

REVIEW ARTICLE

Medicinal plants as a source of natural remedies in the management of diabetes

Zingisa Sitobo¹, Liberty Tinotenda Navhaya², and Xolani Henry Makhoba^{3*}

¹Department of Biochemistry and Microbiology, Faculty of Science and Agriculture, University of Fort Hare, Alice, Eastern Cape, South Africa

²Department of Biochemistry, Microbiology and Biotechnology, Faculty of Science and Agriculture, School of Molecular and Life Sciences, University of Limpopo, Mankweng, Limpopo, South Africa

³Department of Life and Consumer Sciences, College of Agriculture and Environmental Sciences, University of South Africa, Florida Campus, Roodepoort, South Africa

Abstract

Diabetes is a severe chronic illness that has impacted thousands of individuals worldwide. It is caused by the body's failure to produce insulin or insufficient production of insulin. While diabetes is not curable, it can be managed with injectable insulin, which decreases blood glucose levels. However, this treatment has several disadvantages that can affect a patient's health, and it is often unaffordable for some individuals. Previous studies have suggested that phytochemicals can improve insulin sensitivity. Due to the presence of therapeutic phytochemicals in natural plants, medicinal plants emerge as potential candidates for treating diabetes. In addition, compared to conventional diabetes treatments, phytochemical treatment may be affordable for all diabetics and has fewer side effects. This review primarily focuses on the symptoms and treatment options for the four known types of diabetes: type 1 diabetes mellitus, type 2 diabetes mellitus, type 3c diabetes mellitus, and neonatal diabetes. The article reviews medicinal plants that have been used to treat diabetes effectively with minimum side effects, such as *Momordica charantia* L., *Syzygium cumini* (L.) Skeels, and *Ocimum tenuiflorum* L., among others. In addition, some newly approved drugs, such as tirzepatide, sergliflozin, saxagliptin, and liraglutide, recommended for treating patients suffering from various forms of diabetes, are discussed.

***Corresponding author:**
Xolani Henry Makhoba
(makhoxx@unisa.ac.za)

Citation: Sitobo Z, Navhaya LT, Makhoba XH. Medicinal plants as a source of natural remedies in the management of diabetes. *INNOSC Theranostics and Pharmacological Sciences*. 2024;7(3):1885.
doi: 10.36922/itps.1885

Received: September 21, 2023

Accepted: January 16, 2024

Published Online: July 10, 2024

Copyright: © 2024 This is an Open-Access article distributed under the terms of the Creative Commons AttributionNoncommercial License, permitting all non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Publisher's Note: AccScience Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Keywords: Diabetes; Symptoms; Treatment; Medicinal plants; Phytochemicals

1. Introduction

There has been a startling rise in diabetes cases on a global scale in developing countries. Statistically, 537 million people had diabetes worldwide as of 2021, with about 10.5% of adults affected by diabetes mellitus (DM).¹ DM was recognized and explained by ancient Egyptians; the word "diabetes" is derived from the Greek word meaning "passer-by siphon," and "mellitus" means "sweet." DM is a chronic illness that occurs when blood glucose levels are high in the body, causing damage to internal organs such as nerves, kidneys, and blood vessels over a prolonged period.

The primary energy source in the human body, glucose, is obtained from food, specifically from proteins, lipids, and carbohydrates.² Blood glucose concentration is

regulated by several hormones, most of which increase glucose levels in circulation. Hormones such as glucagon, adrenaline, somatotropin, and cortisol are known to increase blood glucose levels. The endocrine gland secretes insulin, an endocrine hormone that helps food-derived glucose enters cells to be used as an energy source.³ Typically, individuals develop diabetes when their body produces insufficient hypoglycemic agents or fails to use them effectively. As a result, glucose does not enter the cells and remains in the blood, increasing its concentration.⁴

The pancreas produces insulin, which helps regulate blood sugar. Insulin is produced by a group of small cells in the pancreas called the “islets of Langerhans”. When blood sugar levels are too high, the islets release insulin, allowing glucose to enter cells.⁵ The liver releases glucose into the bloodstream after being stimulated by glucagon to transform stored glucose (glycogen) into a usable form through a process called glycogenolysis. Several pathogenesis pathways are involved in the development of diabetes, including the destruction of beta-cells (β -cells) in the pancreas, where insulin is produced, and anomalies that lead to insulin resistance.⁶ Diabetes has long-term complications, such as loss of vision, peripheral neuropathy with a risk of foot ulcers, and renal failure.⁷

2. Classification of DM

Diabetes is classified into several types, mainly type 1 DM (T1DM), type 2 DM (T2DM), and gestational DM (GDM). The terms “insulin-dependent” (describing T1DM, which requires external insulin to manage) and “non-insulin-dependent” (describing T2DM, which may be managed without insulin but can develop into insulin dependence) are used to classify the pathophysiological conditions of diabetes.⁸

2.1. T1DM

T1DM is common in children and young adults. It occurs due to auto-immune destruction of insulin-producing β -cells in the pancreas, leading to insulin deficiency resulting from the destruction of β -cells in the pancreas.⁹ T1DM is sometimes referred to as insulin-dependent diabetes because the body is unable to produce sufficient insulin. T1DM is less common than T2DM, accounting for approximately 10% of all diabetes cases. Patients with T1DM require daily insulin injections to survive,¹⁰ follow a specialized diet, and regularly monitor their blood glucose levels.

2.2. T2DM

T2DM, also known as adult-onset diabetes, is the most common form of diabetes, usually affecting middle-aged

and elderly individuals, as well as those who lack exercise. In addition, overweight, obese individuals, and those with visceral fat are at greater risk of developing T2DM. T2DM accounts for about 90% of all diabetic cases worldwide. In T2DM, the body either produces insufficient insulin or uses it improperly,¹¹ or the body’s muscle, fat, and liver cells do not respond to insulin due to insulin resistance. As a result, blood sugar cannot enter the cells to be stored and builds up in the blood. T2DM symptoms can be managed through exercise, weight loss, and a specialized healthy diet.¹² However, T2DM is a progressive disease that gradually gets worse, potentially requiring insulin therapy.

2.3. GDM

The third form of diabetes, GDM, usually occurs in the second or third trimester of pregnancy. This type of diabetes occurs only during pregnancy and can often be resolved after the baby is born, although it might develop into T2DM later in life.¹³ Changes in hormones and weight gain during pregnancy can impair insulin functioning, resulting in high blood glucose levels. Although GDM usually disappears after pregnancy, most women who have had it have a 40 – 60% chance of developing T2DM within 5 – 10 years.¹⁴

2.4. Maturity onset diabetes of the young (MODY)

MODY is a non-autoimmune, monogenic form of diabetes characterized by the destruction of pancreatic β -cells and perturbed insulin biosynthesis.^{15,16} It differs from T1DM and T2DM but is frequently misdiagnosed as one of these types. MODY is caused by a single gene mutation. Its diagnostic criteria include onset between adolescence and early adulthood (below 25 years), a familial background of autosomal dominant diabetes across a minimum of two generations, and β -cell dysfunction with no autoantibodies.¹⁵⁻¹⁷ Assessment methods introduced in the 1990s identified mutations associated with MODY, including *HNF1B*, *HNF1A*, *GCK*, and *HNF4A*.¹⁵ In MODY, disruption in insulin production results in hyperglycemia, which may damage blood vessels, eyes, nerves, and kidneys.¹⁶

2.5. Neonatal diabetes (NDM)

NDM, also termed congenital diabetes, is a rare cause of hyperglycemia caused by mutations in proteins essential for the normal functioning of pancreatic β -cells. NDM typically occurs before the age of 6 months, although it can rarely be present between 6 months and 1 year.^{18,19} NDM arises through two primary mechanisms: the abnormal functionality of existing pancreatic β -cells or anomalies in the pancreas affecting the survival of insulin-secreting cells. The major genetic causes of NDM

involving abnormal β -cell function are mutations in the genes *KCNJ11* or *ABCC8*,^{18,20} which code for the potassium channel in pancreatic β -cells, and anomalies in the 6q24 locus.¹⁸ Patients with mutations in *KCNJ11* or *ABCC8*, as well as 6q24 abnormalities, are compliant with a successful switch from insulin injection (i.e., initially used as a mode of treatment) to oral sulfonylureas.^{18,20}

2.6. Type 3c DM

Type 3c DM, also known as pancreatogenic diabetes or pancreatic DM, results from conditions affecting the exocrine pancreas, such as pancreatic cancer, chronic pancreatitis, and cystic fibrosis.²¹ Due to its association with pancreatic diseases, patients with T3cDM often experience pancreatic exocrine insufficiency, leading to fat malabsorption and undernutrition.²¹ The pathogenesis of T3cDM is due to decreased insulin production, facilitated by both the reduction in the functional capacity of the islets and a decrease in their number due to extensive sclerosis and fibrosis.²² Similar to T1DM and T2DM, controlling hyperglycemia remains the primary target for minimizing the risk of macrovascular and microvascular complications.²² However, there are few studies or randomized trials on the pharmacological treatment of T3cDM due to the unique and variable clinical and metabolic characteristics of these patients.^{21,22}

2.7. Latent autoimmune diabetes in adults (LADA)

LADA is a subtype of T1DM that appears to bridge the gap between T1DM and T2DM. LADA is characterized by a slow progression of autoimmune diabetes and exhibits immunological markers typical of T1DM but does not necessarily require insulin treatment upon diagnosis.²³ Sometimes referred to as type 1.5 diabetes, LADA displays some characteristics closer to T1DM, while others are closer to T2DM.²⁴ The diagnosis of LADA is more commonly made in secondary care settings compared to primary care. The critical diagnostic criteria for LADA include adult onset (>30 years old), the presence of autoantibodies associated with diabetes, and no immediate requirement for insulin therapy post-diagnosis.^{23,24} LADA patients retain functioning β -cells; therefore, it is imperative to initiate therapeutic strategies aimed at improving metabolic control while preserving the insulin-secreting capacity.²⁴

3. Symptoms and treatment of DM

3.1. Symptoms

The symptoms of DM may appear harmless when considered individually, which is the primary reason why people may have diabetes without being aware of the predicament. The symptoms of the different types

of diabetes may vary and develop at different rates. For example, the symptoms of T1DM usually develop over a short period, while those of T2DM develop more slowly. In some individuals, no symptoms are present at all. In GDM, symptoms may or may not develop during pregnancy, necessitating testing for the condition.²⁵ In general, DM often presents asymptotically, but some significant symptoms that develop or indicate a potential diabetic patient include those listed in [Table 1](#).

3.2. Treatment

There is currently no approved cure for DM; therefore, management and treatment of the disease are the primary courses of action. The treatment of DM is complex and involves a combination of exercise, pharmacotherapy, and nutritional therapy as interventions for successful disease management.²⁵ The primary goal of DM treatment is to maintain healthy blood glucose levels to prevent DM-related complications. Patients living with DM are encouraged to consume proteins, carbohydrates, and fats in appropriate nutritional proportions. This recommendation entails carbohydrate intake comprising 55 – 60% of total caloric intake, limiting fat intake to a maximum of 30%, and ensuring protein intake within 10–20% of total daily intake. The expected caloric intake is an average of 30 kcal/kg body weight.²⁷ As part of their treatment regimen, individuals with diabetes are advised to engage in at least 20 min of aerobic exercise per day (at least 150 min/week). This regimen of exercise helps in lowering blood glucose levels. Regular exercise also assists in regulating blood cholesterol levels, lowering blood pressure, and maintaining a healthy body weight.²⁵

Pharmacotherapy treatment depends on the type of DM diagnosed. T1DM is primarily caused by the absence of insulin, so daily insulin injections or the use of an insulin pump is the recommended forms of treatment.²⁵ GDM also requires insulin administration as a mode of treatment. The initial insulin dosage is 0.5–1 unit/kg in individuals with T1DM. Several oral medications are available for managing T2DM ([Table 2](#)), while insulin injections may also be required. The choice of oral drug therapy is complex, and physicians rely on clinical judgment to determine the most effective combination of drugs for the patient. It is important to note that discretion is critically essential over a long period as the treatment of persistent, chronic diseases such as DM are ongoing and unrelenting, and the response to therapy may potentially change over time.^{25–27}

While the oral medications listed in [Table 2](#) are commonly used for managing diabetes, they often fail to completely control the condition and may exhibit

Table 1. Symptoms of diabetes mellitus (DM)

Symptoms	Description	References
Polyuria (frequent urination)	An increased glucose concentration from the blood accumulates in the kidneys and attracts large volumes of water, resulting in frequent urination (from 1.8 L in healthy people to over 3 L in those with DM).	25,26
Polydipsia (excessive thirst)	Loss of substantial amounts of water through excessive urination results in dehydration that, in turn, triggers a thirst that is difficult to satisfy.	25,26
Lethargy/Fatigue	If there is no hormone insulin or it is malfunctioning, there would be no glucose uptake into cells, resulting in listlessness and fatigue.	25,26
Polyphagia (intense hunger)	Large amounts of sugars in the blood are not used in the cells as an energy source due to the absence of insulin or its malfunction. The body's reaction is to try and seek energy, triggering the release of ghrelin and cortisol hormone (hunger hormones), and the patient experiences increased hunger.	25,26
Ketoacidosis	Due to the absence of sugar to fuel metabolism, the body turns to fats and proteins, and the breakdown of fats results in the generation of acetone (ketones) used in metabolism. Ketones lower blood pH (ketoacidosis) and are presented as a fruity smell on the breath, urine, and sweat, as well as Kussmaul breathing (increased breathing rate).	25,26

Table 2. Types of oral medications, their action, and the available drug(s) for diabetes mellitus

Type of oral medication	Action of drug	Available drug	References
Biguanides	Exhibits insulin-sensitizing properties in which it lowers basal and postprandial plasma glucose and increases glucose uptake by the periphery.	Metformin	25,26,28
Sulfonylureas	Stimulates insulin secretion by β -cells of the pancreas, leading to a drop in blood glucose level and a reduction of basal hepatic glucose secretion.	Gliclazide, glimepiride, glipizide, and glibenclamide	25,26,28
α -glucosidase inhibitors	Acts within the small intestines, inhibiting α -glucosidase enzyme, thereby delaying digestion/absorption of ingested carbohydrates and, in turn, lowering postprandial blood glucose.	Miglitol and acarbose	25,26,28
Thiazolidinediones	Targets insulin resistance, enhancing insulin sensitivity to tissues in muscle through activation of intracellular receptors.	Rosiglitazone and pioglitazone	25,26,28
Meglitinides	Increases insulin secretion by triggering pancreatic β -cells.	Netaglinid and repaglinide	25,26,28
Sodium-glucose co-transporter 2 inhibitors	Block glucose reabsorption in the kidneys and improves glucose excretion, in turn lowering blood glucose levels.	Canagliflozin, ipragliflozin, dapagliflozin, and empagliflozin	25,26,28
Dopamine D2 and its receptor agonist	Lowers resistance to insulin and improves insulin sensitivity.	Bromocriptine	25,26,28
Bile acid sequestrant	Develops glucose-lowering effect and improves glucose tolerance.	Colestimide and colesevelam	25,26,28

negative side effects. Therefore, ongoing research is aimed at developing improved treatments for DM.²⁹ Although the drugs that have been and are still being used have proven to be effective, novel classes of innovative targets for diabetic control and antihyperglycemic therapies have emerged to manage diabetes.²⁸ The United States Food and Drug Administration (FDA) approved tirzepatide, a new, unique, first-in-class medication for the treatment of T2DM, on May 13, 2022. The drug is also known as Mounjaro.³⁰ In the following subsections, tirzepatide and

several other medications for T2DM are discussed in detail.

3.2.1. Tirzepatide

Tirzepatide is a dual incretin agonist that decreases blood sugar and promotes weight loss reduction more competently than the usual treatments used for T2DM.³⁰ After meal consumption, the gut secretes hormones known as incretins, which include glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic

polypeptide. Incretins trigger the liver to release stored glucose, which raises blood glucose levels and stimulates the pancreas to release insulin, a hormone that lowers blood glucose and blocks the hormone glucagon.³⁰

3.2.2. Saxagliptin

In July 2009, the FDA authorized saxagliptin, which is generally recommended as an addition to diet and exercise to improve glycemic control in individuals with T2DM. One oral dose of 5 mg of saxagliptin is recommended once daily; this dosage produces broad absorption. Saxagliptin is mostly metabolized by the hepatic cytochrome P450 isoenzyme CYP3A4/5. It is eliminated by both metabolism and renal excretion.³¹

3.2.3. Sergliflozin

Sergliflozin, a sodium-glucose co-transporter 2 inhibitor, has shown dose-dependent urine glucose excretion in animal experiments. In clinical trials, a single oral dose of sergliflozin resulted in dose-dependent glycosuria during fasting and after meals but had no effect on the excretion of electrolytes in the urine. In addition, it significantly reduced weight in healthy obese adults compared to a placebo.³² However, there have been a few mild side effects, such as headache, sore throat, and dyspepsia in diabetic patients. In terms of metabolism, it exhibits a pharmacokinetic profile comparable to that of remigliflozin. Consequently, phase II clinical trials for sergliflozin have halted despite the drug's encouraging profile when treating obese diabetic patients.

3.2.4. Liraglutide

As a GLP-1 counterpart, liraglutide is 97% similar to natural human GLP-1 except for a single amino acid substitution and a side chain of glutamate-linked fatty acids. When used to treat T2DM, it has demonstrated safety, effectiveness, and acceptability as a glucose-lowering medication.³³ Liraglutide reduces insulin resistance while lowering systolic blood pressure, body weight, visceral fat, and other cardiovascular risk factors. It also improves lipid profile. Liraglutide is a desirable alternative for the therapy of insulin resistance because of its positive effects on all aspects of the metabolic syndrome, also known as insulin resistance syndrome, with a low risk of hypoglycemia.³⁴ It has been demonstrated that liraglutide lowers triglyceride levels without changing the concentration of other lipids. The recommended initial dose is 0.6 mg, which can be increased to 1.2 mg or even 1.8 mg if necessary.³⁵

4. Medicinal plants and their health benefits

Medicinal plants have garnered increasing attention from researchers and are reported as one of the natural

sources with the potential to play an important role in the treatment or management of diabetes.³⁶ Approximately 410 medicinal plants have experimentally proven anti-diabetic activities. These medicinal plants contain important anti-diabetic properties without harmful side effects, and nowadays, many individuals from urban and rural areas depend on natural plants to treat various chronic diseases.³⁷ Tannins, alkaloids, flavonoids, and phenolics are rich sources found in medicinal plants, essential for improving the effectiveness of the pancreatic tissues by regulating the intestinal absorption of glucose and the secretion of insulin.³⁸ Therefore, medicinal plants can be used in the treatment of diabetes due to their therapeutically important phytochemicals present in natural plants. This treatment can also be more affordable for everyone suffering from diabetes, making medicinal plants the focus for the development of alternative therapies for DM.

The use of medicinal plants for healing and treatment of diseases dates back to ancient times. In antiquity, people turned to nature for remedies as a means of recovery from diseases. There exists a profound connection between the search for natural remedies and historical mandates, supported by ample evidence from various sources. Humanity's enduring struggle against disease has prompted the utilization of roots, seeds, fruits, stems, barks, and other plant parts as sources of medical drugs. This practice has heightened awareness of the use of medicinal plants.³⁹ To this day, traditional medicinal plant remedies continue to be the easily accessible and most affordable source of treatment within the health-care system, with ethnobotany serving as a rich resource for natural drug research and development in African and Asian countries.^{40,41}

Plants, being living entities, possess the element of life, which is absent from artificial substances. They are capable of working in harmony with the physiological processes of the human body, supporting the normal operation of body systems and facilitating self-healing.⁴⁰ Most modern medicines are designed to suppress symptoms, and research has shown that these treatments are less effective and have more contraindications, making the use of traditional medicinal plants topical once again.³⁹

A medicinal plant is any plant with one or more of its parts or organs containing substances that can be exploited for therapeutic purposes. They are also defined as any plants that are precursors in the synthesis of medicinal drugs for the treatment of various diseases.⁴² Naturally, plants produce metabolites that are not food but are essential to their defense mechanism to protect themselves from harmful insects, pathogenic microbes, and unfavorable environmental changes.⁴² These metabolites are responsible for the medicinal value of these plants and

exhibit physiological effects on people.⁴³ These metabolites are collectively known as phytochemicals (Figure 1).

Phytochemicals are naturally occurring chemical compounds that are biologically active and highly beneficial to human health. Based on their roles in plant metabolism, they are classified as primary metabolites (proteins, sugars, pyrimidines, and purines of nucleic acids, amino acids, and chlorophylls) and secondary metabolites (flavonoids, phytosterols, saponins, alkaloids, phenolics, terpenes, curcumins, glucosides, lignans, and anthraquinones) (Figure 2).^{40,43,44} Phytochemicals can be found in fruits, vegetables, plant-based beverages, and cereal grains. These compounds accumulate in plant parts such as stems, roots, flowers, leaves, and seeds, and they are often concentrated in the outer layers of various plant tissues.⁴⁴ The levels of phytochemicals vary from plant to plant depending on growing conditions, variety, processing, and cooking. Due to the specific properties of phytochemicals, medicinal plants play indispensable roles in people's daily lives and serve as complements or potential substitutes for modern medical treatments.⁴⁰

Phytochemicals can provide direct or indirect defensive mechanisms against harmful ailments or pathogens due to their anticarcinogenic, antimicrobial, antimutagenic, anti-inflammatory, antigenotoxic, anthelmintic, antioxidative, and antiproliferative properties (Figure 2).^{43,44} The consumption of phytochemicals is associated with a decrease in risks of many different types of chronic diseases owing to their free radical scavenging effects and antioxidant properties. A recent review highlighted the potential roles of phytochemicals in increased blood flow and improved endothelial function, supporting the idea that plants containing phytochemicals may beneficially supplement the needs required by the human body.⁴⁴

Phytochemicals offer diverse medical benefits across different health domains. For example, flavonoids and polyphenols exhibit anti-inflammatory and antioxidant properties that can accelerate the healing of wounds. Flavonoids and carotenoids also possess anti-cancer properties, inhibiting the growth of cancer cells by suppressing the formation of tumors and inducing apoptosis.⁴⁵ In oral health, phytochemicals found in plants, such as tea tree oil, contribute to oral health by exhibiting antimicrobial properties that inhibit the growth of bacteria that may potentially cause oral infections.⁴⁶ Certain phytochemicals, such as those in spices and herbs, possess neuroprotective properties. These phytochemicals can mitigate oxidative stress, nerve damage, or other conditions involving neuropathy. Phytochemicals, including quercetin and resveratrol, possess potential positive effects on metabolism, influencing insulin sensitivity, contributing

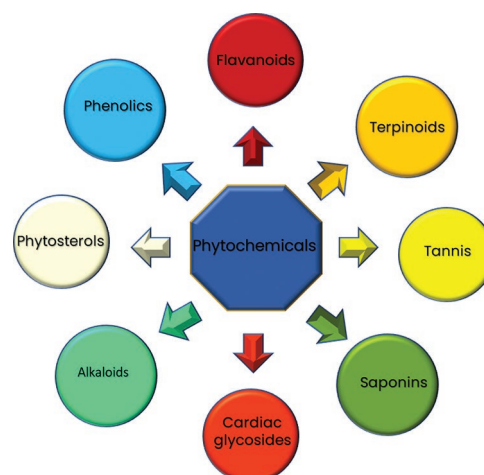


Figure 1. The main phytochemical components present in medicinal plants⁴³

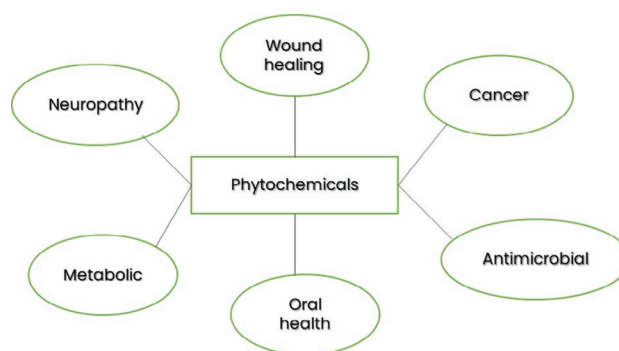


Figure 2. Medical benefits of phytochemicals from medicinal plants.⁴³ Phytochemicals derived from plants contribute to medical benefits due to their diverse bioactive properties, ranging from anti-inflammatory and antioxidant effects to neuroprotective and antimicrobial actions. These properties make phytochemicals valuable in promoting health and addressing various medical issues.

to overall metabolic balance, and regulating blood sugar levels.⁴⁵

5. Medicinal plants with anti-diabetic activity

The use of medicinal plants for healing, treatment, and management of diseases has been extensively explored as an alternative with minimum side effects and lower cost. Here, we focus on medicinal plants readily accessible and known for their anti-diabetic properties with minimal side effects (Table 2).

5.1. *Cinnamomum verum*

Cinnamon, one of the most common spices used in our daily lives, contains active components, such as cinnamate, associated with numerous health benefits. Studies have demonstrated that cinnamon has a 20-fold higher insulin-potentiating effect

compared to many other spices.⁴⁷ In addition, cinnamon contains polyphenols that exhibit anti-diabetic properties, such as regulating glucose levels and repairing pancreatic β -cells responsible for insulin production.⁴⁸

5.2. *Momordica charantia* L.

M. charantia L. has been used as an herbal medicine for years due to its biological properties, such as anti-diabetic, antioxidant, and anti-tumor effects. A study by Oguntibeju⁴⁹ on charantin-rich extract for T1DM and T2DM proved that charantin-rich extract increases plasma glucose tolerance. It was suggested that charantin-rich extract could improve insulin sensitivity in individuals with T2DM, rather than protect patients with T1DM from β -cell abnormalities.⁵⁰

5.3. *Syzygium cumini* (L.) Skeels

The bark and the leaf extract of *S. cumini* have demonstrated the potential for significantly lowering blood glucose levels, as evidenced by the increased volume and size of the pancreatic islets observed in the treated diabetic rats.⁴⁷ In addition, the flavonoid-rich extract obtained from the seed of *S. cumini* has been associated with increased insulin sensitivity and a decrease in triglycerides and low-density lipoprotein (LDL) levels.⁵¹

5.4. *Ocimum tenuiflorum* L.

O. tenuiflorum, considered one of the holy and important medicinal herbs for diabetes treatment, has demonstrated that the oil extracted from its leaves significantly lowers blood glucose levels while concurrently increasing insulin levels.⁵² Over an 8-week period, oral treatment of *Ocimum sanctum* aqueous extract in conjunction with diet significantly lowered serum lipid profiles, lipid peroxidation, and fasting blood glucose levels, while also improving glucose tolerance. Studies in rats found that ethanol, butanol, aqueous, and ethyl acetate fractions of *Ocimum sanctum* induced insulin secretion from the impaired rat pancreas and isolated rat islets, as well as from clonal pancreatic β -cells.⁵³

5.5. *Zingiber officinale* Roscoe

Z. officinale, commonly known as ginger, is considered one of the most common species with several health benefits. Ginger rhizomes have been traditionally used to treat diabetes, fever, toothache, and muscular aches.⁵⁴ According to Gayar *et al.*,⁵⁵ taking a supplement of powdered ginger 3 times a day for 3 months can improve glycemic index and antioxidant activity in T2DM. In addition, a similar study by Ebrahimzadeh *et al.*⁵⁶ found that taking a ginger supplement twice a day can decrease insulin levels without any significant changes in fasting plasma glucose.

5.6. *Allium sativum*

The precursor of allium and garlic oil, S-allyl cysteine sulfoxide, has a higher level of molecular peroxidation regulation than glibenclamide and hormone due to the presence of amino alkanolic acid. A study conducted in 2021⁵⁷ revealed that juice and oil extracts from *A. sativum* reduced blood glucose levels by restoring insulin secretion from the pancreas cells.

5.7. *Coriandrum sativum*

In a review by Paari and Pari,⁵⁸ the stem and leaf extract of coriander demonstrated the ability to improve the antioxidant effects. Sobhani *et al.*⁵⁹ found that the aqueous extract of coriander seeds can normalize decreasing blood glucose levels and increase insulin production from β -cells of pancreatic islets. Diabetic rats induced by streptozotocin demonstrated reduced serum glucose levels and increased insulin-releasing capacity of pancreatic islet β -cells when administered coriander seed ethanol extract (200 mg/kg body weight).⁶⁰

5.8. *Aegle marmelos* (L.) Correa

The fruit of *A. marmelos* is commonly used in various traditional medicinal practices, such as laxatives and the treatment of dysentery, peptic ulcers, and chronic diarrhea.⁶¹ The Tripuri tribe of North East India consumes the juice of this fruit daily on an empty stomach to treat gastrointestinal issues.⁶² The leaf paste is also used to treat high malaria fever. In a study where *A. marmelos* fruit extract was administered orally, twice daily for 4 weeks, at a dose of 250 mg/kg body weight, a significant reduction in blood sugar levels was observed in streptozotocin-induced diabetic Wistar rats. In a complementary study,⁶³ the water-soluble fruit extract was found to protect the pancreatic system by partially reversing the damage caused to pancreatic islets by streptozotocin. It was discovered that rats with mild diabetes and sub-diabetes demonstrated enhanced glucose tolerance.⁶⁴ *A. marmelos* water-soluble fruit extract has been shown to restore the function of pancreatic β -cells and enhance insulin sensitivity by upregulating peroxisome proliferator-activated receptor- γ (PPAR- γ) expression.⁶⁵

5.9. *Murraya koenigii* (L.) Spreng

In streptozotocin-induced diabetic rats, *Murraya koenigii* has been shown to significantly affect postprandial blood glucose levels and insulin sensitivity through koenidine, a metabolically stable alkaloid.⁶⁶ Insulin-resistant mice resulting from dexamethasone treatment showed improvements in insulin sensitivity and glucose

tolerance. Male albinos administered 150 mg/kg body weight of *M. koenigii* ethanolic extract orally for 30 days showed increases in insulin, C-peptide, hemoglobin, and protein levels, along with a decrease in blood glucose and glycosylated hemoglobin.^{67,68} The inclusion of inorganic trace elements in *M. koenigii* leaf extracts may be beneficial in managing glucose tolerance disorders and may play an indirect role in the management of DM. These trace elements include zinc, copper, chromium-vanadium, nickel, iron, sodium, and potassium.

5.10. *Phyllanthus emblica*

P. emblica's high polyphenol content, mostly composed of tannin and flavonoid components, provides the majority of its health advantages. This plant is known to help control blood sugar levels and enhance glucose metabolism, in addition to possessing a variety of anti-inflammatory and anti-cancer effects.⁶⁹ In addition, it stimulates insulin production in the pancreas and the growth of β -cells. Diabetic participants who consumed a daily dose of 3 g of *P. emblica* powder demonstrated a significant reduction in total lipids and LDL cholesterol levels, accompanied by an improvement in high-density lipoprotein cholesterol.⁷⁰ In Wistar rats with T1DM, an improvement in hyperglycemia, oxidative stress, and hyperlipidemia was observed when they were given 1 ml of fruit juice per kg body weight orally every day for 8 weeks.⁷⁰ Furthermore, the cardiovascular function of streptozotocin-induced diabetic Wistar rats was improved by strengthening the antioxidant defense systems in the cardiac tissues.⁷¹ Studies have shown that when the aqueous fruit extract of this plant is administered intraperitoneally to diabetic rats induced with alloxan, blood glucose levels significantly decrease. In addition,

the extract induces hypotriglyceridemia in diabetic rats by lowering triglyceride levels. The aqueous extract was found to improve liver functioning by normalization of the activity of alanine transaminase, a liver-specific enzyme.⁷² Some of the medicinal plants are listed in Table 3 with their main phytochemical components.

6. Anti-diabetic mechanism of natural phenolic compounds

Non-flavonoid phenolics consist of two basic carbon frameworks: hydroxycinnamic and hydroxybenzoic.⁷³ These structures can be divided into four groups: phenolic acids, quinines, stilbenes, and coumarins. Phenolic compounds have been investigated for their antimicrobial properties as well as their nutritional value and potential anti-diabetic effects. Some studies have suggested that phenolics offer nutritional benefits and could aid in managing diabetes.⁷⁴ However, further research is required to validate these findings, especially involving human subjects, as there is limited information about the benefits of pure compounds or diets enriched with phenolics. Cinnamic acid has been shown to enhance the activity of several enzymes, including lipase and angiotensin-converting enzyme, and to reduce the risk of heart and arterial issues in rats fed high-fat diets.⁷⁴

Furthermore, cinnamic acid has been demonstrated to reduce triglyceride and cholesterol levels in rats on a high-cholesterol diet by blocking the actions of acyl-coenzyme A: cholesterol acyltransferases and β -hydroxy β -methylglutaryl-CoA reductase. In addition, it has been discovered to increase AMP-activated protein kinase phosphorylation and adiponectin production,

Table 3. Medicinal plants with anti-diabetic activity

Plant name	Useful plant part(s)	Main phytochemical components	Activity	References
<i>Annona squamosa</i> L.	Leaves and fruit	Flavonoids; alkaloids	Anti-diabetic	78,79
<i>Cocos nucifera</i> L.	Coconut water and drupe	Polyphenols; flavonoids; fatty acids	Antiglycation	80
<i>Curcuma longa</i> L.	Rhizome	Turmerones; curcuminoids	Antioxidant and anti-diabetic	81
<i>Embelia ribes</i> Burm. F.	Berries	Quinone derivatives; embelin	Anti-diabetic	82
<i>Mangifera indica</i> L.	Leaves and fruit	Polyphenols; flavonoids; mangiferin	Anti-diabetic	83
<i>Olea europaea</i> L.	Leaves	Flavonoids; hydroxytyrosol	Anti-hyperglycemic	84
<i>Swertia chirayita</i> (Roxb.)	Whole plant	Xanthones; amarogentin	Anti-diabetic	85
<i>Punica granatum</i> L.	Leaves and fruit	Ellagic acid; anthocyanins	Anti-diabetic	86
<i>Phyllanthus niruri</i>	Aerial parts	Flavonoids; phyllanthin	Anti-diabetic	87
<i>Memecylon umbellatum</i> Burm. F.	Leaves	Ursolic acid; flavonoids, betulinic acid	Anti-diabetic	88

enhancing insulin sensitivity to a degree similar to that of the conventional drug glibenclamide.⁷⁵ Interestingly, hydroxycinnamic acid, a derivative of cinnamic acid, has been demonstrated to inhibit protein tyrosine phosphatase 1B, a major negative regulator of the insulin signaling pathway. Therefore, cinnamic acid appears to possess anti-diabetic, anti-hypertensive, and anti-obesity properties.⁷⁶

Gallic acid may have anti-diabetic effects, as suggested by research on its effects on adipocyte differentiation and adiponectin secretion.⁷⁷ It has been shown to increase the expression of PPAR- γ target proteins and fatty acid binding protein-4, both associated with adipocyte differentiation. In addition, it exhibits antioxidant effects that may be beneficial in reducing oxidative stress and depressive symptoms.

7. Conclusion and future perspectives

The increasing prevalence of diabetes highlights the urgent need for efficient treatment. Medicinal plants have been proposed as potential therapeutic agents for various types of diabetes, supported by both conceptual and empirical data. Clinical investigations have validated the use of phytochemicals derived from naturally occurring plants in the treatment of diabetes. This review summarizes certain medicinal plants with known anti-diabetic properties, proposing that further research is desperately needed to explore additional natural plants with potential anti-diabetic properties and to identify new avenues for future research.

Acknowledgments

None.

Funding

None.

Conflict of interest

The authors declare that they have no competing interests.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

Not applicable.

References

1. Cole JB, Florez JC. Genetics of diabetes mellitus and diabetes complications. *Nat Rev Nephrol.* 2020;16(7):377-390.

doi: 10.1038/s41581-020-0278-y

2. Poznyak A, Grechko AV, Poggio P, Myasoedova VA, Alfieri V, Orekhov AN. The diabetes mellitus-atherosclerosis connection: The role of lipid and glucose metabolism and chronic inflammation. *Int J Mol Sci.* 2020;21(5):1835.
doi: 10.3390/ijms21051835
3. Furman BL, Candasamy M, Bhattamisra SK, Veetil SK. Reduction of blood glucose by plant extracts and their use in the treatment of diabetes mellitus; discrepancies in effectiveness between animal and human studies. *J Ethnopharmacol.* 2020;247:112264.
doi: 10.1016/j.jep.2019.112264
4. Dilworth L, Facey A, Omoruyi F. Diabetes mellitus and its metabolic complications: The role of adipose tissues. *Int J Mol Sci.* 2021;22(14):7644.
doi: 10.3390/ijms22147644
5. Tkinson MA, Campbell-Thompson M, Kusmartseva I, Kaestner KH. Organisation of the human pancreas in health and in diabetes. *Diabetologia.* 2020;63:1966-1973.
doi: 10.1007/s00125-020-05203-4
6. Richardson A, Park WG. Acute pancreatitis and diabetes mellitus: A review. *Korean J Intern Med.* 2021;36(1):15-24.
doi: 10.3904/kjim.2020.020
7. Chen J, Ning C, Mu J, Li D, Ma Y, Meng X. Role of Wnt signaling pathways in type 2 diabetes mellitus. *Mol Cell Biochem.* 2021;476:2219-2232.
doi: 10.1007/s11010-021-04090-2
8. World Health Organization. *Classification of Diabetes Mellitus*; 2019. Available from: <https://apps.who.int/iris/handle/10665/325182> [Last accessed on 2024 Jul 09].
9. Latha S, Kumar R. The facts about diabetes mellitus-a review. *Galore Int J Health Sci Res.* 2019;4:2456-9321.
10. Alamgir AN. Biotechnology, *in vitro* production of natural bioactive compounds, herbal preparation, and disease management (treatment and prevention). In: *Therapeutic Use of Medicinal Plants and their Extracts*. Vol. 2. Germany: Springer; 2018. p. 585-664.
11. Bacanlı M, Dilsiz SA, Başaran N, Başaran AA. Effects of phytochemicals against diabetes. *Adv Food Nutr Res.* 2019;89:209-238.
doi: 10.1016/bs.afnr.2019.03.004
12. Bellary S, Kyrou I, Brown JE, Bailey CJ. Type 2 diabetes mellitus in older adults: Clinical considerations and management. *Nat Rev Endocrinol.* 2021;17(9):534-548.
doi: 10.1038/s41574-021-00497-9
13. Szmulowicz ED, Josefson JL, Metzger BE. Gestational diabetes mellitus. *Endocrinol Metab Clin North Am.* 2019;48(3):479-493.

- doi: 10.1016/j.ecl.2019.05.001
14. McIntyre HD, Catalano P, Zhang C, Desoye G, Mathiesen ER, Damm P. Gestational diabetes mellitus. *Nat Rev Dis Primers*. 2019;5(1):47.
doi: 10.1038/s41572-019-0098-8
 15. Jang KM. Maturity-onset diabetes of the young: Update and perspectives on diagnosis and treatment. *Yeungnam Univ J Med*. 2020;37(1):13-21.
doi: 10.12701/yujm.2020.00082
 16. Yahaya TO, Ufuoma SB. Genetics and pathophysiology of maturity-onset diabetes of the young (MODY): A review of current trends. *Oman Med J*. 2020;35(3):e126.
doi: 10.5001/omj.2020.52
 17. Broome DT, Pantalone KM, Kashyap SR, Philipson LH. Approach to the patient with MODY-monogenic diabetes. *J Clin Endocrinol Metab*. 2021;106(1):237-250.
doi: 10.1210/clinem/dgaa701
 18. Beltrand J, Busiah K, Vaivre-Douret L, et al. Neonatal diabetes mellitus. *Front Pediatr*. 2020;8:540718.
doi: 10.3389/fped.2020.540718
 19. Zübarioğlu AU, Bülbül A, Uslu HS. Neonatal diabetes mellitus. *Med Bull Sisli Etfal Hosp*. 2018;52(2):71-78.
doi: 10.14744/SEMB.2017.87947
 20. Lemelman MB, Letourneau L, Greeley SA. Neonatal diabetes mellitus: An update on diagnosis and management. *Clin Perinatol*. 2018;45(1):41-59.
doi: 10.1016/j.clp.2017.10.005
 21. Bhattamisra SK, Siang TC, Rong CY, et al. Type-3c diabetes mellitus, diabetes of exocrine pancreas-an update. *Curr Diabetes Rev*. 2019;15(5):382-394.
doi: 10.2174/1573399815666190425095441
 22. American Diabetes Association Professional Practice Committee. Classification and diagnosis of diabetes: Standards of medical care in diabetes-2022. *Diabetes Care*. 2022;45:S17-S38.
doi: 10.2337/dc22-sint
 23. Davies S. Latent autoimmune diabetes in adults (LADA): What do primary care professionals need to know? *J Diabetes Nurs*. 2021;25(3):JDN191.
 24. Buzzetti R, Tuomi T, Mauricio D, et al. Management of latent autoimmune diabetes in adults: A consensus statement from an international expert panel. *Diabetes*. 2020;69(10):2037-2047.
doi: 10.2337/db20-0691
 25. Shaikh AA, Kolhatkar MK, Sopane DR, Thorve AN. Review on: Diabetes mellitus is a disease. *Int J Res Pharm Sci*. 2022;13(1):102-109.
 26. Sapra A, Bhandari P. Diabetes mellitus. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing; 2022. Available from: <https://www.ncbi.nlm.nih.gov/books/nbk554495> [Last accessed on 2024 Jul 09].
 27. Karokaro TM, Erika R. The effect of modern dressing treatment on wound healing process of diabetes mellitus. *J Keg Gizi (JKG)*. 2023;5(2):235-240.
doi: 10.35451/jkg.v5i2.1663
 28. Padhi S, Nayak AK, Behera A. Type II diabetes mellitus: A review on recent drug-based therapeutics. *Biomed Pharmacother*. 2020;131:110708.
doi: 10.1016/j.biopha.2020.110708
 29. Dhankhar S, Chauhan S, Mehta DK, et al. Novel targets for potential therapeutic use in Diabetes mellitus. *Diabetol Metab Syndr*. 2023;15(1):17.
doi: 10.1186/s13098-023-00744-6
 30. Dhirani, D, Shahid A, Mumtaz H. A new kind of diabetes medication approved by the FDA: Is there hope for obesity? *Int J Surg*. 2023;109(2):81-82.
doi: 10.1016/j.ijsu.2023.05.064
 31. Yu C, Cui M, Yin Y, et al. Influence of Gegenqinlian decoction on pharmacokinetics and pharmacodynamics of saxagliptin in type 2 diabetes mellitus rats. *Biopharm Drug Dispos*. 2023;44:396-405.
doi: 10.1002/bdd.2376
 32. Liu J, Wei L, Wang Z, et al. Protective effect of Liraglutide on diabetic retinal neurodegeneration via inhibiting oxidative stress and endoplasmic reticulum stress. *Neurochem Int*. 2020;133:104624.
doi: 10.1016/j.neuint.2019.104624
 33. Mirabelli M, Chiefari E, Caroleo P, et al. Long-term effectiveness of liraglutide for weight management and glycemic control in type 2 diabetes. *Int J Environ Res Public Health*. 2020;17(1):207.
doi: 10.3390/ijerph17010207
 34. Neeland IJ, Marso SP, Ayers CR, et al. Effects of liraglutide on visceral and ectopic fat in adults with overweight and obesity at high cardiovascular risk: A randomised, double-blind, placebo-controlled, clinical trial. *Lancet Diabetes Endocrinol*. 2021;9(9):595-605.
doi: 10.1016/S2213-8587(21)00175-2
 35. Zhao X, Huang K, Zheng M, Duan J. Effect of liraglutide on blood pressure: A meta-analysis of liraglutide randomized controlled trials. *BMC Endocr Disord*. 2019;19:4.
doi: 10.1186/s12902-019-0362
 36. Jacob B, Narendhirakannan RT. Role of medicinal plants in the management of diabetes mellitus: A review. *3 Biotech*. 2019;9:4.
doi: 10.1007/s13205-019-1982-4

37. Salehi B, Ata A, Anil Kumar NV, *et al.* Antidiabetic potential of medicinal plants and their active components. *Biomolecules*. 2019;9(10):551.
doi: 10.3390/biom9100551
38. Wadekar AB, Nimbalwar MG, Panchale WA, Gudalwar BR, Manwar JV, Bakal RL. Morphology, phytochemistry and pharmacological aspects of *Carica papaya*, a review. *GSC Biol Pharm Sci*. 2020;14(3):234-248.
doi: 10.30574/gscbps.2020.14.3.0314
39. Awuchi CG. Medicinal plants: The medical, food, and nutritional biochemistry and uses. *Int J Adv Acad Res*. 2019;5(11):220-241.
doi: 10.21474/IJAA-NOV-2019-05
40. Agidew MG. Phytochemical analysis of some selected traditional medicinal plants in Ethiopia. *Bull Natl Res Cent*. 2022;46(1):87.
doi: 10.1186/s42269-022-00611-8
41. Applequist WL, Brinckmann JA, Cunningham AB, *et al.* Scientists' warning on climate change and medicinal plants. *Planta Med*. 2020;86(1):10-18.
doi: 10.1055/a-1060-1475
42. Ullah R, Alqahtani AS, Noman OM, Alqahtani AM, Ibenmoussa S, Bourhia M. A review on ethno-medicinal plants used in traditional medicine in the Kingdom of Saudi Arabia. *Saudi J Biol Sci*. 2020;27(10):2706-2718.
doi: 10.1016/j.sjbs.2020.06.019
43. Bansal A, Priyadarsini C. *Medicinal Properties of Phytochemicals and their Production*. London: IntechOpen; 2021.
44. Kumar Sharma D, Shah KR, Dave RS. Phytochemicals: Promising potential uses in pharmacology. In: *Recent Trends in Pharmaceutical Sciences*. Ch. 6. India: JPS Scientific Publications; 2019.
45. Qadir A, Jahan S, Aqil M, *et al.* Phytochemical-based nano-pharmacotherapeutics for management of burn wound healing. *Gels*. 2021;7(4):209.
doi: 10.3390/gels7040209
46. Kumar M, Prakash S, Kumari N, *et al.* Beneficial role of antioxidant secondary metabolites from medicinal plants in maintaining oral health. *Antioxidants (Basel)*. 2021;10(7):1061.
doi: 10.3390/antiox10071061
47. Przeor M. Some common medicinal plants with antidiabetic activity, known and available in Europe (a mini-review). *Pharmaceuticals (Basel)*. 2022;15(1):65.
doi: 10.3390/ph15010065
48. Alqahtani AS, Ullah R, Shahat AA. Bioactive constituents and toxicological evaluation of selected antidiabetic medicinal plants of Saudi Arabia. *Evid Based Complement Alternat Med*. 2022;2022:7123521.
doi: 10.1155/2022/4435351
49. Oguntibeju OO. Hypoglycaemic and anti-diabetic activity of selected African medicinal plants. *Int J Physiol Pathophysiol Pharmacol*. 2019;11(6):224-237.
50. Mohammed A, Tajuddeen N. Antidiabetic compounds from medicinal plants traditionally used for the treatment of diabetes in Africa: A review update (2015-2020). *S Afr J Bot*. 2022;146:585-602.
doi: 10.1016/j.sajb.2021.07.003
51. Qamar M, Akhtar S, Ismail T, *et al.* Phytochemical profile, biological properties, and food applications of the medicinal plant *Syzygium cumini*. *Foods*. 2022;11(3):378.
doi: 10.3390/foods11030378
52. Martiz RM, Patil SM, Thirumalapura Hombegowda D, *et al.* Phyto-computational intervention of diabetes mellitus at multiple stages using isoeugenol from *Ocimum tenuiflorum*: A combination of pharmacokinetics and molecular modelling approaches. *Molecules*. 2022;27(19):6222.
doi: 10.3390/molecules27196222
53. Sajal H, Patil SM, Raj R, Shbeer AM, Ageel M, Ramu R. Computer-aided screening of phytoconstituents from *Ocimum tenuiflorum* against diabetes mellitus targeting DPP4 inhibition: A combination of molecular docking, molecular dynamics, and pharmacokinetics approaches. *Molecules*. 2022;27(16):5133.
doi: 10.3390/molecules27165133
54. Abdi T, Mahmoudabady M, Marzouni HZ, Niazmand S, Khazaei M. Ginger (*Zingiber Officinale* Roscoe) extract protects the heart against inflammation and fibrosis in diabetic rats. *Can J Diabetes*. 2021;45(3):220-227.
doi: 10.1016/j.cjcd.2021.01.011
55. El Gayar MH, Aboromia MM, Ibrahim NA, Hafiz MH. Effects of ginger powder supplementation on glycemic status and lipid profile in newly diagnosed obese patients with type 2 diabetes mellitus. *Obes Med*. 2019;14:100094.
doi: 10.1016/j.obmed.2019.100094
56. Ebrahimzadeh A, Ebrahimzadeh A, Mirghazanfari SM, Hazrati E, Hadi S, Milajerdi A. The effect of ginger supplementation on metabolic profiles in patients with type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials. *Complement Ther Med*. 2022;65:102802.
doi: 10.1016/j.ctim.2022.102802
57. Anaeigoudari A, Safari H, Khazdair MR. Effects of *Nigella sativa*, *Camellia sinensis*, and *Allium sativum* as food additives on metabolic disorders, a literature review. *Front Pharmacol*. 2021;12:762182.

- doi: 10.3389/fphar.2021.762182
58. Paari E, Pari L. Role of some phytochemicals in the management of diabetes mellitus: A review. *J Med Pract Rev*. 2019;3(4):515-520.
 59. Sobhani Z, Mohtashami L, Amiri MS, Ramezani M, Emami SA, Simal-Gandara J. Ethnobotanical and phytochemical aspects of the edible herb *Coriandrum sativum* L. *J Food Sci*. 2022;87(4):1386-1422.
doi: 10.1111/1750-3841.17233
 60. Sen DB, Balaraman R, Sen AK, Zanwar AS, Greeshma KP, Maheshwari RA. *Anti-Diabetic Activity of Herbal Remedies*. 2023; 373-381.
 61. Nigam V, Nambiar VS. *Aegle marmelos* leaf juice as a complementary therapy to control type 2 diabetes-randomised controlled trial in Gujarat, India. *Adv Integr Med*. 2019;6(1):11-22.
doi: 10.1016/j.aimed.2018.07.003
 62. Birudu RB, Pamulapati P, Manoharan SK. Evaluation of biochemical changes in diabetic rats treated with *Aegle marmelos* (L.) methanolic leaf extract. *Pharmacogn Res*. 2020;12(2):127-130.
doi: 10.4103/pr.pr_53_19
 63. Murthy HN, Bhat MA, Dalawai D. Bioactive compounds of bael (*Aegle marmelos* (L.) correa). In: *Bioactive Compounds in Underutilized Fruits and Nuts*. New York City: Springer International Publishing; 2020. p. 459-486.
doi: 10.1016/B978-0-12-816490-3.00023-1
 64. Kim HS, Lee D, Seo YH, et al. Chemical constituents from the roots of *Angelica reflexa* that improve glucose-stimulated insulin secretion by regulating pancreatic β -cell metabolism. *Pharmaceutics*. 2023;15(4):1239.
doi: 10.3390/pharmaceutics15041239
 65. Ghosh D, Mukherjee PK, editors. *Natural Medicines: Clinical Efficacy, Safety and Quality*. United States: CRC Press; 2019. Available from: <https://www.crcpress.com/natural-medicines-clinical-efficacy-safety-and-quality/ghosh-mukherjee/p/book/9781138745497> [Last accessed on 2024 Jul 09].
 66. Bhupatiraju L, Bethala K, Goh KW, et al. Influence of *Murraya koenigii* extract on diabetes induced rat brain aging. *J Med Life*. 2023;16(2):307-316.
doi: 10.25122/jml-2022-0151
 67. Abeysinghe DT, Alwis DD, Kumara KA, Chandrika UG. Nutritive importance and therapeutic uses of three different varieties (*Murraya koenigii*, *Micromelum minutum*, and *Clausena indica*) of curry leaves: An updated review. *Evid Based Complement Alternat Med*. 2021;2021:5523252.
doi: 10.1155/2021/3649062
 68. Upadhye MC, Deokate UA, Pujari RR. Antidiabetic effect of ethanolic extract of *Murraya koenigii* (Linn.) stem bark in alloxan induced diabetic rats. *Int J Pharmacogn*. 2019;6(6):193-201.
 69. Ahmad B, Hafeez N, Rauf A, et al. *Phyllanthus emblica*: A comprehensive review of its therapeutic benefits. *S Afr J Bot*. 2021;138:278-310.
doi: 10.1016/j.sajb.2020.10.003
 70. Fruit AW. 17 Indian Gooseberry (*Phyllanthus emblica*). In: *Asian Berries: Health Benefits*. United States: CRC Press; 2020. p. 343.
 71. Sharma P, Joshi T, Joshi T, Chandra S, Tamta S. *In silico* screening of potential antidiabetic phytochemicals from *Phyllanthus emblica* against therapeutic targets of type 2 diabetes. *J Ethnopharmacol*. 2020;248:112268.
doi: 10.1016/j.jep.2019.112268
 72. Huang HZ, Qiu M, Lin JZ, et al. Potential effect of tropical fruits *Phyllanthus emblica* L. for the prevention and management of type 2 diabetic complications: A systematic review of recent advances. *Eur J Nutr*. 2021;60:3525-3542.
doi: 10.1007/s00394-021-02621-3
 73. Dabur R, Sharma B, Mittal A. Mechanistic approach of anti-diabetic compounds identified from natural sources. *Chem Biol Lett*. 2018;5(2):63-99.
doi: 10.17795/cbl.31043
 74. Mutha RE, Tatiya AU, Surana SJ. Flavonoids as natural phenolic compounds and their role in therapeutics: An overview. *Future J Pharm Sci*. 2021;7:25.
doi: 10.1186/s43094-021-00176-6
 75. Saikat AS, Hossain R, Mina FB, et al. Antidiabetic effect of garlic. *Rev Bras Farmacogn*. 2021;32:1-11.
doi: 10.1007/s43450-021-00171-2
 76. Kalhotra P, Chittepu VC, Osorio-Revilla G, Gallardo-Velazquez T. Phytochemicals in garlic extract inhibit therapeutic enzyme DPP-4 and induce skeletal muscle cell proliferation: A possible mechanism of action to benefit the treatment of diabetes mellitus. *Biomolecules*. 2020;10(2):305.
doi: 10.3390/biom10020305
 77. Behera PK, Devi S, Mittal N. Therapeutic potential of gallic acid in obesity: Considerable shift! *Obes Med*. 2022;37:100473.
doi: 10.1016/j.obmed.2022.100473
 78. Chowdhury SS, Tareq AM, Tareq SM, Farhad S, Sayeed MA. Screening of antidiabetic and antioxidant potential along with phytochemicals of *Annona* genus: A review. *Future J Pharm Sci*. 2021;7:144.
doi: 10.1186/s43094-021-00300-9
 79. Ahmed RH, Mariod AA. *Annona squamosa*: Phytochemical constituents, bioactive compounds, traditional and

- medicinal uses. In: *Wild Fruits: Composition, Nutritional Value and Products*. Germany: Springer Nature; 2019. p. 143-155.
doi: 10.5772/intechopen.87821
80. Hassan PI, Berinyuy EB. Nutritional management of diabetes mellitus: An appraisal of the role of medicinal plants. *Nat Prod Res*. 2021;1(1):1-27.
doi: 10.1016/j.npr.2021.100001
 81. Chanda S, Ramachandra TV. Phytochemical and pharmacological importance of turmeric (*Curcuma longa*): A review. *Res Rev J Pharmacol*. 2019;9(1):16-23.
doi: 10.37591/rrjph.v9i1.1164
 82. Sharma V, Gautam DN, Radu A, *et al*. Reviewing the traditional/modern uses, phytochemistry, essential oils/extracts and pharmacology of *Embelia ribes* Burm. *Antioxidants*. 2022;11(7):359.
doi: 10.3390/antiox11071359
 83. Samanta S, Chanda R, Ganguli S, Reddy AG, Banerjee J. Anti-diabetic activity of mango (*Mangifera indica*): A review. *MOJ Bioequiv Availab*. 2019;6(2):23-26.
doi: 10.15406/mojbb.2019.06.00184
 84. Idm'hand E, Msanda F, Cherifi K. Ethnopharmacological review of medicinal plants used to manage diabetes in Morocco. *Clin Phytosci*. 2020;6:1-32.
doi: 10.1186/s40816-019-0138-6
 85. Gupta R, Sood H. Optimizing nutrient media conditions for continuous production of shoot biomass enriched in major medicinal constituents, amarogentin and mangiferin of endangered medicinal herb, *Swertia chirayita*. *Vegetos*. 2023;36(3):833-841.
doi: 10.1007/s42535-022-00342-8
 86. Ranjha MM, Shafique B, Wang L, *et al*. A comprehensive review on phytochemistry, bioactivity and medicinal value of bioactive compounds of pomegranate (*Punica granatum*). *Adv Tradit Med*. 2021;1-21.
doi: 10.1007/s13596-021-00526-7
 87. Gupta M, Vaghela JS. Recent advances in pharmacological and phytochemistry studies on *Phyllanthus amarus*. *Pharm Biosci J*. 2019;7:1-8.
doi: 10.2174/25908183219991211114222
 88. Prodhan AH, Mridu FS. Antidiabetic properties of *Nymphaea* species (Water lilies): A review. *Nat Prod J*. 2023;13(1):78-112.
doi: 10.2174/2210315507666210205132344