

Study of Antidiabetic Potential of Polyherbal Formulation

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Abstract: *Diabetes mellitus represents a significant global health burden with increasing prevalence and associated complications. Polyherbal formulations, combining multiple medicinal plants, have emerged as promising therapeutic alternatives for diabetes management. These formulations exploit the synergistic effects of diverse phytochemical constituents, offering enhanced therapeutic efficacy while potentially reducing side effects. This review comprehensively examines the antidiabetic potential of polyherbal formulations through analysis of their phytochemical composition, mechanisms of action, in vitro and in vivo experimental evidence, clinical efficacy, standardization approaches, and safety profiles. Multiple studies demonstrate that polyherbal formulations containing herbs such as *Gymnema sylvestre*, *Momordica charantia*, *Trigonella foenum-graecum*, *Ocimum sanctum*, and *Curcuma longa* exhibit significant antidiabetic activity through inhibition of carbohydrate-digesting enzymes, enhancement of insulin secretion, improvement of insulin sensitivity, and modulation of glucose metabolism. Clinical trials indicate that these formulations produce blood glucose reduction comparable to standard antidiabetic medications while maintaining favorable safety profiles. However, standardization and quality control challenges remain critical barriers to their integration into mainstream therapeutics. This review provides evidence-based insights into the antidiabetic potential of polyherbal formulations and identifies research priorities for their development and validation.*

Keywords: polyherbal formulation, antidiabetic, herbal medicine, *Gymnema sylvestre*, *Momordica charantia*, phytochemicals, synergism, diabetes mellitus

I. INTRODUCTION

Diabetes mellitus represents one of the most significant public health challenges globally, with the World Health Organization reporting that approximately 1.5 million deaths occurred from diabetes in 2019, accounting for 4.6% of mortality from renal disease and 20% of cardiovascular deaths worldwide ^[1]. Type 2 diabetes mellitus (T2DM) accounts for approximately 90% of all diabetes cases and is characterized by disrupted glucose and insulin homeostasis leading to serious complications including neuropathy, cardiovascular diseases, nephropathy, and retinopathy ^[2]. The increasing prevalence of diabetes necessitates the development of safe, effective, and accessible treatment strategies. While conventional synthetic antidiabetic agents such as sulfonylureas, metformin, and insulin analogs offer rapid glycemic control, their long-term use is often associated with significant side effects, high costs, and reduced patient compliance^[3].

Traditional medicine systems, including Ayurveda, Traditional Chinese Medicine, and Unani medicine, have utilized medicinal plants for diabetes management for millennia ^[4] ^[5]. Polyherbal formulations combinations of two or more medicinal plant extracts have been recognized in ancient Ayurvedic texts such as the Sarangdhara Samita for their enhanced therapeutic efficacy ^[6]. Contemporary scientific research has begun validating the antidiabetic potential of these traditional formulations, revealing that polyherbal combinations exploit synergistic effects of diverse phytochemical constituents to achieve therapeutic outcomes superior to individual herb components ^[7]. According to the World Health Organization, approximately 80% of populations in developing countries rely on traditional and polyherbal medicines for primary healthcare ^[8].

The rationale for polyherbal formulations in diabetes management extends beyond simple combination of individual herbs. Multifactorial metabolic diseases like diabetes require comprehensive therapeutic approaches addressing



multiple pathological mechanisms simultaneously. Polyherbal formulations enhance therapeutic action while reducing the concentrations of single herbs, thereby decreasing adverse events and improving tolerability^[9]. Furthermore, crude plant extracts often demonstrate greater potency than isolated constituents, suggesting that synergistic interactions between multiple phytochemicals contribute to enhanced pharmacological activity^[10].

This comprehensive review examines the antidiabetic potential of polyherbal formulations through systematic analysis of their composition, phytochemical profiles, mechanism of action, and experimental evidence from in vitro and in vivo studies, clinical efficacy data, standardization approaches, and safety profiles. The review aims to provide evidence-based insights into the therapeutic promise of polyherbal formulations for diabetes management while identifying critical research priorities for their development, validation, and integration into mainstream therapeutics^[11].

Types of Diabetes

DIABETES MELLITUS

Diabetes mellitus is a chronic metabolic disorder characterised by a high blood glucose concentration - hyperglycaemia (fasting plasma glucose >7.0 mmol/L, or plasma glucose >11.1 mmol/L, 2 h after a meal) - caused by insulin deficiency, often combined with insulin resistance. There are two main types of diabetes mellitus:

1. Type 1 diabetes (previously known as insulin-dependent diabetes mellitus - IDDM or juvenile-onset diabetes), in which there is an absolute deficiency of insulin.
2. Type 2 diabetes (previously known as non insulin-dependent diabetes mellitus - NIDDM - or maturity-onset diabetes), in which there is a relative deficiency of insulin associated with reduced sensitivity to its action (insulin resistance).

Hyperglycaemia occurs because of uncontrolled hepatic glucose output and reduced uptake of glucose by skeletal muscle with reduced glycogen synthesis. Insulin deficiency causes muscle wasting through increased breakdown and reduced synthesis of proteins. Diabetic ketoacidosis is an acute emergency that is predominantly seen in patients with type 1 diabetes. It develops in the absence of insulin because of accelerated breakdown of fat to acetyl-CoA, which, in the absence of aerobic carbohydrate metabolism, is converted to acetoacetate and B-hydroxybutyrate (which cause acidosis) and acetone (a ketone).

Various complications develop as a consequence of the metabolic derangements in diabetes, often over several years. Many of these are the result of disease of blood vessels, either large (macrovascular disease) or small (microangiopathy). Dysfunction of vascular endothelium (see Ch. 23) is an early and critical event in the development of vascular complications. Oxygen-derived free radicals, protein kinase C and non-enzymic products of glucose and albumin called advanced glycation end products (AGE) have been implicated. Macrovascular disease consists of accelerated atheroma (Ch. 24) and its thrombotic complications (Ch. 25), which are commoner and more severe in diabetic patients. Microangiopathy is a distinctive feature of diabetes mellitus and particularly affects the retina, kidney and peripheral nerves. Diabetes mellitus is the commonest cause of chronic renal failure, a huge and rapidly increasing problem, and a major burden to society as well as to individual patients. Co-existent hypertension promotes progressive renal damage, and treatment of hypertension slows the progression of diabetic nephropathy and reduces the risk of myocardial infarction. Angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists (Ch. 23) are more effective in preventing diabetic nephropathy than other antihypertensive drugs, perhaps because they prevent fibroproliferative actions of angiotensin II and aldosterone.

Diabetic neuropathy is associated with accumulation of osmotically active metabolites of glucose, produced by the action of aldose reductase, but aldose reductase inhibitors have been disappointing as therapeutic drugs (see Farmer et al., 2012, for a review).

Type 1 diabetes can occur at any age, but patients are usually young (children or adolescents) and not obese when they first develop symptoms. There is an inherited predisposition, with a 10 to 15-fold increased incidence in first-degree relatives of an index case, and strong associations with particular histocompatibility antigens (HLA types). Identical twins are less than fully concordant, so environmental factors such as viral infection (e.g. with Coxsackie virus or echovirus) are believed to be necessary for genetically predisposed individuals to express the disease. Viral infection may damage pancreatic β cells and expose antigens that initiate a self-perpetuating autoimmune process. The patient



becomes overtly diabetic only when more than 90% of the β cells have been destroyed. This natural history provides a tantalising prospect of intervening in the pre-diabetic stage, and a variety of strategies have been mooted, including immunosuppression, early insulin therapy, antioxidants, nicotinamide and many others; so have disappointed, but this remains a very active field. Type 2 diabetes is accompanied both by insulin resistance (which precedes overt disease) and by impaired insulin secretion, each of which are important in its pathogenesis. Such patients are often obese and usually present in adult life, the incidence rising progressively with age as β -cell function declines. Treatment is initially dietary, although oral hypoglycaemic drugs usually become necessary, and most patients ultimately benefit from exogenous insulin. Prospective studies have demonstrated a relentless deterioration in diabetic control with increasing age and duration of disease. Insulin secretion (basal, and in response to a meal) in a type 1 and a type 2 diabetic patient is contrasted schematically in Fig. 32.2.

There are many other less common forms of diabetes mellitus in addition to the two main ones described earlier (for example, syndromes associated with autoantibodies directed against insulin receptors which cause severe insulin resistance, functional α -cell tumours, 'glucagonomas', and many other rarities), and hyperglycaemia can also be a clinically important adverse effect of several drugs, including glucocorticoids (Ch. 34), high doses of thiazide diuretics (Ch. 30) and several of the protease inhibitors used to treat HIV infection (Ch. 53)⁽¹²⁾.

Etiology of Diabetes Mellitus

The word etiology springs from Greek word —aetiological. Hence, etiology is outlined because the science of finding causes and origins during which a unwellness is arise, It includes –

1. it's presently believed that the juvenile-onset (insulin-independent) type has associated degree autoimmune etiology.
2. Viruses may additionally play a task within the etiology of polygenic disease like coxsackievirus B.
3. epidemic parotitis and German measles viruses all are shown to produce morphologic changes within the islet-cell structure.
4. The genetic role within the etiology of polygenic disease is controversial. probably a genetic attribute makes associated degree = individual's exocrine gland additionally liable to one. Amongst the on top of viruses.

Causes of polygenic disease Mellitus Disturbances or Abnormality in gluco-receptor of β cell in order that they reply to higher aldohexose

Concentration or relative β cell deficiency. In either manner, hypoglycemic agent secretion is Impaired; might progress to β cell failure.

The idea of principal in small vascular UN wellness resulting in neural drive, and therefore the direct effects of hyperglycemia on

Vegetative cell metabolism.

1. Reduced sensitivity of peripheral tissues to insulin: reduction in range of hypoglycaemic agent receptors, 'down regulation' of hypoglycaemic agent receptors. several supersensitized and Hyperinsulinaemic, however traditional glycaemic; and have associated dyslipidaemic, hyperuricaemic, abdominal obesity. so there's relative hypoglycaemic agent resistance, particularly at the extent of liver, muscle and fat. Hyperinsulinaemic has been involved in inflicting angiopathy.
2. way over hyperglycemia internal secretion (glucagon) etc. obesity; causes relative hypoglycaemic agent deficiency – the β cells lag behind. 2 theories have in contestible abnormalities in nitric oxide metabolism, leading to altered perineural blood flow and nerve injury.
3. different rare types of DM area unit those thanks to specific genetic defects (type 3) like —maturity onset diabetes of young (MODY) different endocrine disorders, pancreatectomy and physiological state DM (GDM).
4. thanks to imbalance of specific receptor will cause polygenic disease mellitus. Some specific receptors area unit Glucagon-like peptide-1 (GLP-1) receptor, peroxisomes proliferator activated (γ) receptor (PPAR γ), beta3 (β 3) adrenergic receptor some enzymes like α Glycosidase, dipeptidyl protease IV enzyme etc.
5. Current analysis on diabetic pathology is targeted on oxidative stress, advanced glycation-End merchandise, protein kinase C and therefore the polyol pathway.



Symptoms

Diabetes symptoms depend on how high your blood sugar is. Some people, especially if they have prediabetes, gestational diabetes or type 2 diabetes, may not have symptoms. In type 1 diabetes, symptoms tend to come on quickly and be more severe.

Some of the symptoms of type 1 diabetes and type 2 diabetes are:

- Feeling more thirsty than usual.
- Urinating often.
- Losing weight without trying.
- Presence of ketones in the urine. Ketones are a byproduct of the breakdown of muscle and fat that happens when there's not enough available insulin.
- Feeling tired and weak.
- Feeling irritable or having other mood changes.
- Having blurry vision.
- Having slow-healing sores.
- Getting a lot of infections, such as gum, skin and vaginal infections.
- Type 1 diabetes can start at any age. But it often starts during childhood or teen years. Type 2 diabetes, the more common type, can develop at any age. Type 2 diabetes is more common in people older than 40. But type 2 diabetes in children is increasing⁽¹³⁾.

Pathophysiology of Diabetes Mellitus

Diabetes Mellitus Pathophysiology

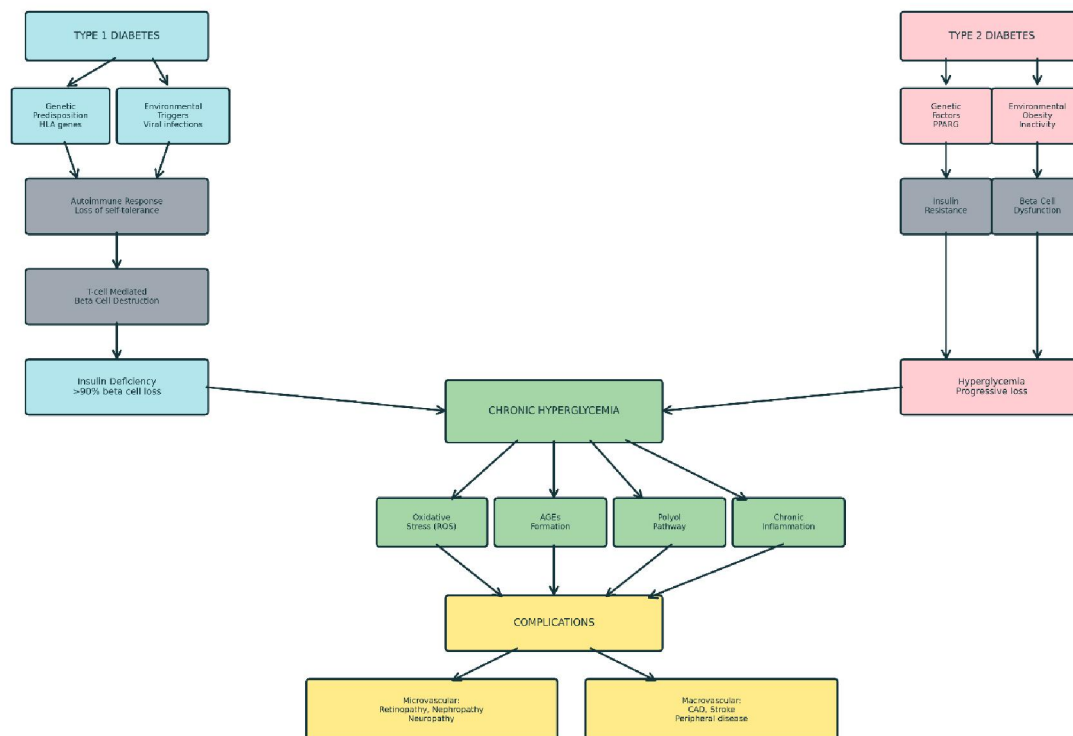


Fig1. Pathophysiology of Diabetes Mellitus

Diabetes mellitus is a complex metabolic disorder characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both⁽¹⁴⁾. The disease represents a heterogeneous group of disorders with distinct etiologies and pathophysiological mechanisms, yet sharing the common hallmark of disrupted glucose homeostasis and vascular complications. While the global prevalence of diabetes continues to rise significantly—affecting over 400 million people worldwide—understanding the underlying pathophysiological mechanisms remains essential for developing targeted therapeutic strategies and improving patient outcomes⁽¹⁵⁾. This comprehensive review examines the distinct pathogenic pathways in Type 1 and Type 2 diabetes mellitus, along with the shared metabolic derangements that ultimately lead to microvascular and macrovascular complications.

Modern Treatment of Diabetes Mellitus

Diabetes mellitus represents one of the most significant global health challenges, affecting over 400 million people worldwide with rapidly evolving treatment paradigms that have transformed management strategies over the past decade. The 2025 Standards of Care released by the American Diabetes Association and numerous international societies reflect a fundamental shift toward personalized, comprehensive management that extends far beyond glycemic control alone, incorporating cardiovascular protection, renal preservation, and individualized therapeutic approaches based on patient comorbidities and clinical context⁽¹⁶⁾.

Type 1 Diabetes Mellitus: From Insulin to Disease-Modifying Therapy

Insulin Therapy: Technological Evolution

Insulin replacement therapy remains the cornerstone of Type 1 diabetes management, with profound technological advances transforming treatment delivery. Modern insulin regimens employ basal-bolus therapy using long-acting insulin analogues (detemir, glargine, degludec) combined with rapid-acting insulins (aspart, lispro) that more closely mimic endogenous insulin secretion patterns⁽¹⁷⁾. Degludec (Tresiba), with its ultra-long duration exceeding 36 hours, provides superior glycemic stability with reduced hypoglycemic episodes compared to earlier formulations. These genetically engineered insulin analogues have been fundamental in enabling intensive diabetes management with significantly improved outcomes⁽¹⁸⁾.

Continuous Glucose Monitoring and Automated Insulin Delivery

The integration of continuous glucose monitoring (CGM) with insulin pump therapy has revolutionized Type 1 diabetes management. Real-time CGM systems provide constant glucose feedback, enabling users to monitor glucose trends and anticipate hypoglycemic events before they occur. Sensor-augmented pump (SAP) therapy, combining CGM with insulin pumps, demonstrates time-in-range (TIR) improvements of 13-15 percentage points compared to pump therapy alone. In clinical trials, adults using fully closed-loop systems (artificial pancreas) achieved mean TIR of 50% compared to 36.2% with pump plus CGM, representing clinically meaningful improvements in glycemic stability. Hybrid closed-loop (HCL) systems represent the most advanced commercially available technology, automatically adjusting basal insulin delivery based on CGM readings while requiring user-initiated prandial (meal-time) boluses. The Medtronic 780G system and Insulet Omnipod 5 have demonstrated HbA1c reductions of 1.4% compared to multiple daily injections with intermittent scanning CGM. These systems provide dual benefits of improved glycemic control and enhanced quality of life, with reduced fear of hypoglycemia, particularly in patients with impaired hypoglycemia awareness⁽¹⁹⁾.

Disease-Modifying Therapy:

In a paradigm-shifting development, teplizumab (Tziel) became the first FDA-approved disease-modifying therapy for Type 1 diabetes in November 2022. This humanized anti-CD3 monoclonal antibody modulates the autoimmune response responsible for beta cell destruction by inducing regulatory T cells and promoting exhausted-like CD8 T cells. In the pivotal trial, teplizumab delayed stage 3 Type 1 diabetes onset by 2.7 years in stage 2 patients and reduced insulin requirements by 0.10 units/kg/day at two years. The mechanism involves preserving endogenous



insulin production, as reflected by maintained C-peptide levels, offering patients the prospect of reduced insulin dependence and improved metabolic outcomes. Adjunctive Therapies in Type 1 Diabetes SGLT2 inhibitors and GLP-1 receptor agonists, historically used in Type 2 diabetes, are increasingly employed as adjunctive therapy in Type 1 diabetes to reduce daily insulin requirements, improve glycemic control, and provide cardiovascular/renal protection⁽²⁰⁾. Trials with dapagliflozin and sotagliflozin in Type 1 diabetes demonstrated HbA1c reductions of 0.4-0.5% alongside 13.6% insulin dose reductions and clinically meaningful weight loss. GLP-1 receptor agonists administered alongside insulin reduce postprandial glucose excursions, decrease hypoglycemic events, and facilitate weight loss in Type 1 patients⁽²¹⁾.

Taxonomy of Herbs

Diabetes mellitus, a chronic metabolic disorder characterized by hyperglycemia, has been managed traditionally using various medicinal plants for centuries. These herbs offer multifaceted therapeutic approaches through diverse mechanisms, including enhancement of insulin secretion, improvement of insulin sensitivity, inhibition of carbohydrate-digesting enzymes, and reduction of oxidative stress. This comprehensive review examines the botanical taxonomy and visual characteristics of major antidiabetic herbs, providing essential information for researchers, practitioners, and students of pharmaceutical sciences⁽²²⁾.

Major Families of Antidiabetic Plants

The medicinal plants used for diabetes management belong to diverse botanical families, each contributing unique phytochemical profiles and therapeutic mechanisms. The most extensively studied antidiabetic herbs are distributed across families including Cucurbitaceae, Apocynaceae, Fabaceae, Lamiaceae, Myrtaceae, Menispermaceae, and Solanaceae. Understanding the taxonomic classification of these plants is crucial for proper identification, cultivation, and standardization of herbal preparations. Cucurbitaceae Family *Momordica charantia* (bitter gourd or bitter melon) represents one of the most widely researched antidiabetic plants from the Cucurbitaceae family⁽²³⁾. This herbaceous, tendril-bearing vine grows up to 5 meters in length and is native to tropical Africa and tropical Asia. The plant bears simple, alternate leaves with 3-7 deeply separated lobes and produces distinctive warty, oblong fruits that are hollow in cross-section⁽²⁴⁾. The fruit contains several bioactive compounds including charantin, polypeptide-p, and vaccine, which demonstrate glucose-lowering effects through multiple mechanisms such as inhibiting protein tyrosine phosphatase 1B (PTP1B), activating AMPK, and enhancing GLUT4 expression⁽²⁵⁾.

Bitter gourd



Fig2: Bitter gourd (*Momordica charantia*) mature fruit, splitting open with seeds

The taxonomic classification of *Momordica charantia* places it in Kingdom Plantae, Class Magnoliopsida, Order Cucurbitales, and Family Cucurbitaceae. The plant exhibits morphological variations with several subspecies including



M. charantia var. *charantia*, *M. charantia* var. *medicate*, and *M. charantia* var. *abbreviate* ⁽²⁶⁾. The fruits are most often consumed green when the flesh is crunchy and watery, though intensely bitter. Apocynaceae Family *Gymnema sylvestre*, commonly known as gram (meaning "sugar destroyer" in Hindi), is a perennial woody climber belonging to the family Apocynaceae, formerly classified under Asclepiadaceae ⁽²⁷⁾. This slow-growing vine is native to regions spanning Asia, Africa, and Australia, and is widely distributed in India, Malaysia, Sri Lanka, Indonesia, Japan, Vietnam, and tropical Africa. The plant features elongated-oval leaves with soft hairs on the upper surface and produces small, yellow, umbelliferous flowers throughout the year ⁽²⁸⁾. The taxonomic position of *Gymnema sylvestre* (Retz.) R.Br. ex Sm. includes Kingdom Plantae, Class Magnoliopsida, Order Gentianales, and Family Apocynaceae. The genus *Gymnema* comprises 49 approved species, with *G. sylvestre* being the most medicinally significant. The plant's leaves contain gymnemic acids, a complex mixture of triterpene saponins that represent the major bioactive constituents ⁽²⁹⁾. These compounds interact with taste receptors on the tongue to temporarily suppress sweetness and demonstrate remarkable antidiabetic activity by stimulating insulin secretion and promoting pancreatic beta cell regeneration. Fabaceae Family the Fabaceae (Leguminosae) family contributes several important antidiabetic herbs, most notably *Trigonella foenum-graecum* (fenugreek) and *Pterocarpus marsupium* (Indian Kino tree) ⁽³⁰⁾.

Fenugreek Seed



Fig3: Fenugreek (*Trigonella foenum-graecum*)

Trigonella foenum-graecum is an annual plant with leaves consisting of three small obovate to oblong leaflets. It is cultivated worldwide as a semi-arid crop and is native to southern Europe and western Asia. The plant grows to a height of 0.3-0.8 meters with cream-colored or yellowish-white flowers, sometimes tinged with lilac ⁽³¹⁾. The taxonomic classification places it in Kingdom Plantae, Class Magnoliopsida, Order Fables, and Family Fabaceae. The seeds contain galactomannan (40-45%), which is responsible for the plant's ant hyperglycemic activity through mechanisms involving increased insulin secretion, enhanced insulin sensitivity, and inhibition of intestinal carbohydrate digestion and absorption ⁽³²⁾. *Pterocarpus marsupium*, known as Malabar Kino or Indian Kino, is a medium-to-large deciduous tree that can grow up to 31 meters tall. Native to India (particularly the Western Ghats), Nepal, and Sri Lanka, this tree belongs to the subfamily Faboideae of the Fabaceae family ⁽³³⁾. The bark and heartwood contain pterostilbene and (-)-epicatechin, which exhibit potent antidiabetic effects by regulating glucose homeostasis, reducing gluconeogenesis, and diminishing oxidative stress. Lamiaceae Family *Ocimum sanctum* (also known as *Ocimum tenuiflorum*), commonly called tulsi or holy basil, is an aromatic perennial plant in the family Lamiaceae ⁽³⁴⁾. This erect, highly branched



subshrub typically grows to a height of 30-75 centimeters and features hairy stems with elliptic, oblong leaves that are slightly serrated and opposite. The flowers are small, purple, and arranged in elongated racemes with closely packed whorls⁽³⁵⁾.

Holy basil



Fig4: Holy basil (*Ocimum tenuiflorum*).

The taxonomic classification of *Ocimum sanctum* includes Kingdom Plantae, Class Magnoliopsida, Order Lamiales, and Family Lamiaceae. The plant is native to tropical and subtropical regions of Asia, Australia, and the western Pacific, with wide cultivation throughout Southeast Asia⁽³⁶⁾. Three main morphotypes are cultivated in India: Ram tulsi (bright green leaves), Krishna or Shyam tulsi (purplish green leaves), and vana tulsi. The plant contains phytochemical constituents including oleanolic acid, ursolic acid, rosmarinic acid, eugenol, carvacrol, and linalool⁽³⁷⁾. Studies have demonstrated that aqueous extract of tulsi leaves produces significant reduction in blood glucose levels, uronic acid, total cholesterol, and triglycerides in both normal and alloxan-induced diabetic rats. Myrtaceae Family *Eugenia jambolana* (synonym *Syzygium cumini*), commonly known as jamun, jambolan, or black plum, is an evergreen tropical tree in the flowering plant family Myrtaceae⁽³⁸⁾. This large tree can reach heights of up to 30 meters and live for more than 100 years. It is native to the Indian subcontinent and Southeast Asia and is favored for its fruit, timber, and ornamental value⁽³⁹⁾.

Eugenia jambolana



Fig6: *Eugenia jambolana*



The taxonomic classification places *Syzygium cumini* in Kingdom Plantae, Class Magnoliopsida, Order Myrtales, and Family Myrtaceae. The tree features elliptic to obovate leaves up to 12 centimeters long, white flowers in few-flowered panicles, and produces purplish-red to black ovoid berries measuring 10-15 millimeters long⁽⁴⁰⁾. In traditional Indian medicine, decoction of kernels has been used as a household remedy for diabetes. The seeds and fruits contain jamboline and ellagic acid, which help lower blood sugar levels and exhibit antioxidant properties. The plant extract enhances insulin secretion from pancreatic islet cells and inhibits insulinase activity in liver and kidney⁽⁴¹⁾. Menispermaceae Family *Tinospora cordifolia*, commonly known as guduchi, giloy, or heart-leaved moonseed, is a large, glabrous, perennial, deciduous climbing shrub belonging to the family Menispermaceae. This herbaceous vine is native to tropical regions of the Indian subcontinent and Southeast Asia, distributed throughout India and China, ascending to altitudes of 300 meters⁽⁴²⁾.

Guduchi



Fig7: *Tinospora cordifolia*, guduchi

The taxonomic classification of *Tinospora cordifolia* (Willd.) Hook. f. and Thoms. includes Kingdom Plantae, Class Magnoliopsida, Order Ranunculales, and Family Menispermaceae. The plant features membranous, cordate (heart-shaped) leaves that are broadly ovate, 10-20 centimeters long, with seven nerves and deeply cordate bases⁽⁴³⁾. The stems are succulent with long filiform fleshy aerial roots, and the bark is creamy white to gray, deeply cleft spirally. Flowers are small, yellow or greenish-yellow, appearing in axillary and terminal racemes, with male flowers clustered and female flowers usually solitary⁽⁴⁴⁾. The Sanskrit name "guduchi" means "one which protects the entire body," while "amrita" refers to its ability to impart youthfulness, vitality, and longevity. Oral administration of root extract has been shown to produce significant reductions in blood glucose, urine glucose, and serum lipids in alloxan-induced diabetic rats⁽⁴⁵⁾.

Phytochemical Constituents

The major phytochemical constituents present in the herbs reviewed for antidiabetic activity include a wide array of bioactive compounds such as flavonoids, alkaloids, phenolics, terpenoids, glycosides, saponins, tannins, and specific secondary metabolites. Common Phytochemical Classes: Flavonoids: Quercetin, rutin, kaempferol, naringenin, apigenin, myricetin, and other flavonoids are present in many antidiabetic herbs including *Trigonella foenum-graecum* (fenugreek), *Momordica charantia* (bitter melon), and *Ocimum sanctum* (tulsi). They contribute to antioxidant activity,



improve glucose uptake, and inhibit sugar-digesting enzymes⁽⁴⁶⁾. Alkaloids: Alkaloids such as berberine (from *Berberis aristata*), herpestine, brahmine (from *Bacopa monnieri*), and vindoline, vindolicine (from *Catharanthus roseus*) are potent modulators of glucose metabolism and insulin sensitivity⁽⁴⁷⁾. Saponins: Triterpenoid saponins like gymnemic acids (in *Gymnema sylvestre*) and bacosides (in *Bacopa monnieri*) stimulate insulin secretion, regeneration of pancreatic β -cells, and mimic insulin action⁽⁴⁸⁾. Phenolic Compounds: These include gallic acid, ellagic acid, chlorogenic acid, and other polyphenols, found in herbs like *Syzygium cumini* (jamun) and *Cinnamomum zeylanicum* (cinnamon). They contribute antioxidative and ant hyperglycemic effects. Terpenoids: Compounds like oleanolic acid and ursolic acid (in tulsi/holy basil) show insulin-mimetic and anti-inflammatory properties⁽⁴⁹⁾. Glycosides: Examples include charantin in *Momordica charantia* and cardiac glycosides in other herbs, helping lower and stabilize blood sugar. Tannins: Present in many antidiabetic plants, tannins exhibit antioxidant properties and help in glucose metabolism⁽⁵⁰⁾.

Plant (Common Name)	Main Phytochemical constituents
<i>Momordica charantia</i> (Bitter Melon)	Charantin, polypeptide-p (plant insulin), vaccine, flavonoids, saponins, phenolics
<i>Gymnema sylvestre</i> (Gurmar)	Gymnemic acids (saponins), gymnemagenin, stigmasterol, quercitol, flavones
<i>Trigonella foenum-Graecum</i> (Fenugreek)	Galactomannan, trigonelline, diosgenin (steroidal saponin), flavonoids, alkaloids, coumarin
<i>Ocimum sanctum</i> (Tulsi)	Eugenol, ursolic acid, rosmarinic acid, oleanolic acid, carvacrol, linalool (volatile oils)
<i>Syzygium cumini</i> (Jamun)	Jamboline, jambosine, ellagic acid, anthocyanins, flavonoids, gallic acid
<i>Tinospora cordifolia</i> (Guduchi)	Tinosporine, tinosporide, berberine, cordifolioside, alkaloids, glycosides, steroids
<i>Cinnamomum zeylanicum</i> (Cinnamon)	Cinnamaldehyde, eugenol, methyl eugenol, coumarin, cinnamic acid, polyphenols
<i>Allium sativum</i> (Garlic)	Allicin, S-allylcysteine, ajoene, diallyl sulfide, flavonoids, saponins
<i>Pterocarpus marsupium</i> (Indian Kino)	Pterostilbene, marsupin, pterosupin, epicatechin, tannins, phenolics
<i>Withania somnifera</i> (Ashwagandha)	Withanolides (steroidal lactones), alkaloids, sitoinosides, flavonoids

Herbal Treatment of Diabetes Mellitus

Herbal medicines are increasingly recognized as complementary options for the management of diabetes mellitus, backed by a growing body of clinical and mechanistic evidence. While these treatments do not replace conventional antidiabetic therapies, they may provide adjunctive glycemic control through a range of bioactive plant compounds and mechanisms. Careful integration under clinical guidance can maximize efficacy and minimize risk, especially regarding herb-drug interactions and product quality⁽⁵¹⁾.

Traditional and Contemporary Use of Herbal Medicines in Diabetes

Prevalence and Examples

The use of herbal remedies in diabetes care is widespread, with up to 56% of diabetic patients in some regions reporting regular use of plant-based treatments. Commonly used herbs include cinnamon, coriander, moringa, fenugreek, bitter melon, jamun, gymnema, aloe vera, and neem, many of which have cultural traditions as well as scientific backing⁽⁵²⁾. These remedies are often employed as adjuncts to standard antidiabetic medications, and their use spans both Type 1 and Type 2 diabetes management. Leading Antidiabetic Plants and Their Evidence Recent systematic reviews and



clinical studies highlight a variety of herbal medicines with substantiated antidiabetic effects: *Momordica charantia* (Bitter melon): Improves insulin sensitivity, enhances peripheral glucose utilization, and inhibits intestinal glucose absorption. Clinical and animal studies report significant hypoglycemic action⁽⁵³⁾.

Gymnema sylvestre (Gurmar): Increases insulin secretion, promotes beta-cell regeneration, and reduces sweet taste perception, leading to decreased sugar intake. *Trigonella foenum-graecum* (Fenugreek): Delays gastric emptying, lowers carbohydrate absorption, and increases insulin secretion. Human trials have documented reductions in fasting and postprandial blood glucose⁽⁵⁴⁾. *Cinnamomum verum* (Cinnamon): Improves insulin sensitivity and cellular glucose uptake, with multiple clinical trials demonstrating benefit. *Aloe vera*: Exhibits insulin-sensitizing effects, reduces gluconeogenesis, and has antioxidant properties. Controlled studies report reductions in fasting blood glucose and HbA1c⁽⁵⁵⁾. *Moringa oleifera*: Contains bioactive compounds that may stimulate insulin secretion and exhibit antioxidant effects, with human pilot studies confirming positive results. *Syzygium cumini* (Jamun): Promotes insulin secretion and inhibits glucose absorption, effective in both animal models and human investigations⁽⁵⁶⁾. The following chart summarizes these plants and their mechanistic, clinical, and safety profiles:

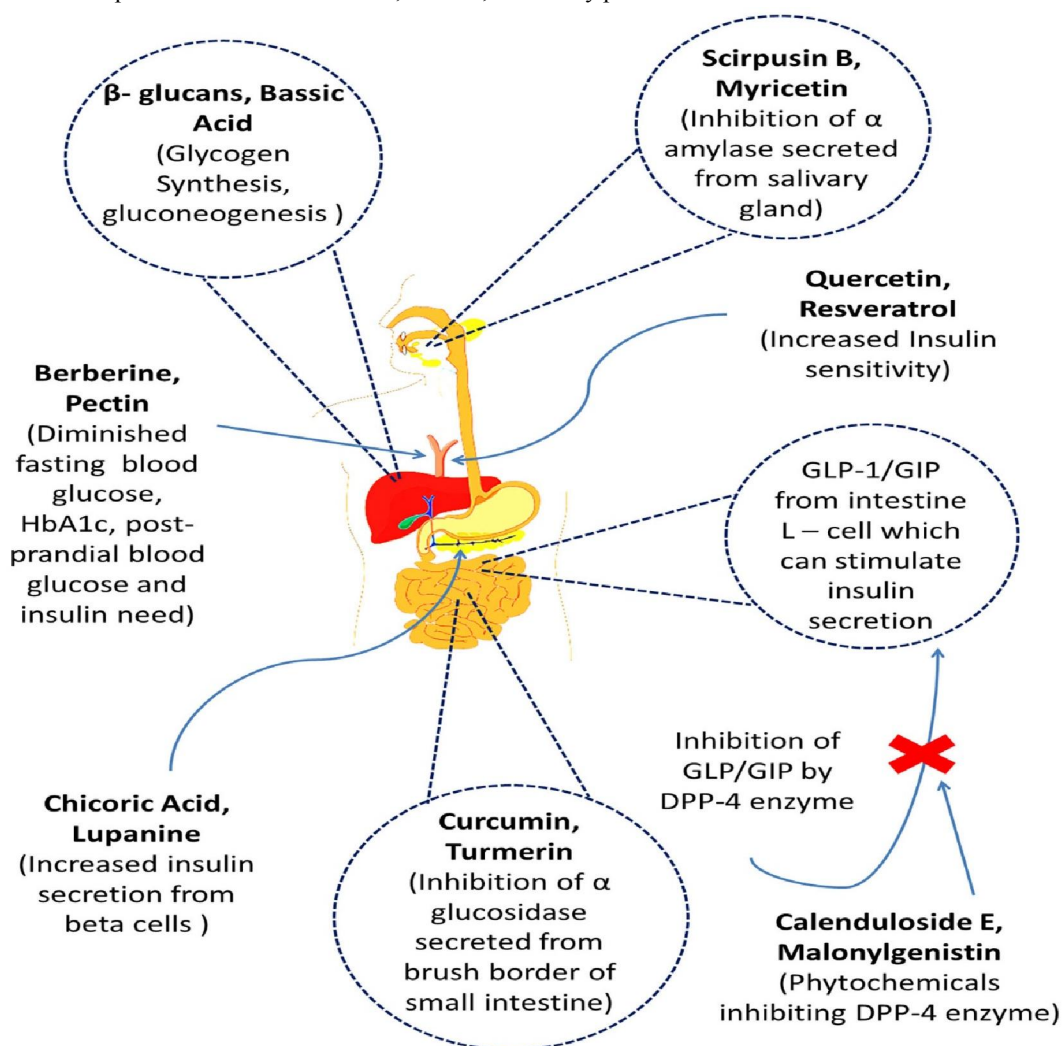


Fig7: The mechanisms of action of several prospective bioactive secondary metabolites (phytochemicals) obtained from different medicinal plants.



Antidiabetic Medicinal Plants

Plant Name	Mechanism	Efficacy	Bioactive	Side Effects
Momordica charantia (Bitter Melon)	Improves insulin sensitivity, enhances glucose uptake, inhibits intestinal glucose absorption	Animal and human studies confirm hypoglycemic effects	Charantin, polypeptide-p, vicine	Possible hypoglycemia if combined with drugs, adulteration risk
Gymnema sylvestre (Gurmar)	Suppresses sweet taste, increases insulin secretion, promotes beta-cell regeneration	Animal and human studies show reduced blood glucose and HbA1c	Gymnemic acids	May interact with antidiabetic meds
Trigonella foenum-graecum (Fenugreek)	Delays gastric emptying, reduces carbohydrate absorption, increases insulin secretion	Human trials show lowered FBG and PPG; animal studies support effect	Furostanolic saponins, 4-hydroxyisoleucine	Allergenicity, possible teratogenic and abortive effects
Cinnamomum verum (Cinnamon)	Improves insulin sensitivity, increases glucose uptake	Multiple human studies show benefit	Cinnamaldehyde and other cinnamic-type compounds	Generally well-tolerated
Aloe vera	Improves insulin sensitivity, inhibits gluconeogenesis, antioxidant properties	Randomized controlled trials show reduced FBG and HbA1c	Aloin, emodin, polysaccharides	Potential GI disturbances, caution with hypoglycemic drugs
Moringa oleifera (Moringa)	Stimulates insulin secretion, antioxidant effects	Pilot human studies show lower FBG and glycemic response	Terpenoids, flavonoids, phenolics	Generally well-tolerated; more data needed
Syzygium cumini (Jamun)	Promotes insulin secretion, inhibits glucose absorption	Human and animal evidence of hypoglycemic effects	Jamboline, ellagic acid	Generally well-tolerated

Table: Comparison of Major Antidiabetic Medicinal Plants: Mechanism, Efficacy, and Safety

Mechanisms of Herbal Antidiabetic Action

Medicinal plants utilize a variety of mechanisms to exert their glucose-lowering effects:

Beta-cell Stimulation:

Compounds like gymnemic acids and polypeptide-p may enhance insulin secretion by stimulating pancreatic beta cells. Insulin Sensitization: Certain phytochemicals (e.g., berberine from *Berberis aristata*) improve cellular insulin uptake and reduce resistance⁽⁵⁷⁾. Inhibition of Glucose Absorption: Bioactives such as saponins, flavonoids, and polyphenols inhibit alpha-glucosidase and alpha-amylase, slowing carbohydrate breakdown and absorption⁽⁵⁸⁾. Other Effects: Antioxidant action, beta-cell preservation, modulation of inflammatory markers, lipid-lowering, and even partial beta-cell regeneration are reported for specific agents like *Moringa oleifera* and *Artemisia* species⁽⁵⁹⁾. The diagram below illustrates these diverse mechanisms as mapped onto human physiology: Clinical Efficacy and Safety Evidence from Clinical Studies Numerous human and animal studies suggest positive effects of herbal treatments: Polyherbal combinations can match the efficacy of standard pharmacological agents (e.g., metformin), improving fasting plasma glucose, HbA1c, and lipid profiles without significant adverse effects⁽⁶⁰⁾. Single-plant treatment with agents such as bitter melon, fenugreek, or aloe vera has shown reductions in blood sugar and improvements in secondary outcomes (lipids, body weight), underlining the clinical potential. Safety, Side Effects, and Quality Control Most studies report that herbal medicines, when used appropriately, are generally well-tolerated. However, issues to consider include: Potential for Hypoglycemia: Especially when combined with standard antidiabetic drugs. Careful monitoring and professional supervision are essential⁽⁶¹⁾. Allergenicity and Toxicity: Allergic reactions (notably fenugreek) and teratogenic risks have been documented. Rare but serious adverse effects include organ toxicity and hematological changes⁽⁶²⁾. Adulteration Risks: Some herbal products are found to contain undeclared pharmaceutical agents, leading to erratic glycemic control and exposure to unintended drugs⁽⁶³⁾. Herb-Drug Interactions: Herbals may inhibit or induce drug-metabolizing enzymes (cytochrome P450), alter gastrointestinal absorption, and modulate pharmacodynamics, requiring careful review before co-administration. Integrating Herbal Medicines with Conventional Therapy Evidence-Based Recommendations Adjunctive Use: Herbal antidiabetics should be considered as complements instead of outright replacements for standard care, primarily in the context of holistic or integrative treatment plans⁽⁶⁴⁾. Patient-Provider Communication: Physicians and patients should engage in transparent discussions about herbal remedy use to coordinate care, avoid interactions, and ensure optimal outcomes. Product Quality: Only



high-quality, standardized herbal products from reputable sources should be used to avoid contamination or adulteration⁽⁶⁵⁾. Monitoring: Regular monitoring of blood glucose and vigilance for signs of hypoglycemia or unusual symptoms is crucial, especially when starting or combining herbal agents with pharmaceuticals⁽⁶⁶⁾.

II. CONCLUSION

Polyherbal formulations represent promising therapeutic approaches for type 2 diabetes management, combining safety profiles of traditional herbal medicines with scientific validation of their antidiabetic potential. Comprehensive evidence from in vitro enzyme inhibition studies, in vivo animal model investigations, and human clinical trials demonstrates that well-formulated polyherbal preparations containing plants such as *Gymnema sylvestre*, *Momordica charantia*, *Trigonella foenum-graecum*, *Ocimum sanctum*, and *Curcuma longa* achieve significant antidiabetic activity through multiple complementary mechanisms including carbohydrate enzyme inhibition, pancreatic β -cell function enhancement, insulin sensitivity improvement, oxidative stress reduction, and anti-inflammatory effects.

The synergistic interactions of phytochemical constituents in polyherbal formulations provide therapeutic advantages over individual herb components, enabling effective disease management at reduced doses with minimal adverse effects. Meta-analysis of clinical trials demonstrates that polyherbal formulations produce blood glucose reduction and lipid profile improvement comparable to or exceeding standard antidiabetic medications, while offering additional hepatoprotective and nephroprotective benefits addressing diabetes complications.

However, significant challenges remain in standardization, quality control, and regulatory integration of polyherbal formulations into mainstream therapeutics. Development of comprehensive standardization protocols accounting for synergistic phytochemical interactions, advancement of modern analytical techniques for quality assurance, and conduction of long-term clinical trials of adequate sample size represent critical priorities for future research. Integration of traditional herbal knowledge with contemporary pharmaceutical science through collaborative efforts between traditional medicine practitioners, pharmaceutical scientists, and regulatory bodies is essential for realizing the therapeutic potential of polyherbal formulations.

Future research should prioritize elucidation of precise molecular mechanisms underlying polyherbal formulation antidiabetic effects through systems pharmacology approaches, advancement of formulation technologies to enhance bioavailability, investigation of optimal herb combinations and ratios for maximal synergistic effects, and conduction of large-scale clinical trials evaluating long-term efficacy and safety. Successfully addressing these research priorities would enable development of effective, safe, and accessible polyherbal formulations as valuable additions to the therapeutic armamentarium for global diabetes management, particularly benefiting populations in developing countries where access to conventional medications remains limited and traditional herbal medicines continue to play central roles in healthcare delivery.

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