

Uncovering the role of *Momordica charantia* in diabetes: therapeutic and biotechnological perspectives

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Abstract

The problem of diabetes mellitus in public health is a worrying one considering the data and forecasts made by the *World Health Organization* and the *International Diabetes Federation* which triggers an alarm signal on nutrition and sedentarism. Even though there are various drugs and treatments available that can treat diabetes, they have side effects so alternative treatments are sought based on the effect of active compounds found in medicinal plants. *Momordica charantia* L. which is rich in secondary metabolites such as polypeptide-p, triterpenes, flavonoids, alkaloids, saponins, volatile oils, gallic acid and chlorogenic acid. The *In Vitro* culture technique makes it possible to quickly produce valuable plant genotypes, including medicinal ones, with a significant advantage of rapid production and preservation of valuable genotypes. Also, the properties of active compounds produced by *Momordica charantia* L. make it beneficial in other diseases such as cancer, respiratory diseases, skin infections, joint diseases, neuronal diseases and viral infections. The pharmaceutical industry offers a wide range of products based on *Momordica charantia* L. extract such as: pills, tablets, syrups, teas, dried fruits, oils, injections, creams, tinctures, foods in the form of bars and drinks in the form of juices.

This review aims to summarize recent research in the field of biotechnology, highlighting its intersection with medicine. It explores how biotechnological advancements can provide a quick and efficient means to produce the necessary active compounds for managing type 2 diabetes effectively.

Keywords: Biotechnology, Diabetes, Active compounds, *Momordica charantia*

Introduction

Diabetes mellitus is a metabolic dysfunction characterized by hyperglycemia, insufficient secretion of insulin, a hormone produced by the endocrine pancreas with a role in regulating blood glucose levels [11]. According to the World Health Organization (WHO) and the International Diabetes Federation (IDF), the number of those affected by diabetes in 2021 was approximately 537 million adults (20-80 years old), more precisely 10.5% of the adult population, also the forecasts are worrying because it is estimated that the number of those affected will exceed 780 million by 2045, representing more than 12% of adults [14] [19] [1].

Type I diabetes is insulin-dependent diabetes that usually has genetic causes that involve the autoimmune destruction of beta cells of the pancreas that play a role in the production of insulin [9].

Type II diabetes also has genetic causes regarding the predisposition of the individual body to acquire the disease, but also complementary causes that include the lifestyle of which we mention unhealthy diet, sedentary lifestyle and obesity [45].

Persistent hyperglycemia leads to damaging stress of tissues in various systems such as cardiovascular, neuronal, renal, epithelial, causing in both types of diabetes symptoms that are manifested by excessive fatigue, frequent urination, excessive hunger and thirst, blurred vision, slow wound healing, dry skin, numb hands and feet, effortless weight loss and diet [24] [45].

For type I diabetes (insulin-dependent) injectable insulin treatment is administered, it may also be necessary in severe cases of type II diabetes [18].

Conventional treatment for diabetes includes the administration of oral medications such as pills, syrups, which have metformin as their active substance or from the sulfonylurea category. It is also very important to adopt a healthy lifestyle that includes balanced diets and physical exercise [29].

Herbal treatments are also very important for their properties on regulating insulin levels, among the most used can be mentioned: *Allium sativum*, *Curcuma longa*, *Aloe vera*, *Ocimum sanctum* and *Momordica charantia* [23].

Studies demonstrate the hyperglycemia-lowering ability of *Momordica charantia* extracts that promote insulin secretion by stimulating pancreatic beta cells that lower blood glucose levels [24]. According to Grover et al. with the help of compounds such as charantin, p-polypeptide, vicin, lectin, flavonoides, saponins, alkaloids, gallic and chlorogenic acids [17].

Momordica charantia (abbreviated MC) also known as "bitter melon" is a plant of the Cucurbitaceae family, with a number of chromosomes $2n = 22$, it is a plant with a natural area widespread in Africa, Southeast Asia and India, today it also has a spread in the temperate zone due to its varieties resistant to colder climates. The fruit of the plant is an edible one famous for its bitter taste and its medical properties [3].

It is a herbaceous plant with a hanging stem that has tendrils reaching a length of up to 5 m. The leaves are placed alternately with lengths of 4-12 cm sectioned into 3-7 lobes. The flowers are unisexual monoecious, flowering taking place between June and July, and fruiting between September and November. The life cycle of the plant is annual in temperate zones and perennial in tropical zones. The MC fruit has an oblong shape that resembles a small cucumber that in the early stage has a light green color, and at maturity the color can vary depending on the varieties from yellow to orange to red [35].

According to the phytochemical studies of Prarthna et. al, MC contains biologically active chemicals, which include glycosides, saponins, alkaloids, fixed oils, triterpenes, proteins and steroids, immature fruits are a good source of Vitamin A and C, phosphorus and iron [10]. MC is a plant used in traditional Asian medicine, which has also been perpetuated in modern medicine due to its therapeutic properties in diseases such as diabetes, cancer, viruses - including HIV, bacteriosis, treating problems such as diarrhea, ulcers, gout, liver diseases, etc. [29].

This review aims to highlight the properties of the medicinal plant MC in diabetes but also the use of biotechnology as a method of increasing the production of biological material, respectively the use of MC in biotechnology.

Biotechnology and *In Vitro* Cultures

Biotechnology is a new, innovative and multidisciplinary field based on biology whose purpose is the use of biological systems (microorganisms or products derived from them, plant and animal cell cultures) for the production of useful substances in agriculture, food, pharmaceutical, etc. for the benefit of human activity. The practical contributions of biotechnology in medicine are represented by pharmaceuticals such as recombinant insulin, gene therapy, vaccines, personalized medicine [15] [13] [4].

In biotechnology there are various techniques, among which we mention: micropropagation and *in vitro* culture, vital tools which are used for the rapid production and preservation of valuable plant genotypes, including medicinal ones. The applications of *In vitro* culture are represented by the production of virus-free plants, different plants under abiotic stress conditions (water stress, salinity, extreme temperatures) and valuable secondary compounds such as alkaloids, flavonoids, terpenes, etc. It also contributes to metabolic engineering to improve the yield of active compounds [22] [31] [38] [32].

Recent *In Vitro* culture research studies at *Momordica charantia*

Kale et al. (2024) tried an *in vitro* regeneration of bitter melon cv. "BSS-1007". For direct multiple shoot induction, auxiliary bud and shoot apical meristem explants were cultured on media with different growth regulators. The results showed that for shoot induction from auxiliary buds, the best concentration was 1.0 mg/l BAP, producing maximum 3.19 numbers of shoots with minimum 7.30 days required for shoot initiation. In case of shoot induction from shoot apical meristem, MS medium with 1.5 mg/l BAP was suitable for producing maximum 2.33 numbers of shoots with minimum 7.67 days required. For *in vitro* rooting of shoots MS medium with 2.0 mg/l IBA was best for rooting the explants obtained and the highest average number of roots (40.71) were produced with minimum average days required for root induction (6.57days) [21].

NaïtchéDé et al. 2023 developed and established an *in vitro* organogenesis protocol to obtain embryogenic callus from immature leaves of *in vivo* grown seedlings and *in vitro* plantlets of *Momordica charantia* L. The results showed that the maximum callus formation frequency (95.09 %) was obtained using Murashige-Skoog media with 1.2 mg/l NAA and 0.5 mg/l TDZ. The results were compared with those of other authors like Malik et al. (2007), Devendra et al. (2009) and Chung & Ouyang (2020) showing the differences and the similarities between the results obtained. Also, for shoot elongation at bitter melon, the MS medium supplemented with 0.75 mg/l GA₃ has been recorded as the most convenient medium. Leaf explants from *in vitro* plantlets produced significantly higher callus and shoot formation frequency than *in vivo* raised seedling explants. [26].

Mobasserimoghadam et al. 2023 obtained *in vitro* plants of *Momordica charantia* through organogenesis from sterilised seeds. According to the results, the highest percentage of callus formation was obtained on MS with 3 g/L 2,4-D, the highest percentage of regeneration was obtained MS with the concentration of 2 mg/L BAP [28].

Naïtchédé et al. (2022) developed the protocol of micropropagation of *Momordica charantia* L. using nodal explants which were obtained from seedlings *in vivo* grown for 30 days in a greenhouse, then grown on media with different concentration of BAP and Kin either alone, or in combination. The best results on shoot induction were obtained using MS with 0.5 mg/L BAP and 0.5 mg/L Kin with a maximum frequency of shoot induction of $72.17 \pm 2.83\%$. Shoots were inoculated on MS 1/2 media without growth regulators or supplemented with IBA, ANA and AIA at different concentrations (0.5-1.5 mg/L) to promote root induction [30].

Secondary metabolites of *Momordica charantia*

Secondary metabolites are chemical compounds that are not directly involved in plant growth or reproduction but have a role in defense, signaling, adaptation to various environmental conditions. In the case of MC, they present various bioactivities making it very valuable for medicine and biotechnologies [13] [42]. The antidiabetic properties of secondary metabolites consist in regulating glucose levels and transmitting its intake into cells, making them effective in the management of type II diabetes [20].

The main secondary metabolites in the management of type II diabetes are represented by:

Charantine - an alkaloid-type mixture of steroids, namely sitosterol and stigmasterol, which has benefits in lowering glucose levels in tissues Jadhav et. Al., 2024 [2].

Vicine – a natural alkaloid with benefits in reducing blood sugar by stimulating insulin secretion [44].

The P- polypeptide is a polypeptide similar to insulin and that mimics its actions, being considered a natural insulinomimetic [7].

Lectin- is a protein that inhibits receptors that play a role in increasing blood sugar after eating [25].

Flavonoids – natural antioxidants, specifically kaempferol and quercetin with a role in reducing oxidative stress associated with diabetes [8].

Saponins - are triterpene glycosides with hypoglycemic and antioxidant effects that contribute to lowering lipid and blood sugar levels [40].

Alkaloids – organic nitrogen-based compounds that help regulate glucose metabolism by reducing glucose absorption in the intestine [5] [27].

Volatile oils and fatty acids – from the lipid category, with a role in promoting the health of beta cells in the pancreas and reducing the risk of cardiovascular complications by supporting lipid metabolism [2].

Gallic acid – is a phenolic acid that helps reduce inflammation and oxidative stress [12].

Chlorogenic acid – phenolic acid that improves insulin sensitivity [33].

Mobasserimoghadam et al. 2023 obtained *in vitro* plants of *Momordica charantia*. Following the regeneration, leaves, roots and fruits were obtained which were tested by GC – MS, the results obtained demonstrated the highest number of secondary metabolites (46 compounds) were found in the fruits of bitter melon [28].

The role of *Momordica charantia* in treating diseases

Also, MC is not only beneficial in treating diabetes, but also in treating other diseases with the help of secondary metabolites such as: Quercetin, Kaempferol in the category of flavonoids have anti-inflammatory, antioxidant and antimicrobial properties used in treating cancer by reducing oxidative stress and inhibiting tumor cells and treating cardiovascular diseases by reducing LDL oxidation and protecting against atherosclerosis [34].

Saponins with antioxidant, immunomodulatory and lipid-lowering properties used in the treatment of conditions such as hyperlipidemia by reducing cholesterol and triglyceride levels. Against cancer through its toxic effect on cancer cells. Against bacterial and fungal infections due to antimicrobial properties [8].

Momordicin is an alkaloid with analgesic, anti-inflammatory and antimicrobial properties that helps in the treatment of malaria through an antiplasmodial effect, also used in the relief of rheumatic and muscle pain [5] [25].

Momordicillin is an antiviral, anticancer and anti-inflammatory terpenoid used in the treatment of conditions such as viral hepatitis, and through its anticancer properties it inhibits cell proliferation and angiogenesis [43] [25].

Steroids have anti-inflammatory properties that reduce inflammation in diseases such as rheumatoid arthritis, and immunomodulatory properties help in the treatment of autoimmune diseases [43].

Lectins have antiviral properties that contribute to the treatment of viral infections by inhibiting the attachment of viruses to cells, including the HIV virus, and by their antitumor character they promote apoptosis of tumor cells. Lectins also have an immunomodulatory role [34].

Gallic acid and chlorogenic acid are phenolic acids that have antioxidant and anti-inflammatory properties, having a use in the prevention and management of neurodegenerative diseases such as Alzheimer's and Parkinson's. It also contributes to the treatment of cardiovascular diseases by reducing vascular inflammation and protecting the endothelium [29].

Glycosides have an antiviral and hypoglycemic role, helping to treat viral infections by inhibiting the replication of some viruses [37].

Triterpenoids have anti-inflammatory properties reducing systemic inflammation and hepatodefensive properties preventing liver damage caused by toxins [14].

Volatile oils have antimicrobial properties helping to treat skin infections caused by bacteria and fungi. Also, the anti-inflammatory properties help in treating respiratory problems such as asthma [29].

Available treatment for type 2 diabetes and the connection with *Momordica charantia*

Different forms of treatment for treating diabetes both natural and chemical substances known as medicines are available in pharmacies. In case of type 2 diabetes, the first medicine prescribed is Metformin (Fortamet, Glumetza, others) which acts by lowering glucose production in the liver and improving the body's sensitivity to insulin so it uses insulin more effectively. The side effects of metformin include nausea, diarrhea, stomachache, loss of appetite, and a metallic taste in mouth.

In the case of patients diagnosed with Type 1 diabetes, they need to inject synthetic insulin to control their disease. The four main ways you can take insulin include injectable insulin with a syringe (shot), insulin pens, insulin pumps and rapid-acting inhaled insulin.

Momordica charantia extracts can be found in capsules or tablets, tinctures, teas, syrups, etc. with different applications in the treatment of diabetes and other diseases.

Capsules or tablets can be used in type 2 diabetes treatment and also as supplements for cholesterol control and immune system support [24].

Powder or dried and ground fruits that are added to drinks and teas for blood sugar control, used as complementary treatments in hypercholesterolemia and detoxification [8].

Dried leaf or fruit teas being beneficial in lowering blood sugar, detoxifying the body and digestive problems [38].

Tincture or concentrated hydroalcoholic extract of the plant used in low doses for the management of diabetes and chronic inflammation with antimicrobial and antioxidant effects [8].

Syrups used in blood sugar control and cough reduction associated with respiratory infections [8].

Fat-soluble oils and extracts used to heal wounds and skin infections with anti-inflammatory and antibacterial effects and with the potential to support skin health [36].

Experimental injections, effective for acute hyperglycemia due to insulin-mimetic effects for severe diabetes [42].

Cream or gel applied to the skin helps heal wounds and treat skin infections [34]

Various functional foods enriched with *momordica* extracts such as: natural juices, smoothies, nutritional bars, chocolate being easy to integrate into the daily diet [26].

Conclusions

The biotechnological potential of *Momordica charantia* is vast, having an important role in different fields such as medicine and agriculture, especially in the treatment of type II diabetes, offering new opportunities for research and therapeutic applications of this medicinal plant.

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