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MOMORDICA CHARANTIA: A POTENTIAL SOURCE FOR TREATING DIABETES MELLITUS: A REVIEW

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Abstract

Diabetes mellitus has one of the highest rates of morbidity and mortality and is a rapidly spreading global health issue. In the 21st century, it has exploded into an epidemic. Unwanted side effects might result from long-term usage of several diabetes medicines. As a result, interest in alternative therapeutic strategies using medicinal plants to manage diabetes has increased. Researchers have looked into *Momordica charantia*, often known as bitter melon or bitter gourd, as a possible herb for treating Type 2 diabetes. Numerous *in vivo* and animal investigations have shown that different forms of bitter melon have hypoglycemic properties. Charantin, vicine, momordicin, protein polypeptide-p, triterpene glycosides, and saponins are only a few of the bioactive compounds having hypoglycemic properties that are thought to be present in bitter melon fruit and seeds. Charantin and polypeptide-p mimic the actions of insulin, and the other key substances, such as momordicin, vicine, and saponin-rich fraction, encourage the pancreas to secrete insulin. Additionally, bitter melon can help to manage blood sugar by increasing the uptake of glucose by cells and reducing the absorption of glucose into the circulation from the small intestine. Several animal investigations have identified the bitter melon's hypoglycemia mechanism. However, in regards to the effects of bitter melon on Type 2 diabetes, results from human clinical trials were conflicting. In order to establish bitter melon as an alternative treatment for Type 2 diabetes, researchers should concentrate on conducting well-planned clinical trials, offering an accurate dosage range without any adverse effects.

Key words: *Memordica charantia*, Bitter melon or Bitter gourd, Diabetes mellitus, Bioactive compounds with anti-diabetic effect, Animal studies and Clinical trials.

Introduction

Diabetes mellitus has one of the highest rates of morbidity and mortality and is a rapidly spreading worldwide health issue. In the twenty-first century, it has spread like an epidemic, posing a serious threat to the global economy, social structure, and health. It happens as a result of rapid lifestyle changes, urbanisation, high disease susceptibility in specific ethnic groups, and longer lifespan (Whiting et al., 2011). An alarming rises in the number of individuals with diabetes globally, from 463 million in 2019 to 700 million by 2045, according to forecasts from the International Diabetes Federation Diabetes Atlas, which is anticipated to place a significant load on the health care system (Saeedi et al., 2019). Long-term usage of diabetes drugs already on the market may result in unwanted side effects. Hence, alternative therapeutic strategies utilising medicinal plants have arisen.

Among the medicinal plants, *Momordica charantia*, a member of the Cucurbitaceae family often known as bitter melon, bitter gourd or balsam pear has been used extensively in the treatment of diabetes (Liu et al., 2021). *M. charantia* has been reported to have hypotensive, hypolipidemic, and anti-diabetic properties (Jandari et al., 2020, Liu et al., 2021). The fruits and seeds of *M. charantia* have been used as a complementary medicine to treat diabetes around the world. The fruits of *M. charantia* exhibit hypoglycemic action in both experimental animal models and people after oral treatment (Yibchok et al., 2006, Rahman et al., 2009). Kim et al., (2020) conducted a randomized; double-blind placebo-controlled clinical trial using unripe fruit extract of *M. charantia* which has revealed a good glucose-lowering impact with no adverse events in patients with type 2 diabetes. These results strongly imply that the fruits and seeds of *M. charantia* contain substances that have hypoglycaemic action.

Cucurbitane glycosides (Tan et al., 2008), saponins (Keller et al., 2011), triterpenes, triterpenoids (Deng et al., 2022) and the steroidal glycoside charantin (Desai et al., 2021) are just a few examples of the bioactive substances which are isolated and characterized with hypoglycemic activity of *M. charantia*. The aim of the present study is to review the animal studies and clinical trials on anti-diabetic potential of *M. charantia* .

Methodology

Using PubMed, Scopus, and Google Scholar, a literature search on bioactive compounds with hypoglycemic activity and anti-diabetic/hypoglycemic effects of M. Charantia was conducted within the past 20 years, primarily using keywords such as ‘Momordica Charantia’, ‘Momordica Charantia and its phytochemicals’, ‘Momordica Charantia and its extracts, ‘Anti-diabetic effect of Momordica Charantia and human clinical trials’, ‘Momordica Charantia and its hypoglycemic components.

1. Nutritional composition

Momordica charantia is mainly composed of water (91.8%), 0.20 % fat, 4.2 % carbohydrates, and 1.4 % fibre. Albumin, globulin, and glutelin are the protein fractions that are present in the amounts of 49.3, 29.3, and 3.1 percent, respectively. The seeds of bitter melon contain nearly 35% to 40% of oil. The fatty acid profile of the seeds indicates the presence of largest amount of polyunsaturated fatty acids (59.96%), 36.71% of saturated fatty acids and 3.33% of monounsaturated fatty acids. α-eleostearic acid, a significant polyunsaturated fatty acid (54.26%) is found in the seeds (Grossmann et al., 2009). The largest concentrations of potassium, magnesium, calcium, sodium, and phosphorus can be found in the seeds of bitter melon (Liu et al., 2010). Along with this, bitter melon seeds are among the greatest sources of natural chromium (5.6 mg/100 g) and zinc (45.45 mg/100 g) (20). In Table 1, the nutritional makeup of bitter melon is briefly mentioned.

Table 1. Nutritional composition of *M.charantia*

Constituent	Quantity	Constituent	Quantity
Water (%)	83.2–92.4	Sodium (mg/100 mg)	3–40
Lipids (%)	0.1–1	Potassium (mg / 100 mg)	8–170
Carbohydrates (%)	4.2–9.8	Zinc (mg/100 mg)	0.1
Proteins (%)	1.6–2.9	Manganese (mg/100 mg)	0.08–0.32
Fiber (%)	0.8–1.7	Copper (mg/100 mg)	0.18–5
Ash (%)	7–18	Vitamin A as carotenes (IU)	210–220
Calcium (mg/100 mg)	20–50	Vitamin C (mg)	70–120
Phosphorus (mg/100 mg)	70–140	Thiamine (mg)	0.05
Iron (mg/100 mg)	2.2–9.4	Riboflavin (mg)	0.03
Magnesium (mg/100 mg)	16	Niacin (mg)	0.4

(Source: Behera et al. 2008; Nagarani et al. 2014; Sorifa 2018; Saeed et al. 2018)

2. Bioactive compounds with anti-diabetic potential of *M. charantia*

Charantin, vicine, momordicin, protein polypeptide-p, and triterpene glycosides are only a few of the phytochemicals with hypoglycemic properties that are thought to be present in the fruit and seeds of *M. charantia*. Charantin and polypeptide-p mimic the actions of insulin, and other important substances including momordicin, vicine, and saponin-rich fraction encourage the pancreas to secrete insulin. The following table provides a quick overview of the identified *M. charantia* compounds having anti-diabetic potential (Table 2).

Table 2. Bioactive compounds with anti-diabetic potential of *M.charantia*

Isolated compound	Functions	Reference
Charantin	Natural steroidal glycoside possess potential hypoglycemic activity Potential agent for increasing insulin-sensitivity in type 2 diabetic (T2D) patients.	Sonal Desai and Pratima Tatke , 2015
Lectin	It has insulin like activity. The insulin-like bioactivity of lectin is due to its linking together to insulin receptors Lectin lowers blood glucose concentrations by acting on peripheral tissues and similar to insulin's effects in the brain, suppressing appetite.	Joseph et al., 2013
P-Insulin	P-insulin is a hypoglycaemic polypeptide Rapidly decreases the blood sugar level in rats	Khanna and Mohan, 1973
Vicine	It is a Pyrimidine nucleoside, which has been found to induce hypoglycemia in rats, when administered intraperitonially.	Barron., et al.,1982
Cucurbitanetype glycosides	They exhibited a hypoglycaemic effect in vitro. Reports indicate that they also improve insulin release from pancreatic beta cells, and repair or promote new growth of insulin-secreting beta cells.	Zhang et al., 2014
Polypeptide-p	It showed effective hypoglycemic activities when administered subcutaneously to langurs, gerbils, and humans.	Khanna et al., 1981
Insulin receptor (IR)-binding protein (mcIRBP) and adMc1proteins	They showed hypoglycemic effects in mice.	Lo et al., 2014
Momordenol and Momordicilin	Active compounds possessing insulin-like chemical structure and properties.	Hazarika et al., 2012
Momordicine II and kuguaglycoside G	They stimulate insulin secretion.	Keller et al., 2011
Triterpenoids	They control the balance of blood glucose via increasing adenosine 5′-monophosphate (AMP)-activated protein kinase (AMPK) activity, which further enhanced glucose uptake and fatty acid oxidation, as well as inhibited lipid synthesis and hepatic glucose output.	Iseli et al., 2013
Momordicosides (Q, R, S, U, and T) and karaviloside XI	They enhance the entry of inducible glucose into cells and stimulate fatty acid oxidation and glucose disposal.	Keller et al., 2011, Tan et al., 2008, Harinamtenaina et al., 2006

5β,19-epoxy3β,25-dihydroxycucurbita- 6,23(E)-diene and 3β,7β,25-trihydroxycucurbita-5,23(E)-dien-19-al	They showed blood hypoglycemic effects at the dosage of 400 mg/kg in diabetes-induced male ddY mice.	Harinamtenaina et al., 2006
25-O-methylkaraviagein D, karaviloside II, and (19R,23E)-5β,19-epoxy-19,25-dimethoxycucurbita-6,23-dien-3β–ol (Cucurbinate Triterpinoids)	They showed remarkable inhibitory activity against Phosphate Tyrosine Phosphatase 1B (PTP1B), an effective target for the therapy of type 2 diabetes and α-amylase.	Yue et al., 2017
9c,11t,13t-CLN	Involved in the activation of PPAR-γ ligand activator, which stimulates the expression of genes involved in lipid catabolism and glucose utilization. Furthermore, PPAR-γ stimulates cellular differentiation, enhances lipid storage, and regulates insulin activities in the adipose tissue. Activators of PPAR-γ also enhance insulin sensitivity.	Rigano et al., 2017, Corrales et al., 2018
Zn-free protein	Insulin like activities	Yibchok et al., 2006

Fig.1 Hypoglycaemic agents of *M.charantia*

3. Potential anti-diabetic effects of *M.charantia*

Various cell-based assays, animal studies and human clinical trials have revealed the powerful anti-diabetic effects of *M. charantia* (Wang et al., 2016)

3.1. Animal studies

Numerous *in vivo* and animal investigations have shown that different parts of bitter melon have hypoglycemic properties. The juice from bitter melon pulp reduced fasting blood glucose levels and increased glucose tolerance in diabetic-induced mice (Mahmoud et al., 2017). The fruit powder of bitter melon also reduced fasting blood glucose levels in diabetic rats fed a high-fat diet (Bai et al., 2016). Alpha-amylase and alphaglucosidase are two carbohydrate-metabolizing enzymes that are inhibited *in vitro* by the amino acid and fatty acid composition that was taken out of the seeds of bitter melon (Ahmad et al., 2012). Additionally, a rat study revealed that bitter melon extract reduced post-meal glucose levels by preventing the action of the alpha-glucosidase enzyme (Uebanso et al., 2007).

Researchers discovered that giving diabetic mice a daily dose of bitter melon extract (20-100 mg/kg body weight) resulted in improved insulin and blood sugar levels as well as improved glucose tolerance tests (Miural et al., 2001). In a rabbit study, it was discovered that giving alloxan-diabetic rabbits fresh fruit juice from bitter melon at a dose of 6 cc/kg body weight reduced their blood sugar levels (Virdi et al.,

2003). With the chronic oral administration of *M. charantia* fruit juice at a dose of 20 mg/kg, blood glucose tolerance in alloxan-induced rats was dramatically improved from days 7 to 22 and returned to normal levels (Chaturvedi et al., 2004. The benefits of *M. charantia* fruit juice for diabetes were also demonstrated by P. B. Aswar et al. in 2012. Mice with alloxan induced diabetes that consumed *M. charantia* juice had lower cholesterol levels. By scavenging free radicals, the juice may quickly defend against lipid peroxidation, lowering the risk of diabetes complications (Eman et al., 2009). Bitter melon fruit juice administration may be helpful as an adjuvant therapy with oral hypoglycaemic medications in the management of diabetes mellitus, as proven by Kaushal Parmar et al. (2011). When tested on rats, alcoholic fruit extracts were discovered to have anti-diabetic and hepatoprotective properties (Yakaiah et al., 2013). Oral administration of the aqueous extract of *M. charantia* fruits could significantly lower blood glucose level in streptozotocin- (STZ-) induced diabetic rats at a dose of 250 mg/kg (Mishra et al., 2015). The aqueous extract of *M. charantia* fruits can stimulate insulin secretion of β cells in pancreatic islets isolated from obese-hyperglycemic mice (Day et al., 1990). Another study showed that *M. charantia* fruit aqueous extract also has hypoglycaemic activity in cyproheptadine-induced diabetic mice (Cakici et al., 1994). One study suggested that bitter guord plays a role in the renewal of β cells in STZ-diabetic rats or recovery of destroyed β cells (Xiang et al., 2007).

The study conducted by Jiang et al., 2020 confirmed that *M.charantia* saponins (MCS) could attenuate the body weight loss of diabetic rats induced by high-fat diet combined with STZ, improve glucose tolerance and reduce FBG with an anti-type 2 diabetes mellitus effect. Further studies found that MCS could improve the lipid metabolism disorder, reduce stress level, and regulate the insulin signalling pathway in diabetic rats, indicating that MCS may exert its anti-diabetic effect by improving the lipid metabolism disorder, reducing the oxidative stress level, and regulating the insulin signalling pathway in diabetic rats. Another study showed that *M.charantia* fruit juice caused a significant reduction of serum glucose, fructosamine, total cholesterol, triglycerides levels, insulin resistance index and pancreatic malondialdehyde content. While it induced a significant increase of serum insulin, HDL-cholesterol, total antioxidant capacity levels, β cell function percent, and pancreatic reduced glutathione (GSH) content and improved histopathological changes of the pancreas. It also increased glucose uptake by diaphragms of normal and diabetic rats in the absence and presence of insulin (Mahmoud et al., 2017).

The administration of whole fruit powder, a lipid fraction, a saponin fraction or the hydrophilic residue of bitter gourd at a daily dosage of 150 mg/ kg body weight for 5 weeks lowered the glycated Hb level in all treatment groups. Saponin and lipid fraction treated group shown reduced lipid peroxidation in adipose tissue and reduced protein tyrosine phosphate 1 B (PTB 1 B) activity in skeletal muscles (first study to demonstrate PTB 1 B regulation) (Klomann et al., 2010). Administration of fruit extract at the rate of 1.5 g /kg of rats for 28 days after induction of diabetes, improved the vascular compilation by decreasing blood pressure, serum total cholesterol, triglyceride levels, aortic tissue MDA level Increased aortic nitrous oxide level (Abas et al., 2015). Oral administration of protein extract from bitter gourd (10 mg/ kg body weight) caused a significant reduction in peak blood glucose and area under the curve (Poovitha & Parani, 2016). *In vivo* study in high sucrose diet induced diabetic rats revealed the decrease in blood glucose level & increasing serum insulin level after the administration of bitter guord fruit powder at the rate of 300 mg/ kg body weight (Mahwish et al., 2018).

In diabetes-induced male ddY mice, the main pure cucurbutanoid compounds of *M. charantia*, 5',19-epoxy-3',25-dihydroxycucurbita-6,23(E)-diene and 3',7',25-trihydroxycucurbita-5,23(E)-dien-19-al, have been shown to have hypoglycaemic effects (). Despite being less effective than glibenclamide at the same concentration (400 mg/kg), the glucose-lowering effects are nonetheless substantial (Harinamtenaina et al., 2006). After 8 to 30 days of therapy, an acetone extract of the whole M. charantia fruit reduced blood sugar levels in albino alloxan diabetic rats by 13 to 50%. (64). Animals with diabetes and normal blood sugar levels both experienced a dose-dependent reduction in blood glucose after receiving *M. charantia* fruit methanol extract for 28 days (Singh and Gupta et al., 2007). Alcoholic extract of *M. charantia* fruit effectively decreased plasma glucose levels by 10-15% at 1 hour in the usual glucose primed rat paradigm (Sarkar et al., 1996). In both healthy and STZ-induced diabetic rats, subcutaneous injection of a protein extract from *M. charantia* fruit pulp dramatically and dose-dependently reduced plasma glucose concentrations (Yibchok et al., 2006). According to several research, *M. charantia's* hypoglycaemic effects are equivalent to those of oral drugs like tolbutamide (Sarkar et al., 1996), chlorpropamide (Ojewole et al., 2006), and glibenclamide (Virdi et al., 2003).

3.2. Human clinical trials

Clinical research on the hypoglycaemic effects of *M. charantia* has been scarce and inconsistent compared to animal trials. In 1956, Lakholia, a doctor, likely became the first to record the beneficial effects of bitter melon using himself as the subject. In a study, Baldwa et al., (1977) examined how bitter melon affected diabetic patients' blood sugar levels. There were 19 participants, including 14 people with type 1 or type 2 diabetes. The diabetic individuals who received bitter melon showed a mean reduction in serum glucose levels, according to the authors. Nine patients with type 2 diabetes mellitus were studied in a case-series investigation by Leatherdale et al. in 1981; eight of them were concurrently taking sulfonylureas. Following juice ingestion, the Glucose Tolerance Test (GTT) revealed a considerable drop in glucose of about 12% after one hour. Additionally, eating fried bitter melon for 8 to 11 weeks decreased HbA1c readings by 8% from starting points. A case series investigation involving 18 individuals who had recently been diagnosed with type 2 diabetes mellitus was described by Welihinda et al. in 1986. Each participant received 100 mL of bitter melon fruit juice 30 minutes before to loading glucose for a GTT. After ingesting bitter melon, 13 (or 73 percent) of the patients' GTT readings improved moderately and significantly. Twelve people with type 2 diabetes mellitus participated in a case series study by Srivastava in 1993 that lasted 21 days. Patients in the powder group displayed a nonsignificant drop of 25% in the mean blood glucose level after three weeks of medication. The mean blood glucose level was significantly reduced in the aqueous extract group by 54 percent, and the mean Hb A1c level decreased from 8.37 percent to 6.95 percent.

Unripe fruit extracts from *M. charantia* showed no significant side events in T2DM patients but were helpful in lowering the average fasting glucose level (Kim et al., 2020). The safety and effectiveness of combining bitter melon powder with glibenclamide were assessed in a larger clinical trial with 112 diabetic patients who had fasting glucose levels between 126 and 240 mg/dl. Bitter melon powder was administered to two randomised groups in doses of either 2 or 4 g/day, and glibenclamide was administered to a third group. In comparison to the glibenclamide group, both groups who received bitter melon powder displayed lower HbA1c and fasting blood glucose levels as well as reduced cardiovascular risks (Rahman et al., 2015).

Sari Amalia et al., 2021 undertook a clinical study to ascertain the impact of the combination of bitter melon and snakehead fish extracts on Advanced Glycation End products (AGEs) levels in type-2 DM patients,. A clinical experimental randomised double-blind control trial was used for this study. The group that got the mixture of bitter melon and snakehead fish extracts had AGE levels that were significantly different between pre- and post-treatment. After receiving the mixture of bitter melon and snakehead fish extracts, AGEs levels changed. It was determined that the combination of both components can be utilised as a supplement to lessen type 2 diabetic problems.

Peter and Sesaazi (2022) conducted a study to create and improve a dosage form for capsules comprising dried fruit extracts of *M. charantia* and *A. esculentus*, The results showed that at day 14, a dose of 281 *M. charantia* and 175 *A. esculentus* (mg/kg) considerably decreased the FPG level when compared to vehicle. A 600 mg capsule (DM083) with a 76 percent drug loading was created using this dose. The DM083 had a total polyphenol content of 40.4 0.62 mg GAE/gDW, an HPLC fingerprint of 12 peaks, and an average disintegration time of 26.6 4.75 min. All of these results demonstrated that a blend of fruit extracts from *M. charantia* and *A. esculentus* may be produced into a stable capsule dosage form with acceptable quality criteria.

In a multicentre, randomised, double blind, active control trial in newly diagnosed type 2 diabetes patients, administration of Bitter melon capsule with 500 mg of dried powder of fruit pulp containing 0.04 – 0.05 (w/w) of charantin at the rate of 500/1000/2000 mg bitter melon per day and 1000 mg metformin per day for 4 weeks resulted modest hypoglycaemic effect and significant reduction in fructosamine levels from baseline in 2000 mg treated patients. (Fuangchan et al., 2011). Significant improvement in reducing symptoms of diabetes, reduced fasting and post prandial blood sugar with the serving of 45 ml of bitter gourd fermented beverage as a morning drink was observed in one randomized clinical trials on diabetic patients (Devaki & Premavalli, 2014).

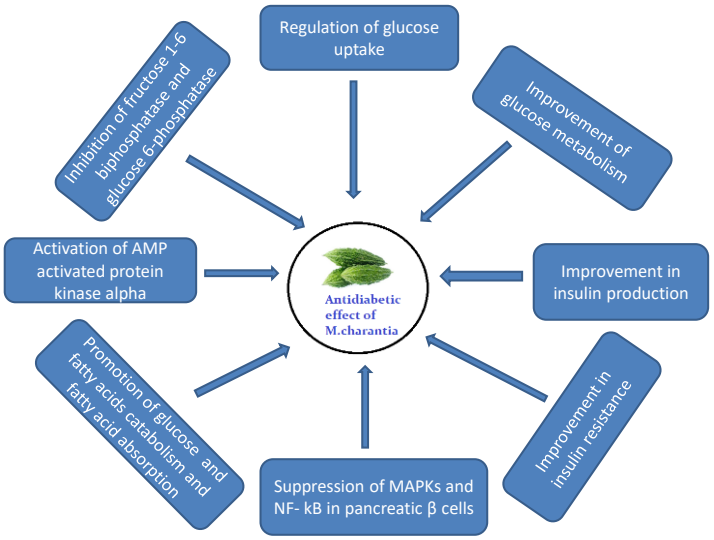
Preliminary clinical trial on non-insulin- dependent diabetes mellitus patients, powdered bitter gourd made into a tablet having a polypeptide of 20 mg. dose of 4 to 6 tablets per day half an hour before meals, for 8 weeks showed effective oral adjunt hypoglycemic effect without no reportable clinical side effects (Salam et al.,2015). Daily bitter gourd consumption of 2.5 g of powder over a course of 8 weeks: Cross over design, 8 weeks for each study period & 4 weeks wash out, lowered fasting plasma glucose in randomized placebo controlled single blinded clinical trial with 52 individuals with prediabetis (Krawinkel et al., 2018). A pilot study conducted on twenty two uncomplicated type2 diabetic patients by Rauniyar et

al., 2021 revealed that add on treatment with 200 ml of *Momordica charantia* along with anti-diabetic drug daily significantly reduced fasting and post prandial blood sugar. Treatment with anti-diabetic drugs only reduced fasting and post-prandial blood sugar but the reduction was not significant. There was improvement in lipid profile by both anti-diabetic drugs alone and *M. charantia* along with anti-diabetic drug, but it was not significant.

An improvement in parameters of glycemic control has been observed with *Momordica charantia* in patients with type 2 diabetes mellitus. A randomized, double-blinded, placebo-controlled, clinical trial was carried out in 24 patients who received *M. charantia* (2000 mg/day) or placebo for 3 months. A 2-h oral glucose tolerance test (OGTT) was done before and after the intervention to calculate areas under the curve (AUC) of glucose and insulin, total insulin secretion (insulinogenic index), first phase of insulin secretion (Stumvoll index), and insulin sensitivity (Matsuda index). In the *M. charantia* group, there were significant decreases in weight, body mass index (BMI), fat percentage, waist circumference (WC), glycated hemoglobin A1c (A1C), 2-h glucose in OGTT, and AUC of glucose. A significant increase in insulin AUC, in total insulin secretion, was observed after *M. charantia* administration (Marisol Cortez et al., 2018).

A randomized, double-blind, placebo-controlled trial to evaluate the hypoglycemic efficacy of the mcIRBP-19 (*M.charantia* Insulin Receptor Binding Protein)-containing *Momordica charantia L.* fruit extracts in the type 2 diabetic subjects revealed that the oral administration of mcIRBP-19-Bitter gourd extract had a significant effect on reducing FBG and HbA1c (Yang et al., 2022). Anti-Diabetic Activity of Polypeptide-K Isolated from *Momordica Charantia*: A Retrospective Study of 142 Cases, result showed that age and duration of disease, pre-treatment of blood glucose and post-treatment of blood glucose showed positive relationship (Sirn, Yong Yean, et al., 2021).

4. Pathways of anti-diabetic effect of *M.charantia* and its extracts



The hypoglycemic effects of *M. charantia* and its extracts are thought to be mediated by a number of different pathways, including improved glucose metabolism, regulation of glucose uptake, improved insulin secretion and resistance, suppression of MAPKs and NF-κB in pancreatic B-cells, induction of PPAR- γ gene expression, activation of AMP-activated protein kinase alpha and inhibition of fructose-1,6-bisphosphatase & glucose-6-phosphatase (Xu et al., 2022, Oyelere et al., 2022).

5. Future outlook

Several research projects on the advantages of bitter melon against Type 2 diabetes have been carried out over the previous ten years. Only a small portion of this research, nevertheless, addressed Type 2 diabetes patients in large-scale clinical trials. Numerous *in vivo* and animal investigations have shown that different forms of bitter melon have hypoglycemic properties. However, in regards to the effects of bitter melon on Type 2 diabetes, results from human clinical trials were conflicting.

In the past, numerous toxicological studies have shown that extracts of *M. charantia* may be toxic in various body organs at varying doses. A decrease in fertility rate and spermatogenesis is one

common side effect of bitter melon extract in animals (Stepka, 1974, Dixit et al., 1978). Clinical trials have revealed gastrointestinal symptoms like abdominal pain and diarrhoea as well as headaches (Dutta et al., 1981), which could suggest that consuming a lot of bitter melon causes hypoglycemic conditions. According to recent review articles on the bitter melon clinical trials, people with glucose-6-phosphate-dehydrogenase deficiency, should abstain from eating bitter melon (Leung et al., 2009). This condition, which can cause red blood cell destruction, may be triggered by bitter melon alkaloids such as vicine (Barbieri et al., 1988, Leung et al., 2009).

According to a study by Khan et al., (2019), *M. charantia* seed extract was fatal to zebrafish embryos with LD50 values of 50 g/ml, and at sub-lethal concentrations, various abnormalities were seen in zebrafish embryos. According to Abdillah et al., 2020, the liver and the kidney could become toxic after receiving an ethanolic extract of *M. charantia* for 28 consecutive days. In order to suggest a safe dose for use, these effects on the body's essential organs need to be clarified further. Unfortunately, there was wide variation in several of these human investigations. Thus, additional clinical studies with more focused criteria can help us to better grasp the potential and restrictions of bitter melon use.

6. Conclusion

Studies on animals and in cell culture have shown that bitter melon has anti-diabetic properties and can regulate blood sugar like a hypoglycemic drug. But during human clinical studies, researchers found conflicting outcomes. A precise dosage range that achieves the required control over hyperglycemia without creating undesirable symptoms is also not currently available from studies. In order to establish bitter melon as an alternative treatment for Type 2 diabetes, researchers should concentrate on conducting well-planned clinical trials, offering an accurate dosage range without any adverse effects.

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