

<https://doi.org/10.48047/AFJBS.6.15.2024.1917-1936>



African Journal of Biological Sciences

Journal homepage: <http://www.afjbs.com>



Research Paper

Open Access

Herbal Remedies and Their Pharmacological Potential in the Management of Diabetes Mellitus: A Comprehensive Review

Mr. Rishu Yadav¹, Dr. Neeru Singh^{1*}, Ms. Akansha Singh¹

¹Faculty of Pharmacy, Swami Vivekanand Subharti University, Meerut, Uttar Pradesh, India

*Corresponding Author- **Dr. Neeru Singh***

Volume 6, Issue 15, Sep 2024

Received: 15 July 2024

Accepted: 25 Aug 2024

Published: 05 Sep 2024

[doi:10.48047/AFJBS.6.15.2024.1917-1936](https://doi.org/10.48047/AFJBS.6.15.2024.1917-1936)

Abstract:

Diabetes mellitus is a long-term metabolic disease characterized by high blood glucose levels resulting from insufficient insulin production, reduced insulin secretion, or a combination of multiple reasons. The number of people exploring additional and complementary therapies, such as herbal supplements, has increased dramatically due to the rising prevalence of diabetes worldwide, especially Type 1 (which needs insulin) and Type 2 (which results in insulin resistance). A comprehensive investigation of the therapeutic potential of several common plants is conducted for the purpose of treating diabetes mellitus. It emphasizes the active bioactive chemicals, mechanisms of action, and clinical efficacy of these drug candidates. Herbal remedies for diabetes mellitus include *Momordica charantia* (bitter melon), *Trigonella foenum-graecum* (fenugreek), *Gymnema sylvestre* (gurmar), and *Ocimum sanctum* (holy basil). These herbs have the ability to regulate blood glucose levels through a variety of ways, including increasing insulin secretion, boosting insulin sensitivity, and limiting carbohydrate absorption. The review also discusses the herbal remedies' safety, efficacy, and limits, highlighting the need for additional clinical trials to establish their therapeutic potential in diabetes management.

Keywords:

Diabetes Mellitus, insulin-dependent, herbal remedies, pharmacological potential, blood glucose regulation, insulin sensitivity, bioactive compounds, complementary therapies.

Introduction:

Long-term endocrine disorders such as diabetes mellitus are defined by diminished insulin efficacy and/or an absolute or relative lack of insulin, which can result in hyperglycemia, or increased blood sugar, and disturbances in the metabolism of proteins, lipids, and carbohydrates. In India, diabetes has become a significant public health issue. A national survey conducted in urban areas in 2005 reported a 15.1% prevalence of diabetes among adults. More recent data highlight the impact of socioeconomic shifts in rural India, where diabetes

prevalence has risen from 2.4% to 6.4% over the past 15 years [1]. Traditional remedies for diabetes management have been used in India since the time of Charaka and Sushruta. Plants have long been valuable sources for drug discovery, with many modern medicines either derived from or inspired by plant compounds. Ethnobotanical research indicates that around 800 plant species may possess potential anti-diabetic properties [2]. Insulin resistance and poor glucose metabolism are hallmarks of diabetes mellitus (DM), a chronic illness that can have a number of long-term consequences. Most cases of diabetes are classified as either Type 1 or Type 2. The autoimmune destruction of pancreatic beta cells leads to insufficient insulin production, which is the cause of type 1 diabetes, commonly referred to as insulin-dependent diabetes mellitus (IDDM). Type 2 diabetes, sometimes referred to as non-insulin-dependent diabetes mellitus (NIDDM), is characterized by a combination of insulin resistance and insufficient insulin production [3]. Increased rates of obesity and changes in lifestyle are largely to blame for the rising occurrence of type 2 diabetes [4]. Microvascular problems are frequently brought on by diabetes, most notably vascular basement membrane thickening, which can harm blood vessels in the kidneys, retina, and heart. Microvascular injury, also known as microangiopathy, is a contributing factor to clinical problems such as hypertension, delayed wound healing, and decreased tissue oxygen delivery [5]. Type 1 and Type 2, the two primary types of diabetes, each have different basic mechanisms. In Type 1 diabetes, also known as insulin-dependent diabetes mellitus, the immune system inappropriately targets and kills the insulin-producing beta cells in the pancreas. Due to little to no insulin production as a result, people must rely on outside insulin to control their blood sugar levels. Conversely, the body's incapacity to react to insulin as intended characterizes Type 2 diabetes, also known as insulin-resistant diabetes mellitus. The pancreas may eventually run out of insulin, even while insulin is still generated, since over time, cells become resistant to its effects. An important symptom of insulin resistance and inadequate insulin synthesis is increased blood sugar [6].

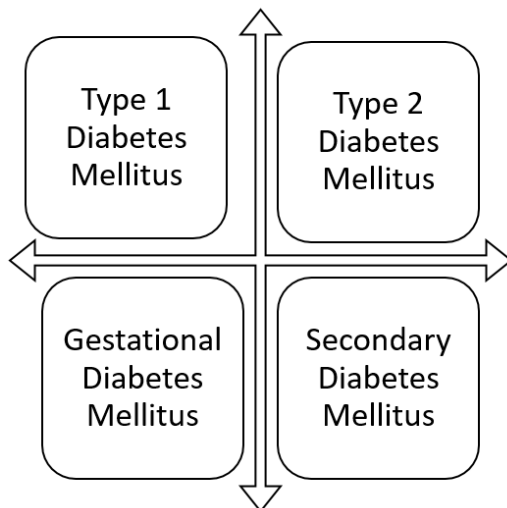


Figure No 1: Types of Diabetes Mellitus

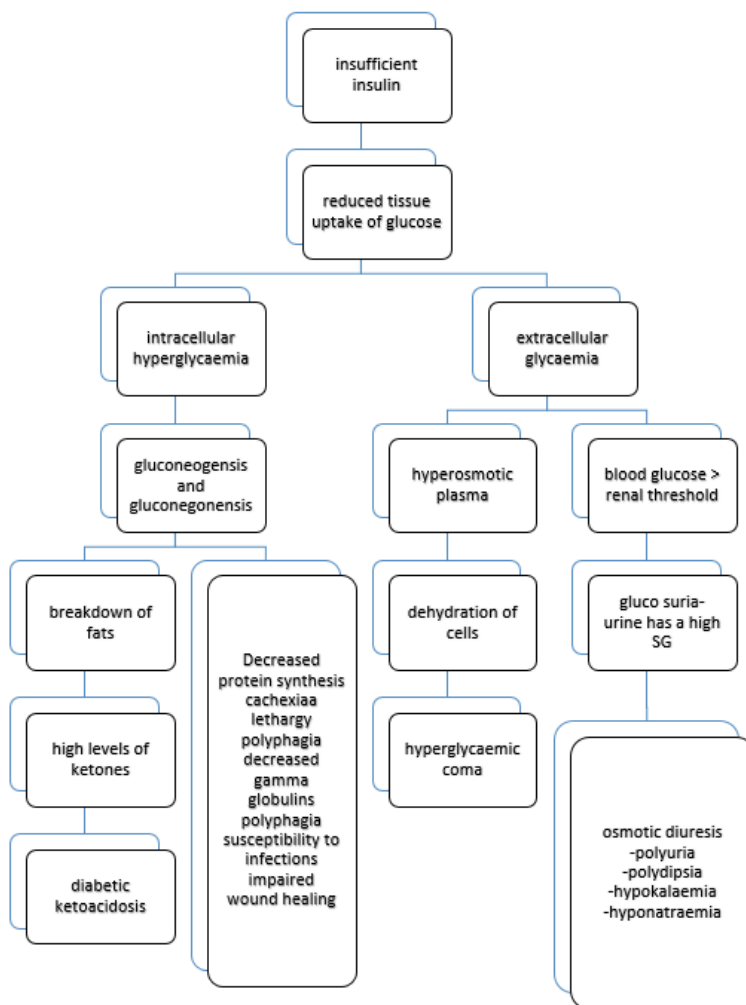


Figure No 2: Pathophysiology of Diabetes Mellitus

The body needs insulin to keep its glucose levels in check. It is created when beta cells in the pancreas, which are mostly found in the liver, muscles, and fat, absorb glucose and lower blood sugar levels. After a meal, increased blood sugar causes the release of insulin into the bloodstream, which enables cells to either use glucose for energy or store it as glycogen in the liver for use at a later time. Insulin also inhibits the liver's ability to produce glucose and stops fat from being broken down into free fatty acids, which helps to keep blood sugar levels steady and avoid hyperglycemia. Blood sugar levels rise when insulin synthesis or function is compromised, as in the case of diabetes, and this can result in a number of health issues [6, 7].

The IDF (*International Diabetes Federation*) predicts that 80% of persons with diabetes worldwide will reside in low- and middle-income nations. According to the IDF's 2011 report, there were 23.7 million diabetics in the US, 61.3 million in India, and 90.0 million in China. These numbers are projected to rise to 101.2 million in India, 29.3 million in the United States, and 129.7 million in China [7, 8].

Diabetes is linked to several systemic problems and is among the top six causes of death worldwide. Treatment for diabetes mellitus often involves glucose-lowering medications such as biguanides, thiazolidinediones, sulfonylureas, and alpha-glucosidase inhibitors, as well as hormone therapy (insulin). Drug discovery remains a key focus for academic institutions and pharmaceutical companies, as one of the primary challenges in managing systemic conditions is identifying treatments with high therapeutic efficacy and fewer side effects [8]. In the United States, 10-25% of patients experience adverse drug reactions, contributing to 3-7% of hospital admissions. [9].

Herbal Remedies in Diabetes Management:

Medicinal plants have been an important part of herbal remedies for diabetic mellitus (DM) for centuries. Ayurveda and Traditional Chinese Medicine, two traditional medicinal systems, acknowledged the usefulness of several herbs in controlling blood sugar levels and associated symptoms. Due to their hypoglycemic qualities, plants including *Trigonella foenum-graecum* (fenugreek), *Momordica charantia* (bitter melon), and *Gymnema sylvestre* were frequently utilised. In recent years, these traditional approaches have gained attention in modern scientific research [10]. The growing field of phytotherapy, which focuses on plant-based treatments, has led to numerous studies investigating the anti-diabetic potential of herbs. Modern research explores the active compounds in these plants, such as flavonoids, alkaloids, and terpenoids, that may contribute to improved insulin sensitivity, glucose metabolism, and overall glycemic

control [11-12]. This renewed interest in herbal remedies is driven by the potential to develop complementary or alternative therapies for diabetes, especially in light of the side effects associated with conventional treatments. The Zingiberaceae family, one of the largest within the Zingiberales order, includes 53 genera and over 1,200 species known for their aromatic rhizomes, which contain significant volatile compounds. In aerobic metabolism, cells generate free radicals, especially reactive oxygen species (ROS), which are regulated by an intricate internal antioxidant defense system [13-14]. An imbalance between pro-oxidants and antioxidants can lead to oxidative stress. The Zingiberaceae family comprises over 1,300 species of aromatic, perennial herbs with either spreading horizontal or tuberous rhizomes. These herbs typically feature a pseudo-stem, a single leaf, and inflorescences with distinctive shapes and colours, and their rhizomes can be bulbous or creep horizontally through the soil [15-17].

Curcuma aeruginosa

The medicinal herb *C. aeruginosa* is widely cultivated in Bangladesh, India, Myanmar, Indonesia, Malaysia, and Thailand. Its rhizome has long been used in Bangladesh to reduce rheumatic disease-related pain and inflammation. Furthermore, this plant's parts are utilized in traditional medicine to treat gastrointestinal problems like diarrhea as well as uterine pain and inflammation [18]. *C. aeruginosa* Roxb. is well-known for its variety of uses and is frequently utilized in traditional Oriental medicine. This herb has been used as a tonic, antifungal, anthelmintic, expectorant, disinfectant, and anti-inflammatory agent [19–20].

Many pharmacological characteristics of *C. aeruginosa* Roxb. have been widely employed in traditional medicine. Researchers have examined its pharmacological actions, which include uterine relaxing, anticancer, antibacterial, anti-dengue, anti-inflammatory, antiandrogenic, anti-nociceptive, antipyretic, antioxidant, and immunostimulant properties. Its antioxidant activity has been examined in studies like George and Britto using assays like nitric oxide scavenging and 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical. The rhizome of *C. aeruginosa* is widely known for its antibacterial action, however further research is needed to identify the specific bioactive antibacterial components of this plant [21–22]. Research has demonstrated that *C. aeruginosa* Roxb. essential oil functions as a chemotherapeutic agent and an immunostimulant when combined with doxorubicin therapy. This plant, which is critically endangered, holds significant ethnomedicinal value. Our research indicates that *C. aeruginosa* contains a considerable number of antioxidants, which may be indicative of its therapeutic potential. Antioxidant levels were observed to increase progressively toward mature tissues.

Furthermore, strong correlations between phenol/flavanol concentration and antioxidant activity indicate that the polyphenolic chemicals found in the plant are probably responsible for the antioxidant benefits [23–24].

Acacia arabica

For 21 days, rats with diabetes caused by streptozotocin (STZ) were administered 200 mg/kg and 100 mg/kg of the plant's bark extract orally. This resulted in elevated serum insulin levels, according to a study assessing *Acacia arabica*'s potential anti-diabetic benefits. In addition, the lipid profile improved and there was a decrease in high serum glucose and insulin resistance. The plant's flavonoid concentration, which includes quercetin, polyphenols, and tannins are thought to be responsible for its anti-diabetic effects. *Acacia arabica* extract was shown to decrease oxidative stress, cure inefficiencies in lipid metabolism, and lower plasma glucose levels in diabetic rats. After two weeks of therapy with a chloroform extract of *Acacia arabica* bark, the diabetic rats also showed significant reductions in their blood glucose levels and improvements in their cholesterol, triglyceride, HDL, and LDL levels [25–26].

Acosmium panamense

The plasma glucose levels of diabetic rats induced by streptozotocin (STZ) were reduced in three hours with the oral administration of 200 and 20 mg/kg of the aqueous extract and 100 and 20 mg/kg of the butanolic extract of *Acosmium panamense*. Following the popular diabetic medication glibenclamide, these plant extracts exhibit hypoglycemic properties [27].

Bael (Aegle marmelos (L.) Correa)

In streptozotocin-induced diabetic Wistar rats, an aqueous extract from *Aegle marmelose* fruit (125 and 250 mg/kg) administered orally twice daily for about 4 weeks headed to significant decreases in plasma thiobarbituric acid reactive substances, hydroperoxides, alpha-tocopherol, and ceruloplasmin. The levels of reduced glutathione and vitamin C in plasma both markedly rose concurrently. The extract at a dose of 250 mg/kg enhanced these parameters more successfully than glibenclamide. These results indicate the hypoglycemic properties of *Aegle marmelose* extract [28-29].

Cynomorium coccineum (Cynomoriaceae)

Studying the pharmacological properties of *Cynomorium* plants has shown a range of biological activities, many of which are backed by conventional medical procedures. These activities include antioxidant, immunity-boosting, antidiabetic, and neuroprotective benefits.

Enzymes like α -glucosidase and α -amylase are necessary for the appropriate post-meal blood sugar regulation and management of hyperglycemia. The aqueous extract of *C. coccineum* exhibited strong inhibition of α -glucosidase and moderate inhibition of α -amylase. This suggests that the extract could be used as a dietary supplement in conjunction with other therapeutic strategies to manage early-stage diabetes [30].

Avicennia marina

The ethanolic leaf extract of *A. marina* was found to successfully reduce blood glucose levels at dosages of 250 and 500 mg/kg. Serum urea levels were also reduced, which may have protective effects on important tissues including the kidneys. Serum phosphorus, albumin, and globulin levels were all improved [22]. After the roots were extracted using methanol, stigmasterol-3-O- β -D-glucopyranoside was found, which may be responsible for the antihyperglycemic action observed in *A. marina* aerial roots [31].

Caralluma sinaica (Asclepiadaceae)

The ethanolic extract of *C. sinaica* was evaluated in rabbits that had been given streptozotocin to induce diabetes. When administered at a 100 mg/kg dose, the extract demonstrated a higher blood glucose-lowering capacity than glibenclamide. Additionally, it helped to avoid hyperglycemia following an oral glucose challenge. The dose was raised from 150 to 200 mg/kg with no discernible toxic or behavioural consequences [26]. In diabetic rats, the plant extract successfully stopped weight loss and increased liver glycogen storage. These outcomes could be attributed to the extract's capacity to raise insulin levels to a sufficient level, which would lessen the impact of metabolic disorders linked to diabetes, including a breakdown of muscle proteins, lipogenesis, and glycogenesis [33].

Allium cepa L. (onion) (Liliaceae)

Onion, or *Allium cepa*, is a regularly grown crop, however related wild species can be found in Central Asia. In diabetic rabbits, a variety of ether-soluble and insoluble fractions of dried onion powder have shown antihyperglycemic benefits. The hypolipidemic and antioxidant qualities of *A. cepa* are well known. S-methyl cysteine sulfoxide (SMCS), an amino acid containing sulfur, was given to rats with diabetes made alloxan-induced at 200 mg/kg for 45 days. This resulted in a considerable reduction in serum lipid levels and blood glucose levels. Liver enzymes such hexokinase, glucose 6-phosphatase, and HMG CoA reductase are all impacted by SMCS. Furthermore, in diabetic patients, a single oral dosage of 50 grams of onion juice significantly reduced post-prandial glucose levels [34].

Garlic (*Allium sativum* L.)

India grows garlic, a perennial herb with considerable antidiabetic benefits when compared to the medication glibenclamide. Oral administration of garlic extracts significantly raised serum insulin levels in diabetic rats while reduced serum levels of urea, uric acid, creatinine, AST, ALT, glucose, total cholesterol, triglycerides, and urea. Normal rats did not exhibit these effects. Garlic may be a good choice for additional diabetes study given the extract's stronger antidiabetic effect [35].

***Aloe vera* (L) Burm. (Asphodelaceae)**

Aloe vera has significant antidiabetic and cardioprotective properties. It is a plant that grows well in dry areas and is widely distributed throughout Africa, India, and other desert places. In diabetic rats, aloe vera gel administered at a dose of 200 mg/kg dramatically lowers increased TBARS, improves glutathione levels fourfold, and restores the activity of catalase and superoxide dismutase [12]. Furthermore, the leaf pulp extract has hypoglycemic effects in rats with insulin-dependent diabetes mellitus (IDDM) as well as non-insulin-dependent diabetic mellitus (NIDDM), and it is more effective than glibenclamide at treating type II diabetes [36].

***Brassica nigra* (L) Koch (Brassicaceae)**

This weedy annual plant, which is grown for its seeds and is endemic to the southern Mediterranean region of Europe, has shown noteworthy effects on diabetic mice. For a month, the daily treatment of 200 mg/kg body weight of its aqueous extract lowers the levels of fasting serum glucose (FSG); in the untreated group, FSG stays increased. Furthermore, the rise in blood lipids and glycosylated haemoglobin (HbA1c) in the treated animals is significantly lower than in the untreated diabetic controls [37–38].

***Bumelia santorum* Mart. (Sapotaceae)**

According to Brazilian tradition, *B. santorum* can be used to cure inflammatory diseases and diabetes. Significant hypoglycemic effects are demonstrated by acid, an unsaturated tri-terpene that is extracted from the root bark of *B. santorum* using ethanol. It significantly raises plasma insulin levels and modifies the patterns of glucose tolerance in rats with alloxan-induced diabetes [39].

***Azadirachta indica* (Meliaceae)**

For testing reasons, an aqueous extract of neem leaves was administered three times a day for 25 days to rabbits with alloxan-induced diabetes. In a dose- and time-dependent way, blood

glucose levels were significantly reduced in the extract group compared to the control. In alloxan diabetic rats, neem root bark extract was also tested for hypoglycemic effects; the results showed that only the higher doses effectively lowered glucose levels. During a 4-week treatment period, the oily neem extract was also helpful in rapidly lowering blood glucose and improving glucose tolerance in alloxan diabetic rats, according to oral glucose tolerance testing [40–41].

Table No 1: Medicinal plant with reported antidiabetic effect on animal

Plant/phytoconstituent	Mechanism of action	References
Aegle marmelose	lowering its oxidative stress and reducing glutathione levels	42
Allium cepa (Onion)	antioxidant activity	43
Cinnamomum zeylanicum	controlling the uncoupling protein-1 (UCP-1) and GLUT4 translocation in the adipose and muscular tissues	44
Grewia asiatica	antioxidant and radical scavenging activity	45
Polygonati Odorati	inhibiting α -glucosidase activity	46
Zingiber officinale	Increasing glucose utilization	47
Aralia elata	Inhibit aldose-reductase activity	48
Allium sativum	Inhibit glycogen-metabolizing enzymes	49

Morus alba	lowers lipid peroxidation and protects pancreatic beta cells from degeneration.	50
Naringin	Antioxidant activity	51
Rutin	Metal chelating activity	52
Chlorogenic acid	Antioxidative activity	53
Trigonella foenumgraecum	Insulin generation and release from beta-pancreatic cells in the islets of Langerhans	54

Bioactive Compounds and Phytochemicals in Herbal Remedies:

Therapeutic management of a number of disorders, including diabetes mellitus (DM), is greatly aided by the phytochemicals and bioactive components found in herbal therapies. They exhibit a range of pharmacological properties that contribute to maintaining glucose homeostasis, improving insulin sensitivity, and protecting against diabetes-related complications [55].

Alkaloids are known for their ability to enhance insulin sensitivity and reduce blood glucose levels by inhibiting enzymes involved in glucose production. Conversely, flavonoids are potent antioxidants that lower inflammation and oxidative stress, two factors connected to the development of diabetes. They also improve insulin secretion and enhance the body's sensitivity to insulin. Saponins, with their cholesterol-lowering effects, help regulate glucose metabolism and insulin sensitivity. Tannins help maintain postprandial blood sugar levels by slowing down the digestion and absorption of carbohydrates [56]. These substances have the added benefit of lowering oxidative stress and inflammation, two major contributors to the development of diabetic complications like neuropathy and nephropathy, in addition to their ability to help control blood glucose levels. Due to these broad therapeutic actions, herbal remedies containing these phytochemicals are being increasingly studied and used as complementary treatments for diabetes management [57].

Table No 2: Phytochemicals and Bioactive Compounds in Herbal Remedies

Compound	Description	Management	Example herbs	Ref
Alkaloids	Organic compounds are often found in plants, known for their pharmacological effects.	Enhance insulin sensitivity, reduce blood glucose levels, and inhibit enzymes involved in glucose production.	<i>Berberis vulgaris</i> (berberine), <i>Catharanthus roseus</i>	[58]
Flavonoids	A group of polyphenolic compounds with antioxidant properties.	Reduce oxidative stress, improve glucose metabolism, and enhance insulin secretion and sensitivity.	<i>Camellia sinensis</i> (green tea), <i>Citrus limon</i>	[59]
Saponins	Glycosides with foaming characteristics found in various plant species.	Modulate glucose metabolism, enhance insulin sensitivity, and reduce cholesterol levels, supporting overall DM management.	<i>Trigonella foenum-graecum</i> (fenugreek), <i>Panax ginseng</i>	[60]
Tannins	Many plants include astringent polyphenols, which are well-known for their capacity to bind and precipitate proteins.	Slow carbohydrate digestion and absorption, lower postprandial blood glucose levels, and exhibit antioxidant properties.	<i>Terminalia chebula</i> , <i>Punicaceae granatum</i> (pomegranate)	[61]

Safety, Efficacy, and Limitations of Herbal Remedies:

The safety, efficacy, and limitations of herbal remedies in diabetes management are important considerations. While many herbal treatments have shown promise in controlling blood sugar

levels, they are not without risks. Toxicity and adverse effects can arise from improper use, overdose, or contamination of herbal products. Some herbs may cause gastrointestinal distress, allergic reactions, or even hepatotoxicity in sensitive individuals. Additionally, the interaction of herbal remedies with conventional diabetes medications is a significant concern. Certain herbs may potentiate or reduce the effects of prescribed medications, leading to either hypoglycemia or reduced therapeutic efficacy. For example, herbs like ginseng and fenugreek can enhance the effects of insulin or oral hypoglycemic agents, potentially causing dangerously low blood sugar levels [62].

Moreover, regulatory and standardization challenges present limitations to the widespread use of herbal remedies. Unlike conventional medications, which undergo rigorous clinical testing and are standardized for dose and purity, herbal products can vary in quality. Differences in plant species, growing conditions, and extraction methods can lead to inconsistencies in active compound concentrations. Regulatory oversight of herbal products is often less stringent, raising concerns about the quality, safety, and efficacy of these treatments. Standardization of dosage, better regulation, and more clinical trials are needed to ensure the safe and effective use of herbal remedies in diabetes management [62].

Future Directions in Herbal Diabetes Treatment:

Future directions in herbal diabetes treatment emphasize the need for more comprehensive clinical studies and standardized research methodologies. While many herbs have shown potential in managing diabetes, large-scale clinical trials are essential to validate their safety and efficacy. Standardized research that includes uniform dosing, quality control, and consistent methodologies will help establish the therapeutic value of these remedies. Additionally, emerging herbs and novel bioactive compounds are drawing attention in diabetes research. Plants such as *Berberis vulgaris* (barberry) and *Salacia reticulata* are being studied for their potential to enhance insulin sensitivity and reduce blood glucose levels. Novel bioactive compounds, including polyphenols and terpenoids, show promise in addressing insulin resistance and oxidative stress, two key factors in diabetes [63].

Moreover, there is increasing interest in integrative medicine approaches that combine herbal treatments with conventional diabetes care. Integrative strategies could provide a holistic approach to diabetes management by incorporating the benefits of herbal remedies alongside pharmaceutical interventions, lifestyle changes, and dietary adjustments. This combined approach has the potential to improve patient outcomes, reduce complications, and offer

personalized care options for individuals with diabetes. However, more research is necessary to explore these possibilities and ensure the safety and efficacy of integrative medicine in diabetes care [63].

Conclusion:

The exploration of herbal remedies for the treat diabetes mellitus (DM) offers promising insights into alternative and complementary approaches for managing this chronic disease. Diabetes, particularly type 2 diabetes, is a global health concern, with its incidence rising significantly due to lifestyle changes and increasing rates of obesity. Traditional medicinal systems such as Ayurveda, Traditional Chinese Medicine, and others have long used herbs to manage blood sugar levels and improve overall health, and these practices are now receiving scientific validation through modern research. This study reviews various aspects of the role of herbal remedies in diabetes treatment, focusing on their mechanisms of action, the bioactive compounds involved, their safety and efficacy, and future directions for research. Herbs such as *Gymnema sylvestre*, *Momordica charantia* (bitter melon), *Trigonella foenum-graecum* (fenugreek), and *Berberis vulgaris* have been recognized for their hypoglycemic properties. These herbs contain bioactive compounds, including alkaloids, flavonoids, saponins, and tannins, which help regulate blood glucose through various mechanisms. These mechanisms include enhancing insulin secretion, improving insulin sensitivity, inhibiting carbohydrate absorption, and exerting antioxidant and anti-inflammatory effects. By acting on multiple pathways involved in glucose metabolism, these phytochemicals provide comprehensive support in managing diabetes and preventing its complications. However, while herbal remedies offer potential, their use is not without risks. Toxicity and adverse effects, particularly from improper use or contamination, pose significant safety concerns. Additionally, interactions between herbal remedies and conventional diabetes medications can lead to complications, such as hypoglycemia or reduced drug efficacy. This highlights the importance of understanding both the benefits and risks of using herbal treatments alongside standard pharmaceutical interventions. One of the major limitations in the widespread adoption of herbal remedies for diabetes is the lack of rigorous, large-scale clinical trials. While many studies show positive results, most are small or conducted in animal models, making it difficult to draw definitive conclusions about the safety and efficacy of these treatments in humans. Standardization of herbal products is another challenge. Variability in plant species, growing conditions, and preparation methods can result in inconsistent levels of active compounds, which complicates dosage and treatment efficacy. Regulatory oversight of herbal products is

less stringent compared to pharmaceuticals, further contributing to these issues. Future directions in herbal diabetes treatment will require more focused clinical research and the standardization of research methodologies. More comprehensive studies, including randomized controlled trials, are needed to confirm the effectiveness of herbal remedies and ensure their safe integration into diabetes care. Emerging herbs and bioactive compounds, such as those from *Salacia reticulata* and other lesser-known plants, are opening new avenues for research. These compounds may provide novel mechanisms to improve insulin sensitivity, reduce oxidative stress, and address the underlying metabolic dysfunctions in diabetes.

The potential for integrative medicine in diabetes care is also worth exploring. By combining herbal treatments with conventional medications and lifestyle interventions, integrative approaches could offer a more holistic management strategy. This would involve careful monitoring to avoid interactions and ensure patient safety. The appeal of herbal remedies lies not only in their potential to manage blood sugar but also in their broader health benefits, including reducing inflammation and oxidative stress, which are critical factors in the development of diabetes complications like neuropathy, nephropathy, and cardiovascular diseases. In conclusion, while herbal remedies present exciting possibilities for diabetes treatment, they must be approached with caution due to the complexities of their use and the need for more thorough scientific validation. The integration of herbal remedies into conventional diabetes care, supported by rigorous research and standardization, holds promise for enhancing patient outcomes and providing more personalized and effective treatments for this growing global health challenge.

References:

1. Anonymous. Diabetes Atlas. 3rd ed. Brussels: International Diabetes Federation; 2006.
2. Puranik N, Kammar KF, Devi S. Anti-diabetic activity of *Tinospora cordifolia* (Wild.) in streptozotocin diabetic rats; does it act like sulfonylurea? *Turk J Med Sci* 2010; 40(2): 265-270.
3. Choudhury, H., Pandey, M., Hua, C. K., Mun, C. S., Jing, J. K., Kong, L., ... Kesharwani, P. (2018). An update on natural compounds in the remedy of diabetes mellitus: A systematic review. *Journal of Traditional and Complementary Medicine*, 8, 361–376. <https://doi.org/10.1016/j.jtcme.2017.08.012>.
4. Dabelea, D., Mayer-Davis, E. J., Saydah, S., Imperatore, G., Linder, B., Divers, J., ... SEARCH for Diabetes in Youth Study. (2014). Prevalence of type 1 and type 2 diabetes

- among children and adolescents from 2001 to 2009. *JAMA*, 311, 1778–1786. <https://doi.org/10.1001/jama.2014.3201>
5. Chawla, A., Chawla, R., & Jaggi, S. (2016). Microvascular and macrovascular complications in diabetes mellitus: Distinct or continuum? *Indian Journal of Endocrinology and Metabolism*, 20, 546–551. <https://doi.org/10.4103/2230-8210.183480>
 6. Zia, T., Hasnain, S. N., & Hasan, S. K. (2001). Evaluation of the oral hypoglycaemic effect of *Trigonella foenum-graecum* L. (methi) in normal mice. *Journal of Ethnopharmacology*, 75(2–3), 191–195. [https://doi.org/10.1016/S0378-8741\(01\)00186-6](https://doi.org/10.1016/S0378-8741(01)00186-6).
 7. Petchi RR, Parasuraman S, Vijaya C. Antidiabetic and antihyperlipidemic effects of an ethanolic extract of the whole plant of *Tridax procumbens* (Linn.) in streptozotocin-induced diabetic rats. *J Basic Clin Pharm* 2013; 4:88-92.
 8. Parasuraman S, Kumar E, Kumar A, Emerson S. Free radical scavenging property and diuretic effect of triglize, a polyherbal formulation in experimental models. *J Pharmacol Pharmacother* 2010; 1:38-41
 9. Javed Ahamad JA, Naquvi KJ, Mir SR, Ali M, Shuaib M. Review on role of natural alpha-glucosidase inhibitors for management of diabetes mellitus.
 10. Alam F, Shafique Z, Amjad ST, Bin Asad MH. Enzymes inhibitors from natural sources with antidiabetic activity: A review. *Phytotherapy Research*. 2019 Jan;33(1):41-54.
 11. Dehghan H, Salehi P, Amiri MS. Bioassay-guided purification of α -amylase, α -glucosidase inhibitors and DPPH radical scavengers from roots of *Rheum turkestanicum*. *Industrial Crops and Products*. 2018 Jul 1;117:303-9.
 12. Mandavi, D’Cruz S, Sachdev A, Tiwari P. Adverse drug reactions and their risk factors among Indian ambulatory elderly patients. *Indian J Med Res* 2012; 136:404-10
 13. Riserus U, Willett WC, Hu FB. Dietary fats and prevention of type-2 diabetes. *Prog Lipid Res* 2009; 48(1): 44-51
 14. Sies H. Oxidative stress: a concept in redox biology and medicine. *Redox biology*. 2015 Apr 1;4:180-3.
 15. Taylor EL, Taylor TN, Krings M. *Paleobotany: the biology and evolution of fossil plants*. Academic Press; 2009 Jan 21.
 16. Christenhusz MJ, Byng JW. The number of known plants species in the world and its annual increase. *Phytotaxa*. 2016 May 20;261(3):201-17.

17. Irayanti A, Putra AA. A narrative review of Zingiberaceae family as antibacterial agent for traditional medication based on balinese local wisdom. *Journal of Pharmaceutical Science and Application*. 2020 Dec;2(2):66-76.
18. Pitopang R, Hamzah B, Zubair MS, Amar AL, Fathurahman F, Basri Z, Poulsen AD. Diversity of Zingiberaceae and traditional uses by three indigenous groups at Lore Lindu National Park, Central Sulawesi, Indonesia. In *Journal of Physics: Conference Series* 2019 Jun 1 (Vol. 1242, No. 1, p. 012039). IOP Publishing.
19. Thaina P, Tungcharoen P, Wongnawa M, Reanmongkol W, Subhadhirasakul S. Uterine relaxant effects of *Curcuma aeruginosa* Roxb. rhizome extracts. *Journal of Ethnopharmacology*. 2009 Jan 30;121(3):433-43.
20. Atun S, Arianingrum R, Aznam N, Ab Malek SN. Isolation of sesquiterpenes lactone from *Curcuma aeruginosa* rhizome and the cytotoxic activity against human cancer cell lines. *International Journal of Pharmacognosy and Phytochemical Research*. 2016;8(7):1168-72.
21. Kartasapoetra, A.G., 1996, *Budaya Tanaman Berkhasiat Obat*, Rineka Cipta, Jakarta
22. George M, Britto SJ. Phytochemical and antioxidant studies on the essential oil of the rhizome of *Curcuma aeruginosa* Roxb. *Int. Res. J. Pharm.* 2015;6(8):573-9. References review article
23. Pangastuti A, Sari SA, Nugraheni ER, Astuti RT. Inhibition of *Pseudomonas aeruginosa* virulence factors expression regulated by quorum sensing system using ethyl acetate extract of Temu Ireng (*Curcuma aeruginosa*). In *IOP Conference Series: Materials Science and Engineering* 2020 Jun 1 (Vol. 858, No. 1, p. 012031). IOP Publishing.
24. Paramita S, Ismail S, Marlina E, Moerad EB. Anti-inflammatory activities of *Curcuma aeruginosa* with membrane stabilization and carrageenan-induced paw oedema test. *EurAsian Journal of BioSciences*. 2019;13(2):2389-94.
25. Choudhury DI, Ghosal MI, Das AP, Mandal PA. Development of single node cutting propagation techniques and evaluation of antioxidant activity of *Curcuma aeruginosa* Roxburgh rhizome. *Int. J. Pharm. Pharm. Sci.* 2013;5(2):227-34.
26. Hegazy GA, Alnoury AM, Gad HG. The role of *Acacia Arabica* extract as an antidiabetic, antihyperlipidemic, and antioxidant in streptozotocin-induced diabetic rats. *Saudi medical journal*. 2013; 34(7):727-33. PMID: 23860893.

27. Anja, B.; Laura, R. The cost of diabetes in Canada over 10 years: Applying attributable health care costs to a diabetes incidence prediction model. *Health Promot. Chronic Dis. Prev. Can.* 2017, 37, 49–53
28. Gupta PD, De A. Diabetes Mellitus and its herbal treatment. *International Journal of Research in Pharmaceutical and Biomedical Sciences.* 2012; 3(2): 706-21.
29. Kumar A, Gnananath K, Gande S, Goud E, Rajesh P, Nagarjuna S. Anti-diabetic Activity of Ethanolic Extract of *Achyranthes aspera* Leaves in Streptozotocin induced diabetic rats. *Journal of Pharmacy Research.* 2011; 4: 3124-5.
30. Andrade-Cetto A, Wiedenfeld H. Hypoglycemic effect of *Acosmium panamense* bark on streptozotocin diabetic rats. *J Ethnopharmacol.* 2004; 90(2): 217-20. doi: 10.1016/j.jep.2003.09.049, PMID: 15013183.
31. Hao-Cong, M.; Shuo, W.; Ying, L.; KUANG, Y.-Y.; Chao-Mei, M. Chemical constituents and pharmacologic actions of *Cynomorium* plants. *Chin. J. Nat. Med.* 2013, 11, 321–329.
32. Phoboo, S.; Shetty, K.; ElObeid, T. In Vitro assays of anti-diabetic and anti-hypertensive potential of some traditional edible plants of qatar. *J. Med. Act. Plants* 2015, 4, 22–29.
33. Das, S.K.; Samantaray, D.; Patra, J.K.; Samanta, L.; Thatoi, H. Antidiabetic potential of mangrove plants: A review. *Front. Life Sci.* 2016, 9, 75–88. [CrossRef]
34. Mahera, S.; Saifullah, S.; Ahmad, V.; Mohammad, F. Phytochemical studies on mangrove *Avicennia marina*. *Pak. J. Bot.* 2013, 45, 2093–2094
35. Mathew PT, Augusti KT. Hypoglycemic effects of onion, *Allium cepa* Linn, on diabetes mellitus- a preliminary report. *Ind J Physiol Pharmacol* 1975, 19, 213-217.
36. Eidi A, Eidi M, Esmaeili E. Antidiabetic effect of garlic (*Allium sativum* L.) in normal and streptozotocin-induced diabetic rats. *Phytomedicine* 2005, 13, 624-629
37. Okyar A, Can A, Akev N, Baktir G, Sütlüpınar N. Effect of *Aloe vera* leaves on blood glucose level in type I and type II diabetic rat models. *Phytother Res* 2001, 15, 157-161
38. Anand P, Murali KY, Tandon V, Chandra R, Murthy PS. Preliminary studies on antihyperglycemic effect of aqueous extract of *Brassica nigra* (L.) Koch in streptozotocin induced diabetic rats. *Indian J Exp Bioi* 2007, 45, 696-701.
39. Karageuzyan KG, Vartanyan GS, Agadjanov MI, Panossian AG, Houlst JR. Restoration of the disordered glucose-fatty acid cycle in alloxandiabetic rats

- bytrihydroxyoctadecadienoic acids from *Bryonia alba*, a native Armenian medicinal plant. *Planta Med* 1998, 64, 417-422.
40. Naik SR, Barbosa Filho JM, Dhuley JN, Deshmukh V. Probable mechanism of hypoglycemic activity of bassic acid, a natural product isolated from *Bumelia sartorum*. *J Ethnopharmacol* 1991, 33, 37-44.
41. Mohammed, S.A.; Al-Awar, A.A.A.M.; Elias, M.A. Antihyperglycemic and Hypolipidemic Effect of *Azadirachta indica* Leaves Aqueous Extract in Alloxan-Induced Diabetic Male Rabbits. *Int. J. Pharm. Biol. Arch.* 2018, 9, 47–51.5.
42. Patil, P.; Patil, S.; Mane, A.; Verma, S. Antidiabetic activity of alcoholic extract of neem (*Azadirachta indica*) root bark. *Natl. J. Physiol. Pharm. Pharmacol.* 2013, 3, 142. [CrossRef]
43. Nagashayana, G.; Jagadeesh, K.; Shreenivas, P.R. Evaluation of hypoglycemic activity of neem (*Azadirachta indica*) in albino rats. *Iosr J. Dent. Med. Sci. (Iosr-Jdms)* 2014, 13, 0411
44. Sabu M, Kuttan R (2004) Antidiabetic activity of *Aegle marmelos* and its relationship with its antioxidant properties. *Indian J Physiol Pharmacol* 48: 81-88.
45. Campos KE, Diniz YS, Cataneo Ac, Faine LA, Alves MJQF, et al. (2003) Hypoglycaemic and antioxidant effects of onion, *Allium cepa*: dietary onion addition, antioxidant activity and hypoglycaemic effects on diabetic rats. *Int J Food sci Nut* 54: 241-246.
46. Shen Y, Fukushims M, Ito Y, Muraki E, Hosono T, et al. (2010) Verification of the antidiabetic effects of cinnamon (*Cinnamomum zeylanicum*) using insulinuncontrolled type 1 diabetic rats and cultured adipocytes. *Biosci Biotechnol Biochem* 74: 2418-2425.
47. Parveen A, Irfan M, Mohammad F (2012) Antihyperglycemic activity in *Grewia asiatica*, a comparative investigation. *Inte J Pharma Pharmaceut Sci* 4: 210- 213.
48. Chen H, Feng R, Guo Y, Sun L, Jiang J (2001) Hypoglycemic effects of aqueous extract of *Rhizoma Polygonati Odorati* in mice and rats. *J Ethnopharmacol* 74: 225-229.
49. Tripathi Ak, Bhoyar PK, Baheti JR, Biyani DM, Khaliq M, et al. (2011) Herbal antidiabetics: A review. *Int J Res Pharm Sci* 2: 30-37.
50. Singab ANB, El-Beshbishy HA, Yonekawa M, Nomura T, Fukai T, (2005) Hypoglycemic effect of Egyptian *Morus alba* root bark extract: Effect on diabetes and lipid peroxidation of streptozotocin-induced diabetic rats. *J Ethnopharmacol* 100: 333-338

51. Zhang J, Yang S, Li H, Chen F, Shi J. Naringin ameliorates diabetic nephropathy by inhibiting NADPH oxidase 4. *Eur J Pharmacol* 2017; 804: 1-6
52. Ganesan D, Holkar A, Albert A, Paul E, Mariakuttikan J, Sadasivam Selvam G. Combination of ramipril and rutin alleviate alloxan induced diabetic nephropathy targeting multiple stress pathways in vivo. *Biomed Pharmacother* 2018.
53. Yan Y, Zhou X, Guo K, Zhou F, Yang H. Use of chlorogenic acid against diabetes mellitus and its complications. *J Immunol Res* 2020; 2020: 1-6.
54. Dey L, Attele AS, Yuan C-S (2003) Alternative therapies for type 2 diabetes. *Textbook of Complementary and Alternative Medicine*. Taylor & Francis, Boca Raton, USA.
55. Tran N, Pham B, Le L. Bioactive Compounds in Anti-Diabetic Plants: From Herbal Medicine to Modern Drug Discovery. *Biology (Basel)*. 2020 Aug 28;9(9):252. doi:10.3390/biology9090252. PMID: 32872226; PMCID: PMC7563488.
56. Al-Ishaq RK, Abotaleb M, Kubatka P, Kajo K, Büsselberg D. Flavonoids and Their Anti-Diabetic Effects: Cellular Mechanisms and Effects to Improve Blood Sugar Levels. *Biomolecules*. 2019 Sep 1;9(9):430. doi: 10.3390/biom9090430. PMID: 31480505; PMCID: PMC6769509.
57. Giacco F, Brownlee M. Oxidative stress and diabetic complications. *Circ Res*. 2010 Oct 29;107(9):1058-70. doi: 10.1161/CIRCRESAHA.110.223545. PMID: 21030723; PMCID: PMC2996922.
58. Swartling U, Helgesson G, Ludvigsson J, Hansson MG, Nordgren A. Children's Views on Long-Term Screening for Type 1 Diabetes. *J Empir Res Hum Res Ethics*. 2014 Oct;9(4):1-9. doi: 10.1177/1556264614544456. Epub 2014 Aug 11. PMID: 25747292.
59. Vorhölter FJ, Schneiker S, Goesmann A, Krause L, Bekel T, Kaiser O, Linke B, Patschkowski T, Rückert C, Schmid J, Sidhu VK, Sieber V, Tauch A, Watt SA, Weisshaar B, Becker A, Niehaus K, Pühler A. The genome of *Xanthomonas campestris* pv. *campestris* B100 and its use for the reconstruction of metabolic pathways involved in xanthan biosynthesis. *J Biotechnol*. 2008 Mar 20;134(1-2):33-45. doi: 10.1016/j.jbiotec.2007.12.013. Epub 2008 Jan 20. PMID: 18304669.
60. Miteniece E, Pavlova M, Rechel B, Groot W. Barriers to accessing adequate maternal care in Central and Eastern European countries: A systematic literature review. *Soc Sci Med*. 2017 Mar;177:1-8. doi: 10.1016/j.socscimed.2017.01.049. Epub 2017 Jan 24. PMID: 28152420.

61. Draycott S, Dabbs A. Cognitive dissonance. 2: A theoretical grounding of motivational interviewing. *Br J Clin Psychol.* 1998 Sep;37(3):355-64. doi: 10.1111/j.2044-8260.1998.tb01391.x. PMID: 9784889.
62. Modak M, Dixit P, Londhe J, Ghaskadbi S, Devasagayam TP. Indian herbs and herbal drugs used for the treatment of diabetes. *J Clin Biochem Nutr.* 2007 May;40(3):163-73. doi: 10.3164/jcbn.40.163. PMID: 18398493; PMCID: PMC2275761.
63. Governa P, Bainsi G, Borgonetti V, Cettolin G, Giachetti D, Magnano AR, Miraldi E, Biagi M. Phytotherapy in the Management of Diabetes: A Review. *Molecules.* 2018 Jan 4;23(1):105. doi: 10.3390/molecules23010105. PMID: 29300317; PMCID: PMC6017385.