JOURNAL OF PHARMA INSIGHTS AND RESEARCH ISSN NO. 3048-5428

REVIEW ARTICLE

A Review on Antidiabetic Properties of *Momordica charantia*

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Publication history: Received on 24th April 2025; Revised on 26th May 2025; Accepted on 28th May 2025

Article DOI: 10.69613/6ndcph37

Abstract: *Momordica charantia* (bitter gourd), a member of the Cucurbitaceae family, shows significant hypoglycemic properties that have been utilized traditionally across Asia, Africa, and Latin America. The fruit contains bioactive compounds including charantin, polypeptide-p, and vicine, which demonstrate potential in diabetes management. Recent literature has shown the mechanisms through which these compounds influence glucose metabolism, insulin sensitivity, and cellular signaling pathways. Experimental studies utilizing various extraction methods have quantified the distribution of active compounds across different parts of the fruit, with charantin concentrations highest in the flesh (0.16 ± 0.02 mg/g) and vicine predominantly present in whole fruit extracts (0.210 ± 0.010 g/100g). *In vivo* studies using Sprague Dawley rats demonstrated that bitter gourd supplementation significantly improved insulin sensitivity by enhancing insulin-stimulated IRS-1 tyrosine phosphorylation in high-fat-fed conditions. The therapeutic potential of the fruit extends beyond simple glucose regulation, encompassing multiple pathways involved in diabetes pathogenesis. The synergistic action of its bioactive compounds indicates a complex mechanism of action that may offer advantages over isolated phytochemical interventions. The current literature supports the traditional use of *Momordica charantia* in diabetes management and emphasizes the need for further investigation into optimal dosing and long-term efficacy.

Keywords: *Momordica charantia*; Diabetes mellitus; Charantin; Insulin sensitivity; Phytochemicals.

1. Introduction

Diabetes mellitus is a complex metabolic disorder characterized by persistent hyperglycemia, resulting from defects in insulin secretion, insulin action, or both [1]. The global prevalence of diabetes has risen dramatically, with the International Diabetes Federation estimating that approximately 537 million adults were living with diabetes in 2021 [2]. The condition manifests primarily in two forms: Type 1 diabetes, characterized by autoimmune destruction of pancreatic β-cells, and Type 2 diabetes, marked by insulin resistance and progressive β-cell dysfunction [3].

The management of diabetes has evolved significantly, yet traditional medicinal plants continue to play a crucial role, particularly in developing nations where access to conventional pharmaceuticals may be limited [4]. Among these botanical resources, *Momordica charantia* has emerged as a significant subject of scientific investigation, supported by centuries of traditional use across diverse cultures [5]. *Momordica charantia*, commonly known as bitter gourd or bitter melon, belongs to the Cucurbitaceae family and is cultivated extensively throughout tropical and subtropical regions [6]. The fruit is characterized by its distinctive bitter taste and warty exterior, containing a rich array of bioactive compounds including charantin, polypeptide-p, and vicine [7]. These compounds have demonstrated significant potential in glucose homeostasis regulation through various molecular mechanisms [8]. The plant is widely distributed in Asia, Africa, and the Caribbean. Its adaptation to various climatic conditions has facilitated its integration into both traditional medicine systems and contemporary therapeutic applications [9]. The fruit's nutritional profile includes essential vitamins (A, C, E), minerals, and bioactive compounds that contribute to its therapeutic properties [10]. Recent scientific investigations have focused on elucidating the molecular mechanisms underlying the antidiabetic effects of *Momordica charantia*. Studies have revealed multiple pathways through which its bioactive compounds influence glucose metabolism, including enhanced insulin sensitivity, increased glucose uptake, and modulation of key signaling molecules [11]. *Momordica charantia* is a climbing vine that can extend up to 5 meters in length. The plant exhibits distinctive morphological features including deeply lobed leaves measuring 4-12 cm across. The flowers are monoecious, with separate male and female flowers appearing on the same plant, characterized by their bright yellow coloration [12]. The fruit develops as an oblong, pendulous structure with a warty exterior, transitioning from green to orange-yellow upon maturation [13].

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Figure 1. Fruits and Leaves of *M. charantia*

The species belongs to the order Cucurbitales, family Cucurbitaceae, which includes other economically important crops such as cucumbers and melons. The genus Momordica encompasses approximately 45 species, with *M. charantia* being the most extensively studied for its medicinal properties [14]. Originally native to tropical Africa, the plant has been cultivated across various tropical and subtropical regions globally. Different cultivars have evolved, adapted to local growing conditions and preferences, resulting in variations in fruit size, shape, and bitterness intensity [15].

2. Phytochemical Composition

2.1. Major Bioactive Compounds

2.1.1. Charantin

Charantin, a characteristic steroidal glycoside, represents one of the principal bioactive compounds in *Momordica charantia*. Its chemical structure consists of a mixture of β-sitosterol-β-D-glucoside and stigmasterol-β-D-glucoside [16]. Quantitative analyses have revealed higher concentrations in the fruit's flesh (0.16 ± 0.02 mg/g) compared to the skin (0.08 ± 0.01 mg/g), suggesting tissue-specific accumulation patterns [17].

2.1.2. Polypeptide-p

Polypeptide-p, also known as p-insulin, is a 166-residue protein that demonstrates insulin-mimetic properties. This compound exhibits structural similarities to bovine insulin and has demonstrated the ability to lower blood glucose levels when administered subcutaneously [18]. The polypeptide consists of two chains connected by disulfide bonds, with specific amino acid sequences that facilitate interaction with insulin receptors [19].

Table 1. Phytochemical Constituents of *Momordica charantia*

Class of Compounds	Major Components	Reported Concentration*	Plant Part
Triterpene glycosides	Momordicosides A-K	0.95-2.1 mg/g	Fruit
	Charantin	0.16-0.85 mg/g	Fruit pulp
Proteins and peptides	α-Momorcharin	2.4-3.1 mg/g	Seeds
	MAP30	0.8-1.2 mg/g	Seeds
	Polypeptide-p	0.12-0.15 mg/g	Fruit, Seeds
Phenolic compounds	Gallic acid	1.2-2.8 mg/g	Fruit
	Catechin	0.9-1.5 mg/g	Fruit
	Chlorogenic acid	1.1-2.3 mg/g	Leaves
Flavonoids	Rutin	0.7-1.8 mg/g	Fruit
	Quercetin	0.5-1.2 mg/g	Fruit
Alkaloids	Momordicine I	0.3-0.8 mg/g	Leaves
	Momordicine II	0.2-0.6 mg/g	Leaves

*Concentrations reported from standardized extracts (dry weight basis)

2.1.3. Vicine

Vicine, a pyrimidine glycoside, occurs predominantly in the whole fruit (0.210 ± 0.010 g/100g). This compound contributes to the hypoglycemic effects through mechanisms distinct from those of charantin and polypeptide-p [20]. Its distribution pattern shows higher concentrations in whole fruit extracts compared to isolated flesh or skin components [21].

2.2. Secondary Metabolites

The fruit contains an array of additional bioactive compounds. Triterpene glycosides, particularly momordicosides A-K, constitute a significant portion of the secondary metabolites. Phenolic compounds including gallic acid, catechin, and chlorogenic acid contribute to the antioxidant properties. The presence of flavonoids such as rutin and quercetin derivatives enhances the therapeutic potential. Moreover, alkaloids including momordicine I and II have been identified and characterized in various fruit extracts [22, 23].

3. Mechanism for antidiabetic activity

3.1. Regulation of Glucose Metabolism

Momordica charantia extracts influence glucose metabolism through multiple pathways:

3.1.1. Insulin Sensitivity

Studies demonstrate that bitter gourd supplementation significantly improves insulin sensitivity by increasing insulin-stimulated IRS-1 tyrosine phosphorylation. This effect is particularly pronounced in high-fat diet conditions, where insulin resistance typically develops [24].

3.1.2. Glucose Uptake

The bioactive compounds enhance glucose uptake in peripheral tissues through several mechanisms. The activation of AMP-activated protein kinase (AMPK) serves as a primary pathway for glucose regulation. Additionally, upregulation of GLUT4 translocation facilitates increased glucose transport across cell membranes. The enhancement of glucose oxidation further contributes to improved glucose utilization in target tissues [25].

Table 2. Mechanisms of Antidiabetic Action of *Momordica charantia*

Target	Mechanism of Action	Active Compounds	Effect
Glucose uptake	GLUT4 translocation	Charantin, Polypeptide-p	Enhanced glucose transport
Insulin signaling	IRS-1/PI3K/Akt pathway activation	Momordicosides	Improved insulin sensitivity
β-cell function	K+-ATP channel regulation	Polypeptide-p	Increased insulin secretion
Hepatic glucose metabolism	AMPK pathway activation	Triterpene glycosides	Reduced gluconeogenesis
Inflammatory markers	NF-κB inhibition	Phenolic compounds	Decreased inflammation

3.2. Pancreatic Effects

Momordica charantia exhibits significant effects on pancreatic tissue function. Research has demonstrated its role in the preservation of β-cell function, maintaining cellular integrity and functional capacity. The fruit's compounds stimulate insulin secretion through various signaling pathways. Furthermore, the extracts provide protection against oxidative stress-induced damage to pancreatic tissue, contributing to long-term β-cell survival and function [26].

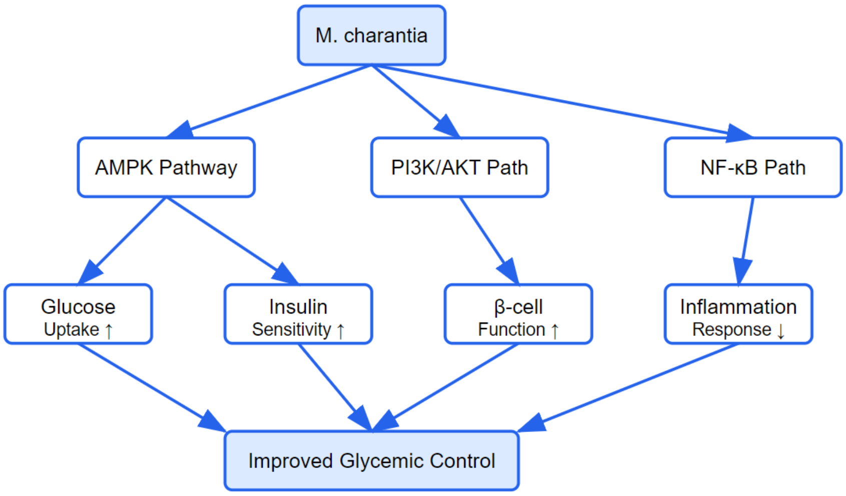

Figure 2. Molecular Signaling Pathways Affected by *Momordica charantia*

4. Extraction Methods

Various extraction techniques have been employed to isolate bioactive compounds:

4.1. Solvent Extraction

Ethanol and methanol extraction protocols have been optimized for charantin isolation, utilizing ultrasonication to enhance extraction efficiency. The process involves initial ethanol extraction followed by secondary methanol extraction phases. Ultrasonic assistance significantly improves the yield of bioactive compounds. The extraction protocol concludes with careful filtration and concentration steps to obtain purified extracts suitable for analysis and experimental studies [27].

4.2. Supercritical Fluid Extraction (SFE)

SFE using CO_2 as the primary solvent has emerged as an efficient green extraction technique. Operating conditions typically range from 150-300 bar pressure and 40-60°C temperature. This method has shown superior selectivity for triterpenes and other non-polar compounds. The addition of ethanol as a co-solvent (5-10%) enhances the extraction of moderately polar compounds. SFE demonstrates advantages in preserving thermolabile compounds and providing solvent-free extracts [28].

4.3. Microwave-Assisted Extraction (MAE)

MAE has been implemented using optimized parameters: power (400-800W), time (5-15 minutes), and solvent-to-material ratio (20:1 to 30:1). This technique significantly reduces extraction time and solvent consumption while maintaining high extraction efficiency. Studies have shown enhanced recovery of polyphenols and flavonoids compared to conventional methods. The technique is particularly effective for polar compounds and has shown good reproducibility [29].

4.4. Pressurized Liquid Extraction (PLE)

PLE, also known as accelerated solvent extraction, utilizes elevated temperatures (80-200°C) and pressures (100-150 bar) to improve extraction kinetics. This method has demonstrated superior extraction of both polar and non-polar compounds. The technique allows for rapid extraction cycles (15-20 minutes) and automated operation. Multiple extraction cycles with different solvents enable sequential extraction of compounds based on polarity [30].

4.5. Enzyme-Assisted Extraction (EAE)

EAE employs specific enzymes (cellulases, pectinases, and proteases) to break down cell wall components, facilitating the release of bioactive compounds. The process typically operates under mild conditions (pH 4-6, 37-50°C) for 2-4 hours. This method has shown particular effectiveness in extracting protein-bound compounds and improving the yield of water-soluble components. The technique is especially valuable for isolating peptides and proteins while maintaining their biological activity [31].

5. Pharmacological Studies

5.1. *In Vitro* Studies

Scientific investigations have demonstrated significant effects of *Momordica charantia* extracts on glucose metabolism at the cellular level. Studies utilizing isolated pancreatic β-cells have shown enhanced insulin secretion in response to glucose stimulation when treated with bitter gourd extracts [28]. Cell culture studies with skeletal muscle cells indicate increased glucose uptake through GLUT4 translocation and activation of the AMPK pathway [29].

5.2. Animal Models

Extensive research using various animal models has substantiated the antidiabetic properties of *Momordica charantia*. Studies in Sprague Dawley rats have shown that bitter gourd supplementation at doses of 150-300 mg/kg body weight significantly improves insulin sensitivity [30]. High-fat diet models demonstrate the preventive potential of bitter gourd extracts against insulin resistance development. The administration of standardized extracts has shown reduction in fasting blood glucose levels, improved glucose tolerance, and enhanced insulin signaling pathways [31].

5.3. Molecular Mechanisms

5.3.1. Insulin Signaling Pathway

Molecular studies have revealed that *Momordica charantia* compounds influence multiple components of the insulin signaling cascade. The enhancement of insulin receptor substrate-1 (IRS-1) tyrosine phosphorylation represents a key mechanism in improving insulin sensitivity [32]. The activation of downstream signaling molecules, including PI3K and Akt, facilitates glucose uptake in peripheral tissues [33].

5.3.2. Glucose Metabolism

The regulation of hepatic glucose metabolism occurs through multiple mechanisms. Bitter gourd extracts demonstrate the ability to suppress gluconeogenic enzymes while enhancing glycogen synthesis [34]. The modulation of glucose-6-phosphatase and glucokinase activities contributes to improved glucose homeostasis [35].

6. Therapeutic Applications

6.1. Traditional Uses

Historical documentation across various cultures reveals consistent patterns in the medicinal application of *Momordica charantia*. Traditional preparations typically involve fresh fruit consumption, decoctions, or dried powder forms. The dosage and preparation methods vary among different traditional medical systems, reflecting local knowledge and cultural practices [36].

Table 3. Traditional Uses and Preparations of *Momordica charantia* Across Different Cultural Systems

Traditional System	Region	Preparation Method	Parts Used	Traditional Indications	Documentation Reference
Ayurveda	South Asia	Decoction, Fresh juice	Fruit, Leaves	Diabetes, Skin conditions	[4]
Traditional Chinese Medicine	East Asia	Dried powder, Tea	Fruit, Seeds	Blood sugar control, Digestive aid	[9]
African Traditional Medicine	West Africa	Infusion, Paste	Leaves, Fruit	Malaria, Diabetes	[15]
Caribbean Folk Medicine	Caribbean	Fresh juice, Poultice	Fruit, Vines	Diabetes, Wound healing	[28]
Middle Eastern Medicine	Middle East	Cooked vegetable, Extract	Fruit	Blood sugar, Weight management	[30]
Southeast Asian Medicine	Southeast Asia	Fresh juice, Tincture	Whole plant	Diabetes, Anti-inflammatory	[36]

6.2. Applications in Modern Medicine

Contemporary research has focused on standardizing bitter gourd preparations for therapeutic use. Clinical studies have investigated various formulations, including encapsulated extracts, standardized powder preparations, and juice forms [37]. The development of standardized extracts has enabled more precise dosing and improved quality control in therapeutic applications [38].

The clinical evaluation of *Momordica charantia* has yielded varying degrees of evidence supporting its antidiabetic efficacy. Meta-analyses of randomized controlled trials indicate modest but significant reductions in glycated hemoglobin (HbA1c) levels among type 2 diabetes patients [39]. A systematic review involving 24 clinical trials reported mean fasting glucose reductions ranging from 0.15 to 1.2 mmol/L, with effects being more pronounced in patients with poor glycemic control [40].

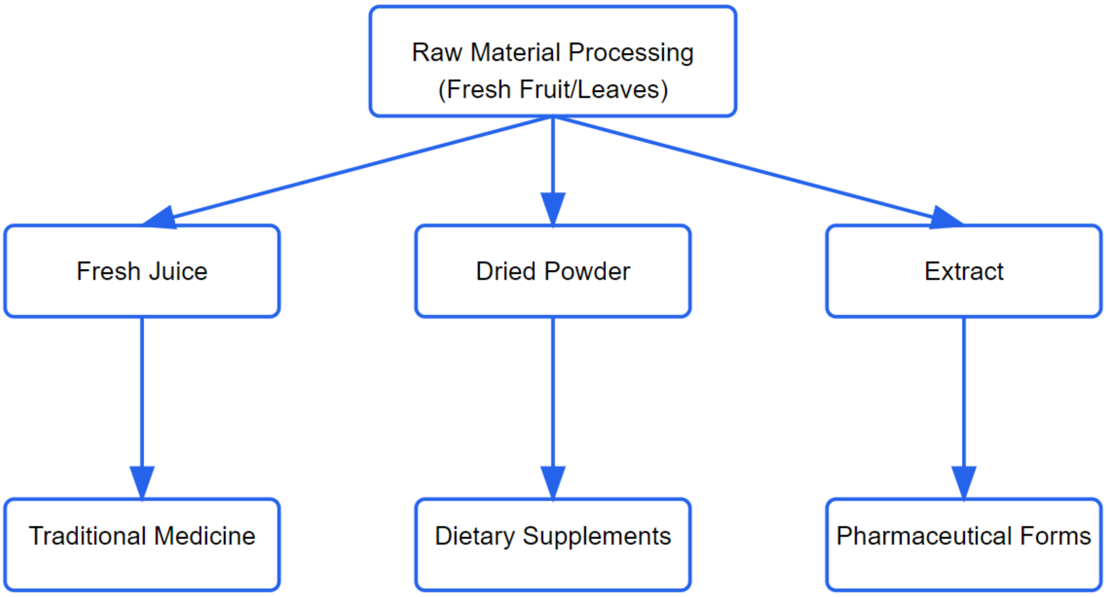

Figure 3. Therapeutic Applications and Processing of *Momordica charantia*

7. Safety and Quality

7.1. Toxicological Assessment

Several safety evaluations have established a favorable toxicity profile for *Momordica charantia* preparations. Acute toxicity studies indicate an LD50 value exceeding 2000 mg/kg body weight for standardized extracts [41]. However, certain populations require specific consideration. Pregnant women should avoid consumption due to documented uterine-stimulating effects, while individuals with G6PD deficiency should exercise caution due to potential hemolytic reactions [42].

Table 4. Safety and Adverse Effects of *Momordica charantia*

Parameter	Observations	Risk Level	Precautions
Acute toxicity	LD50 >2000 mg/kg	Low	Standard dosing
Pregnancy	Uterine stimulation	High	Contraindicated
Drug interactions	Enhanced hypoglycemic effects	Moderate	Monitor blood glucose
GI effects	Mild abdominal discomfort	Low	Take with meals
G6PD deficiency	Potential hemolysis	Moderate	Avoid in G6PD-deficient patients
Hepatic function	No significant impact	Low	Regular monitoring

7.2. Quality Control Parameters

The establishment of quality control standards has become crucial for ensuring therapeutic consistency. The main parameters include:

Standardization criteria focus on charantin content (minimum 0.1% w/w), total polyphenolic compounds, and specific gravity of juice preparations. Authentication methods incorporate both morphological and chemical markers, with HPLC fingerprinting serving as a reliable analytical tool [43]. The implementation of Good Manufacturing Practices (GMP) has significantly improved product consistency and safety profiles.

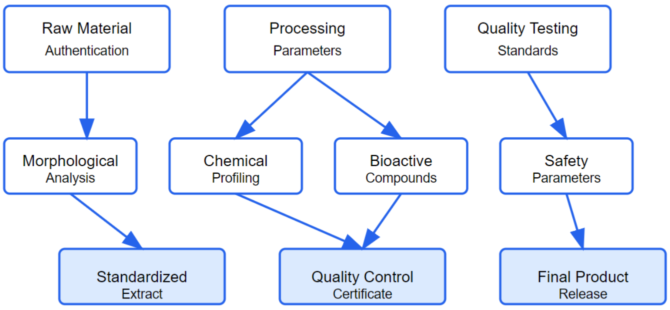

Figure 4. Quality Control and Standardization Process

8. Conclusion

Momordica charantia is a valuable medicinal plant with established antidiabetic properties, supported by both traditional wisdom and scientific evidence. Its phytochemical constituents include charantin, polypeptide-p, and momordicosides, work through multiple molecular pathways to improve glucose metabolism and insulin sensitivity. Clinical studies have shown meaningful reductions in blood glucose levels and enhanced glycemic control, while standardized extraction methods have optimized the isolation of bioactive compounds. The main hypoglycemic mechanisms, including AMPK pathway activation, enhanced GLUT4 translocation, and β-cell preservation, provides a strong mechanistic foundation for its therapeutic applications. However, standardization, dosage optimization, and safety parameters must be thoroughly studied for broader pharmaceutical implementation.

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