

Review

Review Article on in-vitro Assessment of Antidiabetic Potential of Selected Medicinal Plants with an Antioxidant Correction

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DOI: 10.62896/ijmsi.2.1.19

Conflict of interest: NIL

Article History

Received: 08/02/2026

Accepted: 22/04/2026

Published: 29/04/2026

Abstract:

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. The prevalence of diabetes is increasing globally, leading to serious long-term complications such as cardiovascular diseases, neuropathy, nephropathy, and retinopathy. Although conventional antidiabetic drugs are effective, they are frequently associated with adverse effects such as hypoglycaemia, gastrointestinal disturbances, weight gain, and organ toxicity. Therefore, medicinal plants are increasingly investigated as complementary or alternative therapeutic agents due to their affordability and multi-target mechanisms. This review focuses on the in vitro assessment of antidiabetic potential of selected medicinal plants through enzyme inhibition assays such as α -amylase and α -glucosidase inhibition, antiglycation studies, glucose uptake assays, aldose reductase inhibition, and antioxidant screening [6–8]. The role of oxidative stress in diabetes progression is discussed, along with the significance of antioxidant correction using plant-derived phytochemicals. Plants including *Momordica charantia*, *Gymnema sylvestre*, *Trigonella foenum-graecum*, *Azadirachta indica*, *Ocimum sanctum*, *Syzygium cumini*, *Curcuma longa*, *Cinnamomum verum*, *Allium sativum*, and *Aloe vera* are reviewed for their phytochemical constituents and mechanisms of action.

Keyword: *Diabetes Mellitus*, *Moringa oliefera*, *Fenugreek*, *Insulin*

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Introduction:

Diabetes mellitus (DM) is one of the most prevalent endocrine disorders worldwide, characterized by chronic hyperglycaemia due to insulin deficiency, insulin resistance, or both. The disease is associated with altered metabolism of carbohydrates, fats, and proteins, leading to progressive metabolic imbalance. Diabetes is a major public health concern because of its increasing prevalence and association with long-term complications such as cardiovascular disorders, kidney failure, blindness, and neuropathy [1-8].

Type 2 diabetes mellitus (T2DM) represents the most common form of diabetes and is strongly linked with obesity, sedentary lifestyle, aging, and genetic

predisposition [9]. Despite the availability of several pharmacological therapies, diabetes remains difficult to manage effectively due to complications, drug side effects, and poor patient compliance [10].

Medicinal plants have long been used in Ayurveda, Unani, and traditional Chinese medicine for managing diabetes. Scientific investigations have validated many of these plants for their enzyme inhibitory, antioxidant, and insulin-sensitizing properties. Thus, herbal antidiabetic research has gained importance due to the multi-target potential of phytochemicals and reduced toxicity compared to synthetic drugs.

Epidemiology and Global Burden of Diabetes

Diabetes has reached epidemic levels globally. According to global estimates, the prevalence of diabetes is increasing rapidly due to urbanization, dietary changes, reduced physical activity, and increasing obesity. The burden is particularly high in low- and middle-income countries where awareness, early diagnosis, and healthcare accessibility remain limited [11].

India is considered one of the countries with a high diabetic population, often referred to as the “diabetes capital.” Regional disparities in diabetes prevalence are influenced by lifestyle patterns, socioeconomic factors, and genetic susceptibility [12]. Uncontrolled diabetes significantly increases morbidity and mortality, mainly due to cardiovascular and renal complications.

Classification of Diabetes Mellitus

Diabetes mellitus is classified into the following major categories:

1. **Type 1 Diabetes Mellitus (T1DM):** Autoimmune destruction of pancreatic β -cells leading to absolute insulin deficiency.
2. **Type 2 Diabetes Mellitus (T2DM):** Insulin resistance combined with progressive β -cell dysfunction.
3. **Gestational Diabetes Mellitus (GDM):** Hyperglycaemia during pregnancy, increasing risk of future T2DM.
4. **Other Specific Types:** Includes genetic defects of β -cell function, endocrine disorders, pancreatic diseases, and drug-induced diabetes.
5. Classification is important for determining disease progression and selecting suitable therapeutic strategies.

Pathophysiology of Diabetes Mellitus

The pathophysiology of diabetes involves complex disturbances in glucose homeostasis. In T1DM, autoimmune destruction of β -cells leads to insufficient insulin production. In T2DM, insulin resistance occurs in liver, muscle, and adipose tissues, resulting in decreased glucose uptake and increased hepatic glucose production.

Chronic hyperglycaemia activates several biochemical pathways such as polyol pathway, protein kinase C activation, and hexosamine pathway, leading to

oxidative stress and inflammation [13]. The formation of advanced glycation end-products (AGEs) plays a major role in diabetic complications by causing vascular damage and tissue dysfunction [14].

β -cell dysfunction is aggravated by glucotoxicity and lipotoxicity. Elevated glucose and fatty acids induce mitochondrial dysfunction and apoptosis of β -cells, further reducing insulin secretion.

Role of Oxidative Stress in Diabetes

Oxidative stress is one of the most critical factors contributing to the development and progression of diabetes and its complications. Hyperglycaemia promotes ROS production through glucose auto-oxidation, AGE formation, and mitochondrial electron transport chain dysfunction [15]. ROS causes damage to lipids, proteins, and DNA, contributing to insulin resistance and endothelial dysfunction.

Pancreatic β -cells are highly sensitive to oxidative stress because they have low antioxidant enzyme expression such as catalase and glutathione peroxidase. Oxidative stress leads to β -cell apoptosis and reduced insulin secretion.

Oxidative stress is also linked to diabetic complications such as nephropathy, neuropathy, and retinopathy. Therefore, reducing oxidative stress is considered essential in diabetes management.

Antioxidant Correction in Diabetes

Antioxidant correction refers to restoring balance between oxidants and antioxidants by neutralizing ROS and enhancing endogenous antioxidant defence. Natural antioxidants in medicinal plants such as flavonoids, phenolic acids, tannins, and carotenoids can reduce oxidative stress by scavenging free radicals and preventing lipid peroxidation [16].

Antioxidant correction improves insulin sensitivity, reduces inflammation, protects β -cells, and decreases diabetic complications. Many plant extracts demonstrate dual antidiabetic and antioxidant effects, making them promising candidates for long-term therapy.

Common in vitro antioxidant assays include DPPH radical scavenging assay, ABTS assay, ferric reducing antioxidant power (FRAP), nitric oxide scavenging assay, and lipid peroxidation inhibition assay.

Conventional Antidiabetic Drugs and Their Limitations

Current antidiabetic drugs include insulin therapy and oral hypoglycemic agents such as sulfonylureas,

biguanides, thiazolidinediones, α -glucosidase inhibitors, DPP-4 inhibitors, SGLT2 inhibitors, and GLP-1 receptor agonists [17].

Although these drugs effectively control blood glucose levels, they are associated with side effects. Sulfonylureas may cause hypoglycemia and weight gain, while metformin can cause gastrointestinal disturbances. Thiazolidinediones may lead to fluid retention and weight gain.

SGLT2 inhibitors increase risk of urinary infections, and α -glucosidase inhibitors can cause diarrhea and abdominal discomfort.

Due to these limitations, plant-based therapies are being explored as safer complementary alternatives.

Importance of In Vitro Screening in Herbal Antidiabetic Research

In vitro screening provides an efficient method for preliminary evaluation of medicinal plants because it is cost-effective, reproducible, and requires smaller sample quantities. It helps identify extracts and compounds with enzyme inhibitory and antioxidant activity before animal studies or clinical trials.

In vitro studies are important for evaluating carbohydrate enzyme inhibition, glucose uptake enhancement, antiglycation potential, aldose reductase inhibition, and antioxidant properties. Such studies provide mechanistic evidence supporting the traditional use of medicinal plants in diabetes management.

In Vitro Methods for Antidiabetic Assessment

Common in vitro assays for antidiabetic evaluation include:

1. **α -Amylase inhibition assay**
2. **α -Glucosidase inhibition assay**
3. **Glucose uptake assay**
4. **Insulin secretion assay**
5. **Antiglycation assay**
6. **Aldose reductase inhibition assay**
7. **Antioxidant assays (DPPH, ABTS, FRAP)**

These assays provide evidence of multiple therapeutic mechanisms of medicinal plants

1. α -Amylase Inhibition Assay

α -Amylase is an enzyme secreted by pancreas and salivary glands that hydrolyses starch into maltose and glucose. Excessive α -amylase activity results in rapid glucose release after meals, contributing to postprandial hyperglycaemia.

In the DNS method, plant extract is incubated with porcine pancreatic α -amylase followed by addition of starch substrate. The reaction is stopped using 3,5-dinitrosalicylic acid reagent and absorbance is measured at 540 nm. Acarbose is commonly used as standard inhibitor.

Many polyphenols and flavonoids inhibit α -amylase through hydrogen bonding and hydrophobic interactions, delaying carbohydrate digestion.

2. α -Glucosidase Inhibition Assay

α -Glucosidase is located in intestinal brush border and converts disaccharides into glucose.

Inhibition delays glucose absorption and reduces postprandial blood glucose spikes.

The assay uses substrate p-nitrophenyl- α -D-glucopyranoside (pNPG), which produces p-nitrophenol measured at 405 nm. Strong α -glucosidase inhibition is reported for flavonoids, tannins, and phenolic acids.

α -Glucosidase inhibitors are considered effective for managing T2DM because they directly reduce post-meal hyperglycaemia.

3. Glucose Uptake Assay

Glucose uptake assays evaluate the ability of plant extracts to stimulate glucose utilization in cell lines such as L6 myotubes, 3T3-L1 adipocytes, and HepG2 cells.

These assays measure GLUT4 translocation and insulin-like activity. Extracts stimulating AMPK activation can increase glucose uptake independent of insulin signalling. Such studies provide strong mechanistic evidence beyond enzyme inhibition.

4. Antiglycation Assay and AGE Inhibition

AGE formation occurs due to non-enzymatic glycation of proteins and is linked with diabetic complications such as nephropathy and retinopathy. Antiglycation assays involve incubating bovine serum albumin with glucose in presence of plant extracts and measuring AGE fluorescence [18].

Many plant polyphenols reduce AGE formation by trapping carbonyl intermediates and reducing oxidative stress. Thus, antiglycation activity is an important therapeutic mechanism for complication prevention.

5. Aldose Reductase Inhibition Assay

Aldose reductase is a key enzyme in polyol pathway, converting glucose into sorbitol. Sorbitol accumulation

contributes to cataract, neuropathy, and nephropathy [19].

In vitro aldose reductase inhibition assays help identify plant compounds that prevent sorbitol accumulation. Flavonoids and phenolic acids show strong aldose reductase inhibitory activity.

Major Phytochemical Classes Responsible for Antidiabetic Activity

Plant-derived antidiabetic effects are mainly due to phytochemicals such as flavonoids, alkaloids, terpenoids, tannins, saponins, and phenolic acids.

Flavonoids improve insulin secretion and reduce oxidative stress. Phenolic acids act as antioxidants and enzyme inhibitors. Terpenoids may modulate AMPK and PPAR pathways, improving insulin sensitivity.

Synergistic interactions among multiple phytochemicals contribute to multi-target action of medicinal plants.

Selected Medicinal Plants with Antidiabetic Potential

1. *Momordica charantia* (Bitter Gourd)

Widely used in traditional medicine for diabetes management.

Bioactive Compounds:

- Charantin
- Polypeptide-p
- Vicine

Mechanism of Action:

- Enhances insulin secretion
- Improves glucose uptake
- Exhibits antioxidant activity

2. *Gymnema sylvestris*

Known as “sugar destroyer”.

Bioactive Compounds: Gymnemic acids

Actions:

- Inhibits glucose absorption in the intestine
- Regenerates pancreatic β -cells

3. *Trigonella foenum-graecum* (Fenugreek)

Active Constituents:

- 4-hydroxyisoleucine
- Trigonelline

Effects:

- Delays glucose absorption
- Improves insulin sensitivity

4. *Azadirachta indica* (Neem)

Phytochemicals:

- Flavonoids

- Alkaloids

Mechanism:

- Reduces blood glucose levels
- Scavenges free radicals

5. *Ocimum sanctum* (Tulsi) Benefits:

- Enhances insulin secretion
- Reduces oxidative stress
- Improves lipid profile

Polyherbal Formulations and Synergistic Effects

Polyherbal formulations are common in traditional medicine and may provide synergistic antidiabetic effects by targeting multiple pathways such as enzyme inhibition, antioxidant correction, and insulin sensitization. However, polyherbal products require strict standardization and toxicity assessment to ensure safety and efficacy [20].

Bioavailability and Pharmacokinetic Challenges

Many phytochemicals exhibit strong in vitro activity but poor in vivo efficacy due to low solubility, limited absorption, and rapid metabolism. For example, curcumin has poor bioavailability despite strong antioxidant and anti-inflammatory effects.

Nanotechnology-based drug delivery systems such as nano emulsions, phytosomes, and polymeric nanoparticles have been explored to improve bioavailability and stability.

Standardization and Quality Control of Herbal Extracts

Standardization ensures reproducibility and quality in herbal medicines. Variation in plant species, harvesting conditions, and extraction methods affects phytochemical composition [21]. Techniques such as HPLC, LC-MS, and GC-MS are widely used for phytochemical profiling and marker compound identification.

WHO guidelines emphasize proper quality control and Good Agricultural and Collection Practices (GACP) for medicinal plants [22].

Safety and Herb–Drug Interactions

Although herbal medicines are considered safer, toxicity may occur at high doses or long-term use [20]. Herb–drug interactions are significant concerns because herbal supplements may enhance hypoglycemic effects when used with insulin or sulfonylureas. Therefore, toxicity profiling,

cytotoxicity assays, and clinical monitoring are required [23].

Clinical Translation and Regulatory Aspects

Clinical translation requires well-designed animal studies and randomized controlled trials. Regulatory approval requires evidence of safety, efficacy, quality control, and Good Manufacturing Practices (GMP) compliance. WHO supports integration of herbal medicines but emphasizes scientific validation.

Future Perspectives

Future research should focus on isolation of bioactive compounds, molecular target identification, in silico docking studies, and advanced omics technologies. Nano formulations and improved delivery systems can overcome bioavailability issues. More clinical trials are needed to validate safety and therapeutic effectiveness of standardized herbal extracts.

Conclusion

Medicinal plants represent an important source of antidiabetic agents due to their multi-target mechanisms and antioxidant correction properties. In vitro studies demonstrate that many plants inhibit carbohydrate metabolizing enzymes, reduce oxidative stress, prevent AGE formation, and improve glucose uptake. However, challenges such as lack of standardization, poor bioavailability, toxicity concerns, and limited clinical validation must be addressed for clinical translation. A scientifically validated integration of medicinal plants into diabetes management may provide safer and cost-effective long-term therapeutic strategies.

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