eyes, and bitter melon seemed to perhaps lessen some of these problems in different animal models. These results are very primary; thus, they cannot be used to support a recommendation to prevent complications due to diabetes. However, even though this while being quite preliminary, they show promise, and more study is needed. Also keep in mind that these advantages might be secondary to improve better blood glucose regulation (Kathy et al, 2005).

For example, the most common cause of end-stage renal disease is diabetes (Grover et al, 2004). Mice with diabetes produced by streptozotocin exhibit higher levels of blood creatinine, urinary albumin, urine volume, compared to normal mice’s renal weight. Mice given harsh medicine despite not being adjusted, melon's values for these characteristics had been greatly improved. Leg ache, dysfunctional sexual life, among other undesirable signs are caused by diabetic neuropathy. Tail flick amount of delay increases significantly (by 74%) in mice who have diabetes (Kathy et al, 2005). An aqueous extract of bitter melon (200 mg/kg) greatly

decreased this rise in a rat study, raising the prospect that future studies will one day show that patients with diabetes may benefit from eating bitter melon (Grover et al, 2004).

Diabetic enteropathy is another consequence of diabetes, which causes a syndrome of dyspepsia, heartburn, dizziness, and nausea, fecal incontinence, diarrhea, constipation, and stomach pain. Traditional remedies have utilized bitter melon to enhance gastrointestinal function, and it may have some advantages for those who suffer from diabetic enteropathy (Kathy et al, 2005).

In one investigation on mice, those with diabetes had an 83 percent shorter transit time than those without the condition (Grover et al, 2004). Aqueous bitter melon extracts nearly brought the animals' travel back to normal, while simultaneously lowering their blood sugar levels (Kathy et al, 2005). For a rat, type of syndrome X, watery bitter (hyperglycemia linked to obesity, hyperinsulinemia, and hypertriglyceridemia). In contrast to the control group, melon extract (400 mg/day) administered to rats on a fructose-rich diet prevented hyperinsulinemia and hyperglycemia effects felt by the animals in control (Grover et al, 2004).

Moreover, diabetes is a significant cataract risk factor. As part of an experiment, aqueous bitter melon extract onset of cataracts in diabetic rats given alloxan (120 days onset versus 100 days in controls) (Rathi et al, 2002). In a subsequent investigation, also included heavy doses of bitter melon fruit (4 g/kg) for two months. In rats with diabetes, the onset took place later (140–180 days as opposed to 90–100 days) (Srivastava et al, 1998).

9. Medicinal herbs other than bitter gourd possessing antidiabetic effect

a. Acacia arabica (Babhul)

It is distributed throughout India, primarily in the wild habitat. The plant extract functions as a secretagogue to release insulin, making it an anti-diabetic medication. In control rats, it causes hypoglycemia but not in alloxanized animals. Powdered Acacia arabica seeds when consumed (2,3 and 4 g/kg body weight) produced hypoglycemia in normal rabbits by beginning insulin secretion from pancreatic beta Cells [Wadood et al, 1989].

b. Aegle marmelos: (Bengal quince, Bel, Bilva)

Ingestion of aqueous extract of leaves stimulates digestion and lowers blood glucose levels, urea, and serum cholesterol levels in alloxanized rats as compared to control. Along with hypoglycemic effects, this extract also inhibited the peak rise in blood sugar at 1 hour in an oral glucose tolerance test [Karunanayake et al, 1984].

c. Allium cepa: (Onion)

In diabetic rabbits, various ether soluble and insoluble portions of dried onion powder have anti-hyperglycemic impact. Allium cepa also has antioxidant and hypolipidemic effects. S-methyl cysteine sulphoxide (SMCS) (200 mg/kg for 45 days) administration to alloxan-induced diabetic rats significantly controlled blood glucose as well as lipids in serum and tissues and normalized the activities of liver hexokinase, glucose 6-phosphatase, and HMG Co A reductase [Roman-Ramos et al,1995, Kumari et al, 1995]. When diabetic patients were given a single oral dose of 50 g onion juice, their post-prandial glucose levels were dramatically reduced [Mathew et al, 1975].

d. Allium sativum: (Garlic)

This perennial herb is grown all over India. The sulfur-containing component allicin, which gives garlic its strong aroma, has been found to have considerable hypoglycemic action [Sheela et al, 1992]. Increased liver function, increased production of insulin from pancreatic beta cells, and/or an insulin sparing effect are suggested to be the causes of this impact [Bever et al, 1975]. aqueous homogenate of garlic (10 ml/kg/day) given orally to rabbits fed on sucrose (10g/kg/day in water for 2 months) significantly boosted hepatic glycogen as well as free amino acid content, lowered fasting blood sugar, and decreased levels of triglycerides in serum compared with sucrose controls [Zacharias et al, 1980].

e. Azadirachta indica: (Neem)

This plant's hydroalcoholic extracts showed anti-hyperglycemic activity in streptozotocin-treated rats, which is due to an increase in glucose absorption and glycogen accumulation in isolated rat hemidiaphragm [Chattopadhyay et al, 1987, Chattopadhyay et al, 1987]. This plant not only has anti-diabetic properties, but it also possesses anti-bacterial, antimalarial, antifertility, hepatoprotective, and antioxidant properties [Biswas et al, 2002].

f. Eugenia jambolana: (Indian gooseberry, jamun)

The extract of jamun pulp exhibited hypoglycemic action in streptozotocin-induced diabetic rats after 30 minutes, whereas the seed of the same fruit took 24 hours. In diabetic rats, oral administration of the extract resulted in a rise in serum insulin levels. Insulin secretion was discovered to be boosted by incubating plant extract with isolated Langerhans islets from normal and diabetic rats. These extracts also decreased the activity of insulinase in the liver and kidney [Acherekar et al, 1991].

g. Mangifera indica: (Mango)

Although the leaves of this plant are employed as an anti-diabetic medication in Nigerian folk medicine, an aqueous extract given orally had no effect on blood glucose levels in normoglycemic or streptozotocin-induced diabetic rats. However, anti-diabetic efficacy was shown when the extract and glucose were provided concurrently, as well as when the extract was supplied 60 minutes before the glucose. The findings suggest that an aqueous extract of Mangifera indica has hypoglycemic action. This could be attributed to a decrease in glucose absorption in the intestine [Aderibigbe et al, 1999].

10.Conclusion

Food as medicine is a major theme in dietetics and nutritional studies. M. charantia has been utilized for generations as a dietary supplement and ethnomedicine to treat symptoms and diseases related to what we now call diabetes. M. charantia has been widely explored for its therapeutic qualities to cure a variety of diseases [Leung et al, 2009]. It is explained as a versatile herb capable of treating practically any disease known to man. This could be because the plant has approximately 225 different therapeutic constituents [Taylor et al, 2002]. These numerous substances can exert their therapeutic effects either singly or in combination. In terms of diabetes, only charantin, insulin-like peptide, and alkaloid-like extracts have hypoglycemic characteristics like the plant or its pure extracts. These various substances appear to exert their therapeutic effects on diabetes mellitus control and treatment via a variety of mechanisms [Joseph and Jini, 2013]. Although, charatin in bitter gourd is responsible for hypoglycemic activity but when the two chemicals in charatin were individually examined, they did not show any changes in blood sugar levels, hence we can say that there is any other component present in charatin which is responsible for the hypoglycemic activity so, there is need for further research.

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