



Review Article

Utilization Of Herbal Medication & Home Remedies In The Management Of Diabetes Mellitus Type-II: A Comprehensive Review

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ABSTRACT

Diabetes mellitus is a chronic metabolic disorder characterized by elevated levels of blood glucose (hyperglycemia) due to either insufficient insulin production by the pancreas or the body's inability to effectively use insulin. Insulin, a vital hormone, plays a pivotal role in the regulation of blood sugar levels by facilitating the absorption of glucose into cells, where it is utilized for energy. The increasing prevalence of diabetes mellitus poses a significant global health challenge, with a lack of a permanent remedy despite the availability of chemicals and biochemical agents for diabetes control. The adverse effects associated with the prolonged use of certain synthetic agents underscore the ongoing need for non-toxic and cost-effective pharmaceutical alternatives. Throughout human history, traditional treatments have held immense value as a source of medicine. Their widespread global use underscores the growing integration of herbs into modern, high-tech medical practices. Extensive research has led to the discovery of various traditional medicines, and substances derived from natural resources, particularly plants, stand out as a promising arsenal for effectively managing and treating diabetes and its associated complications. This review will highlight recent advancements in the realm of herbal drugs for diabetes treatment, the prevention of secondary complications associated with diabetes, and the exploration of various herbal medication currently undergoing different stages of clinical trial.


INTRODUCTION

Diabetes mellitus, a complex syndrome marked by elevated glucose levels, altered lipid, carbohydrate, and protein metabolism, stands as the prevailing chronic metabolic ailment. Stemming from a deficiency in insulin, the

condition manifests diverse complications over time, impacting the eyes, kidneys, heart, and nerves. Noteworthy symptoms include polyuria, fatigue, weight loss, delayed wound healing, and blurred vision. The destruction of pancreatic beta-cells, a consequence of immune system

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dysregulation, particularly the attack on lymphocytes and pancreas, may lead to insulinitis and insulin-dependent diabetes. Various environmental and genetic factors contribute to the intricate interplay influencing the immune system and paving the way for this intricate disorder. ⁽¹⁾ Type 2 diabetes mellitus (T2DM) stands as the predominant form of diabetes, constituting roughly 90% of all diabetes cases. Numerous scientific investigations have underscored the profound impact of diabetes on human quality of life, posing substantial risk

factors for severe complications including stroke, amputation, kidney failure, and blindness. This results in noteworthy morbidity and premature mortality, as evidenced by various studies. Illustrated in Figure 1, the International Diabetes Federation (IDF) projected a staggering increase in the prevalence of diabetes, estimating around 463 million affected adults in 2019. The numbers are anticipated to surge to approximately 578 million by 2030 and a staggering 700 million by 2045. ⁽²⁾

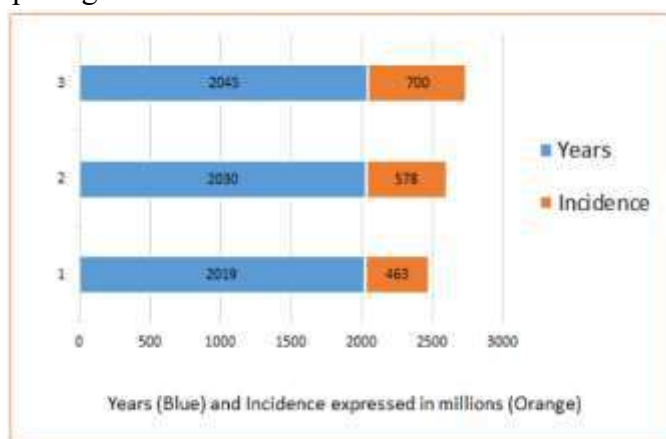


Fig 1. Graph of an increased incidence of diabetes patients worldwide. ⁽²⁾

Types of diabetes mellitus-

The World Health Organization categorizes diabetes into six distinct classes: type 1 diabetes, type 2 diabetes, hybrid forms such as slowly evolving immune-mediated diabetes of adults and ketosis-prone type 2 diabetes, hyperglycemia first detected during pregnancy, "other specific types," and "unclassified diabetes". Contrary to previous perceptions, diabetes is now recognized as a more diverse condition, with individuals often

presenting with a combination of these various forms. ⁽³⁾

- 1) Insulin-dependent diabetes
- 2) Non-insulin-dependent
- 3) Gestational diabetes
- 4) Impaired glucose tolerance.

Each type of diabetes has its own set of risk factors, symptoms, and treatment approaches. It's essential for individuals with diabetes to work closely with healthcare professionals to manage their condition effectively. ⁽⁴⁾

Table No. 1. Classification of diabetes mellitus: ⁽⁵⁾

Types	Condition	Age	Severity	Risk factor	Treatment
Type -1	Body fails to production of insulin. Also, destruction of B-cells.	In childhood and early adulthood.	10 %	Environmental factor, nutritional factor and destruction of immune system.	Insulin injection.
Type-2	Delayed insulin secretion and	Age of 40 years.	80%	Obesity, family history, defect in	By using synthetic drug.

	excessive glucagon secretion.			insulin receptor and history of gestational DM.	By using natural drug.
Gestational diabetes	Hormonal changes in during pregnancy.	Any phase of pregnancy.	4 %	Metabolic change.	Regular exercise and proper diet.
Impaired glucose tolerance	Transition state between normality and diabetes mellitus.	Older than 50 years.	6 %	Hypertension, smoking, family history and increasing age.	Proper diet, daily exercise, antidiabetic medication.

In this comprehensive review article, the author focus on the predominant form of diabetes is type 2, typically diagnosed in adults, characterized by insulin resistance or insufficient insulin production. Over the last three decades, the incidence of type 2 diabetes has surged globally across various income levels. For individuals grappling with diabetes, affordable access to essential treatments, notably insulin, is imperative for their well-being. ⁽⁶⁾ According to the International Diabetes Federation's projections, the global prevalence of diabetes, standing at 10.5% in 2021, is anticipated to rise to 11.3% by 2030 and further to 12.2% by 2040. Individuals with Type 2 Diabetes Mellitus (T2DM) face an elevated risk of organ dysfunction and failure, particularly impacting the kidneys, eyes, and nerves. This heightened vulnerability contributes to escalated medical care expenses and a diminished quality of life. Furthermore, studies indicate that those with T2DM confront a 15% higher likelihood of premature death, resulting in an approximate 20-year reduction in life expectancy. ⁽⁷⁾

✚ Non-insulin-dependent / Type-II Diabetes Mellitus-

Formerly referred to as adult-onset diabetes, Type 2 diabetes (T2D) represents a form of diabetes mellitus characterized by elevated blood sugar levels, insulin resistance, and a relative deficiency of insulin. Common manifestations encompass increased thirst, frequent urination, unexplained weight loss, and fatigue. Additional symptoms may manifest as heightened hunger, a tingling

sensation akin to pins and needles, and non-healing sores. The onset of symptoms is often gradual. Prolonged exposure to elevated blood sugar levels in T2D can lead to severe complications, including heart disease, strokes, diabetic retinopathy culminating in blindness, kidney failure, and impaired blood flow in extremities, potentially necessitating amputations. ⁽⁸⁾

- Constituting 85–90 percent of all diabetes cases, type 2 diabetes stands as the predominant form within this spectrum of metabolic disorders.
- Typically emerging in adults aged 45 and older, type 2 diabetes is increasingly prevalent among younger demographics, encompassing children, adolescents, and young adults.
- The likelihood of developing type 2 diabetes is higher in individuals with a familial history of the condition or those from specific ethnic backgrounds.
- Some individuals may first recognize the presence of type 2 diabetes through complications such as heart attacks, vision impairments, or slow-healing wounds.
- Management of type 2 diabetes involves a multifaceted approach, encompassing regular physical activity, balanced nutrition, and weight reduction. Given its progressive nature, many individuals may require oral medications or insulin injections in conjunction with lifestyle modifications over time. ⁽⁹⁾



Sign and Symptoms-

The symptoms commonly associated with diabetes include frequent urination, excessive thirst, heightened hunger despite regular eating, profound fatigue, blurred vision, delayed healing of cuts and bruises, and sensations of tingling, pain, or numbness in the hands and feet, particularly observed in type 2 diabetes. However, it's noteworthy that some individuals with type 2 diabetes may experience such mild symptoms that they remain unnoticed.

Recognizing and addressing diabetes in its early stages can significantly diminish the likelihood of complications associated with the condition, underscoring the importance of early detection and prompt treatment for optimal health outcomes. ⁽¹⁰⁾



Fig 2. Sign & symptoms of type-2 diabetes ⁽¹¹⁾

Causes and risk factors of type 2 diabetes- The primary cause of Type 2 diabetes, the prevalent variant of diabetes, stems from a combination of factors such as lifestyle choices and genetic predisposition.



Fig 3. Risk factor of type-2 diabetes ⁽¹²⁾

A multitude of risk factors have been identified in association with the onset of type 2 diabetes, including a

- Familial predisposition to diabetes
- Excess weight, an unhealthy dietary pattern
- Insufficient physical activity
- Advancing age
- Elevated blood pressure
- A history of gestational diabetes
- Suboptimal nutrition during pregnancy.

These factors collectively contribute to the increasing prevalence of type 2 diabetes, with changes in diet and physical activity, particularly in rapidly developing urban environments, playing a significant role in the rising numbers of individuals affected by this metabolic disorder. ^(13,14)

Diagnosis of type 2 diabetes- The diagnosis of type 2 diabetes is commonly conducted through the glycated hemoglobin (A1C) test, a blood examination reflecting the average blood sugar level over the preceding two to three months. The results are interpreted as follows:

- Below 5.7% is within the normal range.
- In the range of 5.7% to 6.4%, the diagnosis is classified as prediabetes.
- A measurement of 6.5% or higher, confirmed by two separate tests, signifies the presence of diabetes.

In instances where the A1C test is unavailable or certain conditions impede its accuracy, healthcare providers may resort to alternative tests for the diagnosis of diabetes. ⁽¹⁵⁾



Fig 4. Blood glucose chart ⁽¹²⁾

TYPE 2 DIABETES TREATMENT-

The management of type 2 diabetes involves a comprehensive approach that combines lifestyle modifications with medication. Adopting a healthy lifestyle is paramount and typically includes

- changes in diet
- regular physical activity
- weight management.
- Dietary adjustments may involve monitoring carbohydrate intake, choosing whole foods, and maintaining a balanced diet. ⁽¹⁶⁾

Synthetic Medication- Indeed, the management of type 2 diabetes encompasses a variety of medications, and finding the most suitable one, along with the appropriate dosage, may require some time and adjustments.

1. Metformin- It stands as the predominant medication for managing type 2 diabetes, playing a key role in maintaining optimal blood sugar levels. Administered in tablet form, it is typically taken with or following meals. While metformin is generally well-tolerated, common side effects may include nausea and diarrhea. ⁽¹⁷⁾

2. Sulfonylureas- It have been a longstanding and commonly utilized treatment for type 2

diabetes. Operating by augmenting the production of insulin within the body, they contribute to a reduction in blood sugar levels, typically by around 20 percent. However, they remain a viable option as a secondary treatment due to their cost-effectiveness, widespread availability, and well-established history of use.

3. DPP-4 inhibitors- Including drugs like sitagliptin (Januvia), saxagliptin (Onglyza), linagliptin (Tradjenta), alogliptin (Nesina), and vildagliptin (Galvus), are a group of medicines that help lower blood sugar levels. They achieve this by increasing insulin release from the pancreas after meals. These medications can be used alone if someone cannot tolerate the first-line medicine (metformin) or in combination with other oral medicines if blood sugar levels are still higher than the target. ⁽¹⁸⁾

4. SGLT2 inhibitors- Including drugs like canagliflozin (Invokana), empagliflozin (Jardiance), dapagliflozin (Farxiga), and ertugliflozin (Steglatro), help lower blood sugar by making your body remove sugar through urine. They are about as effective as DPP-4 inhibitors. These medications might be a good option for people with heart failure or kidney disease because they can offer cardiovascular, renal, and mortality benefits.

5. GLP-1 receptor agonists- They are injectable medications that enhance insulin release during meals and slow down digestion. Examples include exenatide (Byetta), exenatide extended release (Bydureon), liraglutide (Victoza), dulaglutide (Trulicity), lixisenatide (Adlyxin), and semaglutide (Ozempic or Rybelsus). These injections or tablets can be beneficial for individuals whose blood sugar is not well-managed with the highest dose of one or two oral medicines. ⁽¹⁹⁾

6. Meglitinides- Drugs like repaglinide (Prandin) and nateglinide (Starlix), help lower blood sugar levels, acting similarly to sulfonylureas but with a

quicker effect. These pills should be taken right before a meal. Meglitinides might be suggested for those allergic to sulfonylureas. Although they can be used in patients with kidney failure, they are not typically the first choice due to their higher cost compared to sulfonylureas.

7. Thiazolidinediones- Drugs like pioglitazone (Actos) and rosiglitazone (Avandia), help lower blood sugar by enhancing the body's response to insulin. These pills are taken orally and are often prescribed in combination with other medications like metformin, a sulfonylurea, or insulin.

8. Alpha-glucosidase inhibitors- Drugs such as acarbose (Precose) and miglitol (Glyset), function by disrupting the absorption of carbohydrates in the intestine, aiding in lowering blood sugar

levels. While not as potent as metformin or sulfonylureas, they can be used in combination with other medications if the initial treatment is not sufficiently reducing blood sugar levels. ⁽²⁰⁾

Common adverse effects of synthetic medication- Like all medications, oral diabetes medications may have potential side effects, and these can vary depending on the specific type of medication. It's important to discuss the possible side effects of the diabetes medication you are thinking of starting with your healthcare provider or pharmacist, as they can provide valuable information. Typically, common side effects of oral diabetes medications represent in following table no.2 ⁽²¹⁾

S/N	Drug class	Example of drugs	Adverse effects
1	Insulin and analogues	Regular Insulin	Hypoglycemia, Weight gain, Insulin allergy, Lipodystrophy at injection sites
2	Sulphonylureas	Glibenclamide	Hypoglycaemia, Weight gain, Cardiovascular risk, rash, Cholestatic jaundice, Bone marrow damage, Photosensitivity
3	Meglitinides	Repaglinide	Hypoglycemia, Sensitivity reactions
4	Biguanides	Metformin	Gastrointestinal effects, Lactic acidosis
5	GLP-1 agonists	Exenatide	Gastrointestinal effects, Pancreatitis, risks for cancer and cardiovascular events
6	DPP-4 inhibitors	Saxagliptin	Pancreatitis, risk for cancer, acute hepatitis and kidney impairment
7	Thiazolidinedions	Pioglitazone	Hepatitis, Cardiovascular risk, Bladder cancer, Water retention and weight gain
8	Dual PPAR agonists	Saroglitazar	Gastritis, asthenia and pyrexia
9	Alpha-glucosidase inhibitors	Acarbose	Gastrointestinal effects, Hepatitis,
10	Amylin analogues	Pramlintide	Hypoglycemia, Allergy
11	SGLT 2 inhibitors	Canagliflozin	Glycosuria, Cardiovascular concern

Table No. 2. Conventional antidiabetic drugs and their major adverse effects: ⁽²²⁾

Herbal Medication- Presently, the primary and effective approach for managing diabetes involves the use of insulin and hypoglycemic drugs. However, these medications are associated with numerous adverse side effects. Medicinal plants, with a rich history of traditional use, are gaining widespread attention and utilization in the treatment of various diseases. The escalating interest in medicinal plants is driven by several factors, including their exploration for potential antidiabetic effects. ⁽²³⁾ This review article

highlights some of the most significant medicinal plants known for their hypoglycemic properties, drawing from reliable clinical and laboratory evidence. Additionally, it explores the traditional use of medicinal plants in Iranian traditional medicine for the treatment of diabetes.

- **Fenugreek**
- **Eugenia jambolana**
- **Aegle marmelos**
- **Allium cepa**
- **Silybum marianum:**

+ Fenugreek:



Fenugreek seeds, known scientifically as *Trigonella foenum-graecum*, have a dual role as both a food supplement and a traditional remedy for labor induction, digestion aid, and overall health improvement. Animal studies have demonstrated that fenugreek seed extract can effectively lower blood glucose levels, making it a promising option for managing diabetes and its complications. The plant's glucose-lowering action is attributed to its ability to reduce insulin resistance. Active compounds like diosgenin, GII, galactomannan, trigoneoside, and 4-hydroxyisoleucine are identified in fenugreek, with diosgenin specifically noted for its potential in reducing insulin resistance by affecting adipocyte differentiation and inflammation. A clinical study also suggests that fenugreek contributes to hypoglycemic control by enhancing insulin sensitivity. ⁽²⁴⁾

+ *Eugenia jambolana*: (Indian gooseberry, jamun)



In India, the kernels of *Eugenia jambolana*, commonly known as jamun, are widely used as a home remedy for diabetes and are a key ingredient in many herbal formulations. Studies have shown that extracts and lyophilized powder from jamun have antihyperglycemic effects,

leading to a reduction in blood glucose levels. The extent of this reduction varies with different diabetes levels, with a 73.51% decrease in mild diabetes (plasma sugar >180 mg/dl), 55.62% in moderate (plasma sugar >280 mg/dl), and 17.72% in severe diabetes (plasma sugar >400 mg/dl). The hypoglycemic activity of jamun pulp extract was observed in diabetic mice within 30 minutes, while the seeds required 24 hours. Additionally, oral administration of the extract increased serum insulin levels in diabetic rats and stimulated insulin secretion when incubated with isolated islets of Langerhans from both normal and diabetic animals. These extracts also demonstrated inhibitory effects on insulinase activity from the liver and kidney. ⁽²⁵⁾

+ *Aegle marmelos*:



Aegle marmelos, commonly known as bael, is recognized for its medicinal properties, including antidiabetic effects. In a study with twenty Type 2 diabetes (T2D) patients having postprandial blood glucose (PPBG) of 201 ± 6 mg/dL, a daily decoction of 5 g *A. marmelos* leaf powder for 16 weeks led to a significant decrease in their PPBG to 159 ± 5 mg/dL. Another study demonstrated that this decoction (5 g/day for 1 month) enhanced the hypoglycemic effects of standard oral drugs in T2D patients. Similar findings were reported in a double-blind placebo trial, where T2D patients receiving a combination of sulfonylurea drug and *A. marmelos* leaves (2 g/twice a day) showed more effects on fasting blood glucose (FBG), PPBG, and urinary glucose levels after 8 weeks compared to those receiving sulfonylurea plus a placebo. ⁽²⁶⁾

Allium cepa:



In an early study by Mathew and Augusti (1975), it was found that consuming *Allium cepa* (onion) orally could enhance glycemic control in diabetes. A self-controlled study on twenty Type 2 diabetes (T2D) patients also revealed an acute hypoglycemic effect of *A. cepa*. Furthermore, it was observed that *A. cepa* could reduce the rise in plasma glucose 2 hours after glucose ingestion by 37%. In a more recent study, the intake of 100g of *A. cepa* was associated with decreased fasting blood glucose (FBG) levels and improved glucose tolerance tests (GTT) in both Type 1 (T1D) and Type 2 diabetes (T2D) patients (Eldin et al., 2010).⁽²⁷⁾

Silybum marianum:



Silybum marianum, commonly known as milk thistle, is renowned in herbal medicine for its therapeutic effects on liver-related issues. Interestingly, studies have also revealed the positive impact of *S. marianum* and its flavonolignans, known as silymarin, in reducing glucose and lipids in diabetic patients. In a 2-month clinical study involving 30 Type 2 diabetes (T2D) patients, silymarin (200 mg three times a day) significantly lowered fasting blood glucose (FBG), HbA1c, total cholesterol, LDL, triglycerides (TG), serum glutamic oxalacetic

transaminase (SGOT), and serum glutamic pyruvic transaminase (SGPT) when combined with conventional therapy. Similar results were observed in another trial with 25 T2D patients receiving the same silymarin dose for 4 months, demonstrating reductions in glucose, lipids, and hepatic enzymes. Additionally, the beneficial effects of silymarin (200 mg/day) on FBG, HbA1c, and postprandial blood glucose were noted in T2D patients already on glibenclamide therapy.⁽²⁸⁾

CONCLUSION

Diabetes mellitus poses a significant health challenge in today's lifestyle, with many individuals, especially those with type 2 diabetes, remaining undiagnosed. While synthetic formulations are available and exhibit effective clinical and pharmacological activity, they often come with notable adverse effects like hypoglycemia, weight gain, gastrointestinal effects, cardiovascular risk etc. This review emphasizes the importance of creating awareness among individuals with type 2 diabetes about the use of herbal preparations, which have demonstrated potent antidiabetic actions. The herbal drugs discussed in this review are easily accessible or can be prepared easily, presenting a favorable option with minimal side effects compared to synthetic drugs. Consequently, the preference for herbal drugs is advocated to mitigate the risk of serious side effects associated with synthetic medications.

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