Herbal Medicine for the Treatment of Diabetes and CVDs

Aqsa Farooq[1,*] and Madiha Ilyas[1]

[1]Department of Nutritional Sciences, Government College Women University Faisalabad (GCWUF)
*Corresponding author: aqsafarooq@gcwuf.edu.pk

Abstract

Diabetes and Cardiovascular diseases are leading contributors to morbidity and mortality and are becoming major health concerns globally due to high prevalence rates. The use of herbal medicinal plants has emerged as a potential alternative treatment for several health conditions, including cardiovascular diseases, and diabetes. Recently, there has been an increasing interest in integrating herbal remedies into modern medicine. This trend is largely driven by their perceived therapeutic benefits, safety, and affordability compared to conventional treatments. *Nigella sativa, Trigonella foenum-graecum, Zingiber officinale, Allium sativum, Moringa Oleifera, Curcuma longa, Gymnema sylvestre and Ocimum sanctum* are some commonly used herbal plants for the treatment of diabetes and CVDs. Bioactive compounds present in these plants are responsible for their pharmaceutical properties, including hypoglycemic, antioxidant, anti-inflammatory, and anti-hyperlipidemic properties. These phytochemicals contribute to improving insulin function, managing blood sugar levels, and modulating lipid metabolism, thereby playing a crucial role in lowering the risks and complications related to cardiovascular diseases and diabetes. However, the presumed safety of herbal treatments necessitates more thorough scientific validation. Consequently, it is essential to raise public awareness about the safety profiles of medicinal herbs, their serious adverse effects, their potential toxicity, and the risk of interactions with pharmaceutical drugs.

Keywords: Herbal Therapeutics, Phytochemicals, Insulin Resistance, Hyperglycemia, cardiovascular diseases

Cite this Article as: Farooq A and Ilyas M, 2025. Herbal medicine for the treatment of diabetes and CVDs. In: Khan A, Hussain R, Tahir S and Ghafoor N (eds), Medicinal Plants and Aromatics: A Holistic Health Perspective. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 151-158. https://doi.org/10.47278/book.HH/2025.21

A Publication of Unique Scientific Publishers

Chapter No: 25-023

Received: 01-Jan-2025
Revised: 18-March-2025
Accepted: 08-May-2025

Introduction

Diabetes mellitus comprises a range of physiological conditions marked by elevated blood glucose concentration caused by insulin resistance, inadequate insulin production, or excessive glucagon release (Blair, 2016). Diabetes can develop for various reasons, and its management depends on the specific type (Ojo et al., 2023). Cardiovascular disease (CVD) is a significant cause of illness and death in people with diabetes (Almourani et al., 2019). Diabetes is considered as an independent risk factor for heart disease and stroke (De Rosa et al., 2018). People with diabetes face a doubled risk of developing CVDs, including heart attacks, strokes, and peripheral vascular disease. CVD represents a major cause of death among diabetic patients (Abdul-Ghani et al., 2017).

Herbal medicine has been practiced for thousands of years in both developed and developing countries because it is derived from natural sources (Jamshidi-Kia et al., 2017). Botanical compounds can be used to cure multiple diseases and conditions (Abbas et al., 2025). The safe and effective treatment of diabetes mellitus without adverse effects remains a significant challenge for medical practitioners (Nikpour et al., 2022). Globally, ethnobotanical research identifies around 800 medicinal plants as being used to manage diabetes mellitus. Of these, clinical evidence confirms that 450 possess antidiabetic properties, with 109 having their mechanisms of action fully elucidated (Verma et al., 2018). In recent years, the integration of herbal medicine into mainstream healthcare has garnered increasing attention. This trend acknowledges the therapeutic potential of herbal treatments and their ability to complement conventional treatments, often offering fewer side effects and broader patient acceptance (Parvin et al., 2023).

1. Pathophysiology of Diabetes and CVDs

1.1. Mechanisms underlying diabetes

The pathogenesis of diabetes encompasses a complex interaction of genetic, environmental, and immune factors that eventually disrupt glucose metabolism. The two major mechanisms behind Type-II diabetes are decreased insulin secretions from pancreatic β-cells and insulin resistance in peripheral tissues (Banday et al., 2020). β-cell malfunction leads to reduced insulin secretion, which lowers the body's capacity to regulate normal glucose levels. In contrast, insulin resistance (IR) results in enhanced glucose production by the liver and decreases glucose uptake in muscle, liver, and adipose tissue (Zheng et al., 2018). However, both processes occur early in disease development and contribute to its initiation, β-cell dysfunction tends to be more evident than IR. However, when both β-cell dysfunction and IR are present, hyperglycemia worsens, thereby advancing the progression of Type-II diabetes mellitus (Galicia-Garcia et al., 2020).

Diabetes exacerbates when the pancreas can no longer compensate for this resistance by increasing insulin production. Additionally, impaired glucagon secretion from α-cells worsens hyperglycemia. β-cell failure in type 2 diabetes is linked to both a decrease in β-cell number and declining cell function, with chronic high blood glucose further damaging insulin release, creating a cycle that exacerbates hyperglycemia

(Brereton et al., 2016). Aging, obesity, physical inactivity, alcohol consumption, and smoking are key risk factors in disease pathogenesis. Specifically, obesity, particularly visceral fat from a sedentary lifestyle, reduces muscle mass and triggers insulin resistance, which is strongly linked to the growing prevalence among middle- and older-aged individuals. Dietary shifts, including higher fat and simple sugar intake, along with reduced starch and dietary fiber, also contribute to obesity and worsening glucose tolerance (Kohei, 2010). The mechanisms responsible for hyperglycemia are shown in Fig. 1.

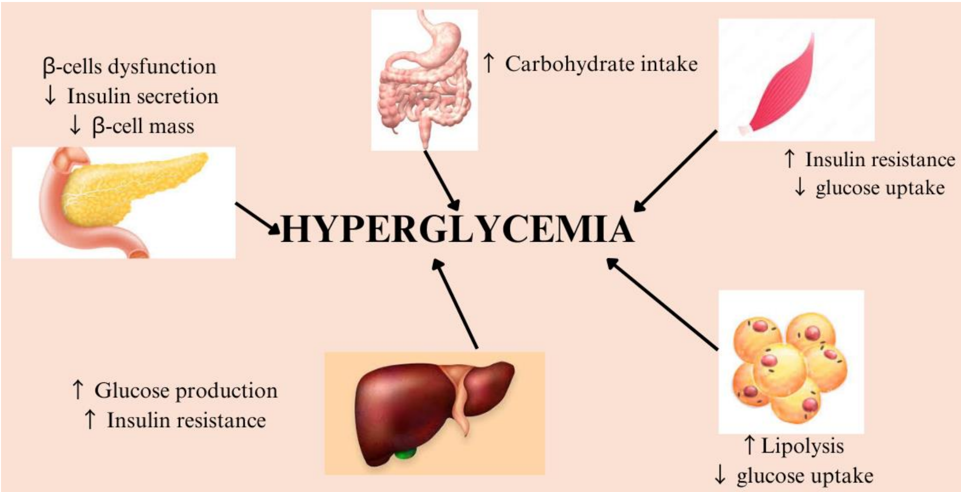

Fig. 1: Mechanisms leading towards hyperglycemia/ diabetes

1.2. Pathophysiological Links Between Diabetes and CVDs

Chronic diabetes leads to changes in cardiac function and structure, driven by abnormal myocardial metabolism and insulin resistance (IR), regardless of the presence of atherosclerotic coronary artery disease (Oktay et al., 2023). Individuals with diabetes show a higher prevalence of dyslipidemia, associated with raised triglycerides and low-density lipoprotein (LDL) levels, accompanied by reduced high-density lipoprotein cholesterol (HDL-C) levels (Abdissa and Hirpa, 2022).

The primary mechanism driving dyslipidemia in individuals with diabetes is insulin resistance. Peripheral IR upsurges the release of free fatty acids (FFAs) from adipose tissue, which are subsequently taken up by the liver. This process enhances triglyceride production in hepatic cells. Additionally, the liver's stimulation by triglyceride synthesis leads to increased ApoB secretion and the production of triglyceride-rich very low-density lipoprotein (Sharma et al., 2020). The triglyceride-rich VLDL particles transfer triglycerides to HDL and LDL, enriching them with cholesterol through the action of cholesterol ester transfer protein. These triglyceride-loaded LDL particles lead to the formation of small, dense LDL as they are hydrolyzed by hepatic lipase (Murtaza et al., 2019).

Diabetic cardiomyopathy refers to impaired myocardial structure and function occurring in people with diabetes mellitus, independent of other cardiac risk factors like hypertension (HTN), coronary artery disease (CAD), or significant valvular disease (Jia et al., 2018). Diabetic cardiomyopathy arises from insulin resistance, hyperglycemia, and associated metabolic disturbances like lipotoxicity and glucotoxicity, leading to mitochondrial dysfunction, oxidative stress, and inflammation (Figure 2). Activation of the RAAS, autonomic neuropathy, epigenetic changes, and autoimmunity further exacerbate cardiac damage. These processes result in structural and functional alterations, including cardiomyocyte death, fibrosis, and microvascular changes, culminating in diastolic and/or systolic dysfunction and impaired cardiac performance (Salvatore et al., 2021).

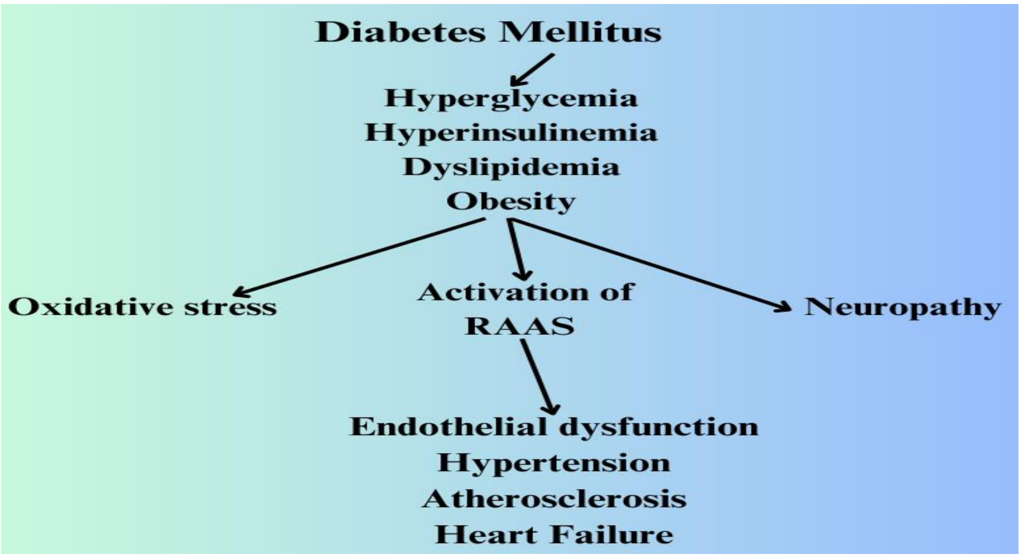

Fig. 2: Pathophysiological linkages between diabetes and CVDs

2. Pharmacological Perspectives on Herbs for Diabetes and CVDs Treatment

Recent research has highlighted various plants with potential hypoglycemic and hypolipidemic properties, offering a basis for alternative approaches to diabetes and CVD management. The active compounds responsible for the hypoglycemic and hypolipidemic effects of some herbal plants are summarized in Table 1.

Table 1: Bioactive components of some herbal plants

Scientific Name	Common name	Bioactive components	Reference
Nigella sativa	Black seeds	Thymoquinone, Thymohydroquinone, Dithymoquinon, and Thymol	Kooshki et al., 2020
Trigonella foenum-graecum	Fenugreek	Trigonelline, Quercetin, Luteolin, Steroidal sapogenins	Alu'datt et al., 2024
Zingiber officinale	Ginger	Gingerol, Diarylheptanoids, Phenylalkanoids, Sulfonates, 6-gingerol and 6-shogaol	Zhang et al., 2021
Allium sativum L.	Garlic	Alliin, allicin diallyl sulfide, Ajoenes, Vinyldithiins, quercetin, Diallyl trisulfide, Ajoene, Diallyl disulfide, and S-allyl-cysteine	El-Saber Batiha et al., 2020
Moringa Oleifera	Moringa	Gallic acid, Chlorogenic acid, Ellagic acid, Isoquercitrin, Epicatechin, Kaempferol, Myricetin	Hassan et al., 2021
Curcuma longa	Turmeric	Desmethoxycurcumin, Bisdemethoxycurcumin, Cyclocurcumin, Ar-turmerone	Silva et al., 2021
Gymnema sylvestre	Gurmar	Gurmarin, Gymnemic acids, Saponins, Flavonol, Glycosides,	Gupta et al., 2023
Ocimum sanctum	Holy tulsi	Aponins, Flavonoids, Triterpenoids, Tannins, Apigenin and Isothymusin	Bhadra and Sethi 2020

Nigella sativa

Nigella sativa, commonly referred to as black seeds and belongs to the family Ranunculaceae, exhibits therapeutic potential for various health conditions, including asthma, inflammatory diseases, digestive disorders, and diabetes (Kooti et al., 2016). Polysaccharides from *Nigella sativa* seeds, administered at doses of 35, 70, and 140mg/kg, have been shown to lower FBS (fasting blood sugar), TNF-α (Tumor necrosis factor-alpha), IL-6 (Interleukins-6), GSP (Glycosylated serum protein), and IL-1β levels while enhancing insulin, total anti-oxidant capacity, SOD (superoxide dismutase), and CAT (catalase) levels in male Kunming mice (Dong et al., 2020). Endothelial dysfunction induced by diabetes is a key risk factor for atherosclerosis and heart diseases. Nigella sativa exerts a protective effect against diabetes-induced endothelial dysfunction through multiple mechanisms. These include reducing inflammatory and apoptotic markers, alleviating hyperglycemia, hyper-lipidemia, and antioxidant activity, preventing platelet aggregation, and regulating the expression of LOX-1, eNOS, and VCAM-1, genes associated with endothelial dysfunction (Mohebbati and Abbasnezhad, 2020).

Trigonella foenum-graecum

Trigonella foenum-graecum, commonly referred to as fenugreek, possesses various pharmacological properties, including hypoglycemic, hypocholesterolemic, anti-inflammatory, and antioxidant effect (Haxhiraj et al., 2024). In hyperlipidemic animals generated by the reduction of cAMP responsive element binding protein H (CREBH), fenugreek seed supplementation enhances PPARα expression and fatty acid β-oxidation, reducing hepatic lipid buildup and secretion of VLDL. It also alleviates ER stress and metabolic inflammation, leading to improved insulin efficiency and lipid metabolism (Khound et al., 2018). Fenugreek seed extract demonstrated significant effects by reducing serum sugar, cholesterol, and triglyceride concentration. It also modulated oxidative stress markers, including thiobarbituric acid-reactive substances (TBARS), superoxide dismutase (SOD), catalase (CAT), and total thiol groups (SH) activity, while influencing apoptotic cell death (Bafadam et al., 2021).

Zingiber officinale

Zingiber officinale (ginger), a member of the Zingiberaceae family, is widely recognized for its immunomodulatory, anti-carcinogenic, anti-fungal, anti-bacterial, anti-hyperglycemic, and anti-atherosclerotic properties (Li et al., 2019). *Zingiber officinale* rhizome extract alleviates hyperglycemia, hyperlipidemia, and kidney dysfunction in diabetic rats while minimizing kidney histological damage. It reduces oxidative stress, inflammation, and apoptosis, enhancing antioxidant defenses (Hroob et al., 2018). Ginger extract effectively reduced serum glucose levels and significantly decreased serum concentration of aspartate aminotransferase, lactate dehydrogenase, and creatine kinase-muscle/brain in all treated groups in comparison to the diabetic group. Additionally, fibrosis and collagen content in heart tissue were markedly lower in ginger-treated groups. Ginger extract also reduced inflammatory cell infiltration and improved cardiac tissue arrangement compared to the diabetic group. Furthermore, the expression of angiotensin II type 1 receptor, TGF-β1, and TGF-β3 genes was downregulated in all treated groups relative to the diabetic group (Abdi et al., 2021).

Allium sativum L.

Garlic (*Allium sativum* L.) displays a wide range of biological functions, including antioxidants, cardiovascular protective, anti-cancer, anti-inflammatory, anti-diabetic, immunomodulatory, anti-obesity, and anti-bacterial effects (Shang et al., 2019). Dipeptidyl peptidase-4 (DPP-4) inhibitors are appealing oral anti-hyperglycemic agents for managing diabetes. Scientific evidence demonstrates that garlic extracts can inhibit DPP-4 activity (Kalhotra et al., 2020). Garlic affects blood glucose by exhibiting insulin-like properties, inhibiting insulinase activity, improving insulin secretion, regenerating pancreatic β-cells, increasing liver glycogen, and reducing carbohydrate absorption via fiber (Saikat et al., 2021). Garlic extract has the potential to slow coronary artery calcification progression and effectively reduce IL-6, glucose concentration, and blood pressure in patients with elevated risk of cardiovascular events (Wlosinska et al., 2020). Garlic has shown the ability to inhibit the formation and accumulation of free and esterified cholesterol, phospholipids, and collagen within the aortic media. Additionally, it reduced serum lipid content and decreased the atherogenic potential of blood serum (Sobenin et al., 2016). Garlic owns anti-atherogenic properties by its direct action on the arterial wall, helping to reduce and prevent lipid deposition. A detailed meta-analysis indicates that garlic effectively lowers total cholesterol levels, with a greater impact observed in individuals with hyper-cholesterolemia (Ribeiro et al., 2021).

Moringa oleifera

Moringa, belongs to the Moringaceae family, is a rich in nutrients and renowned for its diverse pharmaceutical activities, including anti-microbial, hepatoprotective, anti-tumor, anti-inflammatory, antioxidant, neuroprotective, cardioprotective, and tissue-protective properties (Dhakad et al., 2019). Diabetes interrupts nitric oxide homeostasis and prevents the activities of constitutive paraoxonase-1 (PON1), and nitric oxide synthase (cNOS) leading to oxidative stress. Oral administration of *moringa extract* in diabetic rats efficiently decrased glucose concentration, advanced glycation end-products (AGEs), triglycerides, and HbA1c. Additionally, *moringa oleifera* treatment considerably restored cNOS and PON1 activity compared to the untreated diabetic group (Sierra-Campos et al., 2018). The methanolic extract of *Moringa* exhibits dose-dependent benefits, including improved lipid profiles and enhanced vascular endothelium protection. These findings support its traditional application in managing dyslipidemia and endothelial disorders associated with cardiovascular conditions (Madkhali et al., 2019).

Curcuma longa

Turmeric *(Curcuma longa)* exhibits a wide range of pharmacological and biological effects, demonstrated through both *in vitro* and *in vivo* studies, including antioxidant, cardioprotective, nephroprotective, hepatoprotective, anti-inflammatory, hypoglycemic, antimicrobial, antineoplastic, immunomodulatory, and anti-rheumatic properties (Pivari et al., 2019). Curcumin has demonstrated notable antidiabetic activity, primarily due to its potent antioxidant and anti-inflammatory properties. Curcumin NF-κB and reduces caspase-12 levels while cleaving caspase-3 in response to endoplasmic reticulum stress. Additionally, curcumin restores streptozotocin induced reductions in (Nrf-2) and heme oxygenase-1 levels (Rashid and Sil, 2015). Curcumin plays a role in alleviating oxidative stress and its downstream pathways, which are key contributors to diabetic complications. Curcumin inhibits oxidative stress, which otherwise activates pathways such as NF-κB, p38 MAPK/ERK, PKC, sphK1-S1P, and AP-1. These pathways lead to the production of pro-inflammatory and damaging molecules, including TNF-α, IL-6, Bax, VEGF, TNF-β, and fibronectin. The resulting inflammation, endothelial dysfunction, and cellular damage further exacerbate diabetic complications (Roney et al., 2024).

Gymnema sylvestre

Gymnema sylvestre (GS), referred to as Gurmar, is renowned for its anti-diabetic effects and is frequently incorporated into Ayurvedic formulations used to treat conditions such as inflammation, eye diseases, dental caries, and asthma (Jamadagni et al., 2021). Gurmar leaves powder significantly reduced the fasting blood glucose and hemoglobin A1c (HbA1c) concentrations in type 2 diabetic patients (Vyas et al., 2024). In a randomized, double-blind, placebo-controlled clinical trial, Gurmar was shown to significantly reduce 2-hour OGTT levels, A1C, body weight, BMI, and LDL cholesterol (Gaytán Martínez et al., 2021). *Gymnema Syylvestre* leaves significantly reduced the thyroid stimulating hormone, leptin, total cholesterol (TC), triglycerides, LDL, VLDL, and atherogenic index (AI) while increased the HDL, T3 and T4 levels in obese albino rats fed on high fat diet (Rahman and khateib, 2020).

Ocimum sanctum

Ocimum sanctum, commonly knwon as holy basil or tulsi, is a member of the Lamiaceae family and is renowned for its therapeutic properties, including anti-inflammatory, antimicrobial, and antioxidant effects (Singh and Majumdar, 2019). The aqueous-methanolic extract (100 mg/kg) of tulsi leaves demonstrated restoration of body weight (BW), fasting blood glucose (FBG), serum glucose, insulin, HbA1c, ALT, AST, ALP levels, and histopathological analysis revealed an increase in pancreatic islet size (Ramzan et al., 2020). Consumption of *Ocimum sanctum* (OS) leaves notably elevated plasma lipid levels and the atherogenic index in the high-fat diet group. However, OS supplementation significantly decreased plasma total cholesterol, triglycerides, lipoproteins, and the atherogenic index in OS-treated rats (Khan et al., 2022). *Ocimum sanctum* exerts significant effects in the treatment and prevention of cardiovascular diseases by lowering blood lipid levels, alleviating ischemia and stroke, reducing hypertension, and leveraging its potent antioxidant properties. Additionally, it plays a critical role in preventing platelet aggregation and mitigating the risk of pulmonary hypertension (Sharma and Chanda, 2018)

2.1. Mechanisms of Action of Antidiabetic Herbs

Hypoglycemic herbs exert their therapeutic effects by influencing different interconnected mechanisms that target cellular, molecular, and metabolic pathways. These mechanisms involve increasing insulin secretion and sensitivity, stimulating the regeneration of pancreatic beta-cells protecting them from oxidative damage, and preventing the absorption of intestinal carbohydrates (Xie et al., 2011). *Gymnema sylvestre* encourages glucose uptake in peripheral tissues by regulating GLUT4 translocation (Kumar et al., 2016). Trigonella foenum-graecum reduces blood glucose levels through at least three mechanisms, including the inhibition of amylase, glucosidase, and sodium-glucose co-transporter 2, and enhanced GLP-1 secretion (Ahda et al., 2023). Curcumin functions as a potent inhibitor of α-glucosidase and α-amylase enzymes, which are released from the brush border of the small intestine (Alam et al., 2022). Phytochemicals in Moringa have been shown to substantially reduce fasting blood glucose concentration and serum HbA1c levels while improving insulin sensitivity (Figure 3). Additionally, they inhibit the passage of glucose and fructose via GLUT2 in the brain and facilitates the translocation and expression of GLUT4 in skeletal muscle (Villarruel-López et al., 2018).

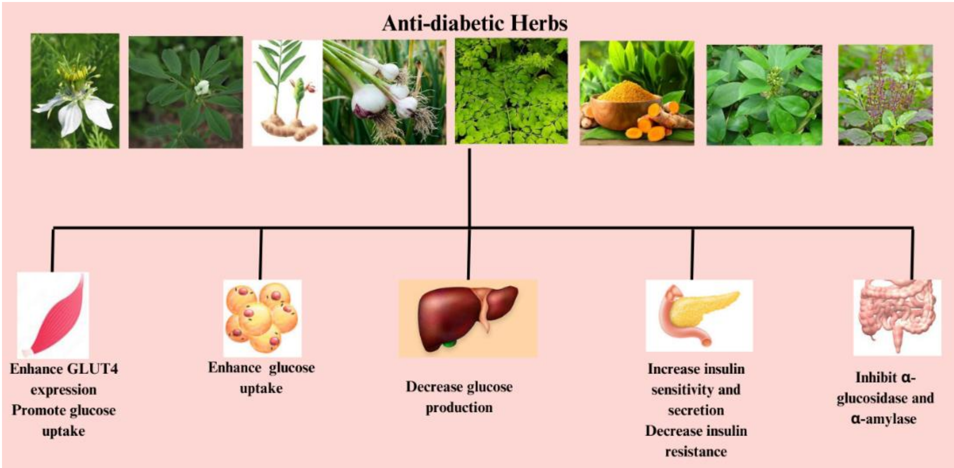

Fig. 3: Mechanism of action of anti-diabetic herbs

2.2. Mechanism of action of herbs against CVDs

Polyphenols, flavonoids, and other phytochemicals present in medicinal plants are vital bioactive compounds that play a momentous role in preventing cardiovascular diseases. These compounds demonstrate a remarkable ability to inhibit the oxidation of low-density lipoproteins (LDL), thereby improving lipid profiles. Additionally, they contribute to maintaining endothelial health by modulating apoptotic processes, supporting overall cardiovascular function (Bachheti et al., 2022). Curcuma longa demonstrates cardioprotective properties by effectively reducing oxidative stress. Its active component, curcumin, plays a key role in neutralizing reactive oxygen species, decreasing lipid per-oxidation, and boosting the activity of antioxidant enzymes, reduce the blood viscosity, formation of thrombus, prevents the platelet aggregation and reduce arterial sclerosis, thus protecting cardiac tissues and promoting heart health (Fu et al., 2021; Wang et al., 2021). *Moringa oleifera* and *Ocimum sanctum* help lower blood cholesterol levels and reduce blood pressure, contributing to improved cardiovascular health (Adekanmi et al., 2020; Mohammadi Pour et al., 2021). *Nigella sativa* lowers oxidative stress and helps to regulate blood pressure (Shamlan, 2021). *Zingiber officinale* improves fibrinolytic activity, lowers lipid peroxidation, helps to regulate blood glucose, blood pressure, and lipid concentrations, contributing to overall metabolic and cardiovascular health (Hesari et al., 2021).

Challenges and Limitations

Plant-based medicines have gained global recognition for their health benefits and affordability, often being more economical than modern synthetic treatments (Hossain et al., 2022). However, their use is challenged by issues such as ensuring botanical identity and traceability of herbs, ecological concerns, regulation of over the counter (OTC) herbal products, and communication gaps between patients and physicians (Choudhury et al., 2023). Many traditional practices lack sufficient evidence on efficacy, quality, and safety, compounded by inadequate oversight, unclear standards, and the absence of certification or legal requirements for business (Silveira et al., 2018). Moreover, the complex composition of herbal products, with unidentified active constituents, complicates their evaluation and stability (Verma, 2016).

Future perspective

Modern research offers the opportunity to address common concerns associated with herbal drugs, such as similar popular names for products from various origins, structural variations in plant-derived compounds influenced by environmental conditions, inconsistencies in harvesting, extraction, and storage methods, and limited toxicity data. These gaps can be addressed by using advanced technologies and techniques (Kesharwani et al., 2019). The incorporation of nanotechnology with herbal drugs proposed substantial advancements by enhancing bioavailability, reducing toxicity, and increasing therapeutic efficacy. However, challenges in conventional medicine's safety, nanotechnology-based herbal formulations exhibit immense potential. These herbal nanomedicines are known for being safer and more effective than traditional herbal and synthetic drugs. This approach paves the way for innovation in herbal medicine research (Teja et al., 2022).

Conclusion

Herbal drugs hold significant promise as a potential strategy for the management of diabetes and cardiovascular diseases, which remain a major global health challenge. The phytochemicals found in medicinal plants offer a comprehensive approach to treatment by helping regulate blood glucose levels, improve insulin sensitivity, and promote healthy lipid metabolism. Despite the growing evidence supporting the therapeutic effects of these herbs, more research is needed to validate their safety, effectiveness, and possible interactions with conventional drugs. Educating the public on their benefits, alongside ensuring proper scientific evaluation, will be crucial for incorporating herbal therapies into mainstream healthcare.

References

Abbas, R. Z., Qureshi, M. A., & Saeed, Z. (2025). Botanical compounds: A promising control strategy against Trypanosoma cruzi. *Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas*, *24*(3), 308-327.

Abdi, T., Mahmoudabady, M., Marzouni, H. Z., Niazmand, S., & Khazaei, M. (2021). Ginger (*Zingiber Officinale Roscoe*) extract protects the heart against inflammation and fibrosis in diabetic rats. *Canadian Journal of Diabetes*, *45*(3), 220-227.

Abdissa, D., & Hirpa, D. (2022). Dyslipidemia and its associated factors among adult diabetes outpatients in West Shewa zone public hospitals, Ethiopia. *BMC Cardiovascular Disorders*, *22*(1), 39.

Abdul-Ghani, M., DeFronzo, R. A., Del Prato, S., Chilton, R., Singh, R., & Ryder, R. E. (2017). Cardiovascular disease and type 2 diabetes: has the dawn of a new era arrived?. *Diabetes Care*, *40*(7), 813-820.

Adekanmi, A. A., Adekanmi, S. A., & Adekanmi, O. S. (2020). Qualitative and quantitative phytochemical constituents of moringa leaf. *International Journal of Engineering and Information Systems*, *4*(5), 10-17.

Ahda, M., Jaswir, I., Khatib, A., Ahmed, Q. U., Mahfudh, N., & Ardini, Y. D. (2023). A review on selected herbal plants as alternative anti-diabetes drugs: chemical compositions, mechanisms of action, and clinical study. *International Journal of Food Properties*, *26*(1), 1414-1425.

Alam, S., Sarker, M. M. R., Sultana, T. N., Chowdhury, M. N. R., Rashid, M. A., Chaity, N. I., & Mohamed, I. N. (2022). Antidiabetic phytochemicals from medicinal plants: prospective candidates for new drug discovery and development. *Frontiers in Endocrinology*, *13*, 800714.

Almourani, R., Chinnakotla, B., Patel, R., Kurukulasuriya, L. R., & Sowers, J. (2019). Diabetes and cardiovascular disease: an update. *Current Diabetes Reports*, *19*, 1-13.

Alu'datt, M. H., Rababah, T., Al-ali, S., Tranchant, C. C., Gammoh, S., Alrosan, M., & Ghatasheh, S. (2024). Current perspectives on fenugreek bioactive compounds and their potential impact on human health: A review of recent insights into functional foods and other high value applications. *Journal of Food Science*, *89*(4), 1835-1864.

Bachheti, R. K., Worku, L. A., Gonfa, Y. H., Zebeaman, M., Deepti, Pandey, D. P., & Bachheti, A. (2022). [Retracted] Prevention and treatment of cardiovascular diseases with plant phytochemicals: a review. *Evidence-Based Complementary and Alternative Medicine*, *2022*(1), 5741198.

Bafadam, S., Mahmoudabady, M., Niazmand, S., Rezaee, S.A. and Soukhtanloo, M., 2021. Cardioprotective effects of Fenugreek *(Trigonella foenum-graceum)* seed extract in streptozotocin induced diabetic rats. *Journal of Cardiovascular and Thoracic Research*, *13*(1), 28-36.

Banday, M. Z., Sameer, A. S., & Nissar, S. (2020). Pathophysiology of diabetes: An overview. *Avicenna Journal of Medicine*, *10*(04), 174-188.

Bhadra, P., & Sethi, L. (2020). A review paper on the Tulsi plant (*Ocimum sanctum*). *Indian Journal of Natural Sciences*, *10*(60), 20854-20860.

Blair, M. (2016). Diabetes mellitus review. *Urologic Nursing*, *36*(1).

Brereton, M. F., Rohm, M., & Ashcroft, F. M. (2016). β-Cell dysfunction in diabetes: a crisis of identity?. *Diabetes, Obesity and Metabolism*, *18*, 102-109.

Choudhury, A., Singh, P. A., Bajwa, N., Dash, S., & Bisht, P. (2023). Pharmacovigilance of herbal medicines: Concerns and future prospects. *Journal of Ethnopharmacology*, *309*, 116383.

De Rosa, S., Arcidiacono, B., Chiefari, E., Brunetti, A., Indolfi, C., & Foti, D. P. (2018). Type 2 diabetes mellitus and cardiovascular disease: genetic and epigenetic links. *Frontiers in Endocrinology*, *9*, 2.

Dhakad, A. K., Ikram, M., Sharma, S., Khan, S., Pandey, V. V., & Singh, A. (2019). Biological, nutritional, and therapeutic significance of *Moringa oleifera Lam*. *Phytotherapy Research*, *33*(11), 2870-2903.

El-Saber Batiha, G., Magdy Beshbishy, A., G. Wasef, L., Elewa, Y. H., A. Al-Sagan, A., Abd El-Hack, M. E., & Prasad Devkota, H. (2020). Chemical constituents and pharmacological activities of garlic *(Allium sativum L.):* A review. *Nutrients*, *12*(3), 872.

Fu, Y. S., Chen, T. H., Weng, L., Huang, L., Lai, D., & Weng, C. F. (2021). Pharmacological properties and underlying mechanisms of curcumin and prospects in medicinal potential. *Biomedicine & Pharmacotherapy*, *141*, 111888.

Galicia-Garcia, U., Benito-Vicente, A., Jebari, S., Larrea-Sebal, A., Siddiqi, H., Uribe, K. B., & Martín, C. (2020). Pathophysiology of type 2 diabetes mellitus. *International Journal of Molecular Sciences*, *21*(17), 6275.

Gaytán Martínez, L. A., Sánchez-Ruiz, L. A., Zuñiga, L. Y., González-Ortiz, M., & Martínez-Abundis, E. (2021). Effect of Gymnema sylvestre administration on glycemic control, insulin secretion, and insulin sensitivity in patients with impaired glucose tolerance. *Journal of Medicinal Food*, *24*(1), 28-32.

Gupta, V. K., Vikash, A., & Pankaj, (2023). N. Gymnema sylvestre R. BR. (gurmar, meshasringi): A review. *International Journal of Pharmcognosy*, 10(7): 356-361.

Hassan, M. A., Xu, T., Tian, Y., Zhong, Y., Ali, F. A. Z., Yang, X., & Lu, B. (2021). Health benefits and phenolic compounds of *Moringa oleifera* leaves: A comprehensive review. *Phytomedicine*, *93*, 153771.

Haxhiraj, M., White, K., & Terry, C. (2024). The role of fenugreek in the management of type 2 diabetes. *International Journal of Molecular Sciences*, *25*(13), 6987.

Hesari, M., Mohammadi, P., Khademi, F., Shackebaei, D., Momtaz, S., Moasefi, N., & Abdollahi, M. (2021). Current advances in the use of nanophytomedicine therapies for human cardiovascular diseases. *International Journal of Nanomedicine*, 16, 3293-3315.

Hossain, C. M., Gera, M., & Ali, K. A. (2022). Current status and challenges of herbal drug development and regulatory aspect: a global perspective. *Asian Journal of Pharmaceutical and Clinical Research*, *15*, 31-41.

Hroob, A. M., Abukhalil, M. H., Alghonmeen, R. D., & Mahmoud, A. M. (2018). Ginger alleviates hyperglycemia-induced oxidative stress, inflammation and apoptosis and protects rats against diabetic nephropathy. *Biomedicine & Pharmacotherapy*, *106*, 381-389.

Jamadagni, P. S., Pawar, S. D., Jamadagni, S. B., Gautam, M., Gaidhani, S. N., Prasad, G. P., & Gurav, A. M. (2021). Recent Updates in Research on Gymnema sylvestre. *Pharmacognosy Reviews*, *15*(30), 128-133.

Jamshidi-Kia, F., Lorigooini, Z., & Amini-Khoei, H. (2017). Medicinal plants: Past history and future perspective. *Journal of Herbmed Pharmacology*, *7*(1), 1-7.

Jia, G., Hill, M. A., & Sowers, J. R. (2018). Diabetic cardiomyopathy: an update of mechanisms contributing to this clinical entity. *Circulation Research*, *122*(4), 624-638.

Kalhotra, P., Chittepu, V. C., Osorio-Revilla, G., & Gallardo-Velazquez, T. (2020). 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*, *10*(2), 305.

Kesharwani, R. K., Misra, K., & Singh, D. B. (2019). Perspectives and challenges of tropical medicinal herbs and modern drug discovery in the current scenario. *Asian Pacific Journal of Tropical Medicine*, *12*(1), 1-7.

Khan, Z., Shamim, M., & Khan, N. I. (2022), Effect of *Ocimum Sanctum* (Tulsi) leaf on high-fat-diet induced hyperlipidemic rat. *Biosight,* 03(01), 16-20.

Khound, R., Shen, J., Song, Y., Santra, D., & Su, Q. (2018). Phytoceuticals in fenugreek ameliorate VLDL overproduction and insulin resistance via the insig signaling pathway. *Molecular Nutrition & Food Research*, *62*(5), 1700541.

Kohei, K. (2010). Pathophysiology of type 2 diabetes and its treatment policy. *JMAJ*, *53*(1), 41-46.

Kooshki, A., Tofighiyan, T., Rastgoo, N., Rakhshani, M. H., & Miri, M. (2020). Effect of Nigella sativa oil supplement on risk factors for cardiovascular diseases in patients with type 2 diabetes mellitus. *Phytotherapy Research*, *34*(10), 2706-2711.

Kooti, W., Hasanzadeh-Noohi, Z., Sharafi-Ahvazi, N., Asadi-Samani, M., & Ashtary-Larky, D. (2016). Phytochemistry, pharmacology, and therapeutic uses of black seed (Nigella sativa). *Chinese Journal of Natural Medicines*, *14*(10), 732-745.

Kumar, P. M., Venkataranganna, M. V., Manjunath, K., Viswanatha, G. L., & Ashok, G. (2016). Methanolic leaf extract of Gymnema sylvestre augments glucose uptake and ameliorates insulin resistance by upregulating glucose transporter-4, peroxisome proliferator-activated receptor-gamma, adiponectin, and leptin levels in vitro. *Journal of Intercultural Ethnopharmacology*, *5*(2), 146.

Li, H., Liu, Y., Luo, D., Ma, Y., Zhang, J., Li, M., & Yang, K. (2019). Ginger for health care: An overview of systematic reviews. *Complementary Therapies in Medicine*, *45*, 114-123.

Madkhali, H. A., Alharthy, K. M., Asiri, M. A., Ganaie, M. A., Ansari, M. N., Rehman, N. U., & Hamad, A. M. (2019). *Moringa oleifera Lam.*(family Moringaceae) leaf extract attenuates high-fat diet-induced dyslipidemia and vascular endothelium dysfunction in Wistar albino rats. *Tropical Journal of Pharmaceutical Research*, *18*(12), 2597-2604.

Mohammadi Pour, P., Farzaei, M. H., Soleiman Dehkordi, E., Bishayee, A., & Asgary, S. (2021). Therapeutic targets of natural products for the management of cardiovascular symptoms of coronavirus disease 2019. *Phytotherapy Research*, *35*(10), 5417-5426.

Mohebbati, R., & Abbasnezhad, A. (2020). Effects of Nigella sativa on endothelial dysfunction in diabetes mellitus: A review. *Journal of Ethnopharmacology*, *252*, 112585.

Murtaza, G., Virk, H. U. H., Khalid, M., Lavie, C. J., Ventura, H., Mukherjee, D., & Paul, T. K. (2019). Diabetic cardiomyopathy-a comprehensive updated review. *Progress in Cardiovascular Diseases*, *62*(4), 315-326.

Nikpour, S., Mehrdad, N., Sanjari, M., Aalaa, M., Heshmat, R., Mafinejad, M. K., & Ghezeljeh, T. N. (2022). Challenges of type 2 diabetes mellitus management from the perspective of patients: Conventional content analysis. *Interactive Journal of Medical Research*, *11*(2), e41933.

Ojo, O. A., Ibrahim, H. S., Rotimi, D. E., Ogunlakin, A. D., & Ojo, A. B. (2023). Diabetes mellitus: From molecular mechanism to pathophysiology and pharmacology. *Medicine in Novel Technology and Devices*, *19*, 100247.

Oktay, A. A., Paul, T. K., Koch, C. A., & Lavie, C. J. (2023). Diabetes, cardiomyopathy, and heart failure. *Endotext [Internet]*.

Parvin, K., Srivastava, A., Hidangmayum, N., Bansal, S., Meher, R., & Awasthi, R. (2023). Exploring the evolving role of herbal and alternative medicine in modern healthcare. *Acta Traditional Medicine*, *2*, 35-42.

Pivari, F., Mingione, A., Brasacchio, C., & Soldati, L. (2019). Curcumin and type 2 diabetes mellitus: prevention and treatment. *Nutrients*, *11*(8), 1837.

Rahman, A. N. A., and khateib B.R.M., (2020). Anti-obesity and hypolipidemic Effects of gymnemasyylvestre Leaves on Rats Fed on High Fat Diet. *Journal of Research in the Fields of Specific Education*, 6 (28): 613-630.

Ramzan, T., Aslam, B., Muhammad, F., Faisal, M. N., & Hussain, A. (2020). Influence of Ocimum sanctum (L.) extract on the activity of gliclazide in alloxaninduced diabetes in rats. *Revista de Chimie*, *71*(10), 101-110.

Rashid, K., & Sil, P. C. (2015). Curcumin enhances recovery of pancreatic islets from cellular stress induced inflammation and apoptosis in diabetic rats. *Toxicology and Applied Pharmacology*, *282*(3), 297-310.

Ribeiro, M., Alvarenga, L., Cardozo, L. F., Chermut, T. R., Sequeira, J., Moreira, L. D. S. G., & Mafra, D. (2021). From the distinctive smell to therapeutic effects: Garlic for cardiovascular, hepatic, gut, diabetes and chronic kidney disease. *Clinical Nutrition*, *40*(7), 4807-4819.

Roney, M., Huq, A. M., Rullah, K., Zamri, N. B., & Mohd Aluwi, M. F. F. (2024). Curcumin, a bioactive compound of Turmeric *(Curcuma longa)* and its derivatives as α-amylase and α-glucosidase inhibitors. *Cell Biochemistry and Biophysics*, 1-19.

Saikat, A. S. M., Hossain, R., Mina, F. B., Das, S., Khan, I. N., Mubarak, M. S., & Islam, M. T. (2021). Antidiabetic effect of garlic. *Revista Brasileira de Farmacognosia*, 1-11.

Salvatore, T., Pafundi, P. C., Galiero, R., Albanese, G., Di Martino, A., Caturano, A., & Sasso, F. C. (2021). The diabetic cardiomyopathy: the contributing pathophysiological mechanisms. *Frontiers in Medicine*, *8*, 695792.

Shamlan, G. (2021). Ethanolic and aqueous extracts of avocado *(Persea americana)* seeds attenuates doxorubicin-induced cardiotoxicity in male albino rats. *Arabian Journal for Science and Engineering*, *46*, 5265-5274.

Shang, A., Cao, S. Y., Xu, X. Y., Gan, R. Y., Tang, G. Y., Corke, H., & Li, H. B. (2019). Bioactive compounds and biological functions of garlic *(Allium sativum L.). Foods*, *8*(7), 246.

Sharma, A., Mittal, S., Aggarwal, R., & Chauhan, M. K. (2020). Diabetes and cardiovascular disease: inter-relation of risk factors and treatment. *Future Journal of Pharmaceutical Sciences*, *6*, 1-19.

Sharma, V., & Chanda, D. (2018). Ocimum: The holy basil against cardiac anomalies. *The Ocimum Genome*, 25-36.

Sierra-Campos, E., Valdez-Solana, M. A., Pérez-Velázquez, J. R., García-Arenas, G., Téllez-Valencia, A., & Avitia-Domínguez, C. (2018). *Moringa oleifera* leaves extract regulate the activity of nitric oxide synthases and paraoxonase 1 in diabetic rat. *MOJ Biorganic and Organic Chemistry*, *2*(5), 236-241.

Silva, P. A. S. N., Arawwawala, L. D. A. M., Kumari, M. W. S. J., & Galappatthy, P. (2021). Effect of Curcuma longa L. and curcumin on diabetes

and it’s complications: A review. *Journal of Ayurvedic and Herbal Medicine*, *7*(2), 109-118.
Silveira, D., Prieto, J. M., Freitas, M. M., & Mazzari, A. L. (2018). Herbal medicine and public healthcare: Current and future challenges. *Natural Products as Source of Molecules with Therapeutic Potential: Research & Development, Challenges and Perspectives*, 495-515.
Singh, S., & Majumdar, D. K. (2019). Therapeutic potential of Tulsi: A holy herb of ancient India. *Pharmacognosy Reviews,* 13(26), 49-56.
Sobenin, I. A., Andrianova, I. V., Lakunin, K. Y., Karagodin, V. P., Bobryshev, Y. V., & Orekhov, A. N. (2016). Anti-atherosclerotic effects of garlic preparation in freeze injury model of atherosclerosis in cholesterol-fed rabbits. *Phytomedicine*, *23*(11), 1235-1239.
Teja, P. K., Mithiya, J., Kate, A. S., Bairwa, K., & Chauthe, S. K. (2022). Herbal nanomedicines: Recent advancements, challenges, opportunities and regulatory overview. *Phytomedicine*, *96*, 153890.
Verma, N. (2016). Current regulatory challenges and approaches in the registration of herbal drugs in Europe. *Clinical Research and Regulatory Affairs*, *33*(1), 9-24.
Verma, S., Gupta, M., Popli, H., & Aggarwal, G. (2018). Diabetes mellitus treatment using herbal drugs. *International Journal of Phytomedicine*, *10*(1), 1-10.
Villarruel-López, A., López-De La Mora, D. A., Vázquez-Paulino, O. D., Puebla-Mora, A. G., Torres-Vitela, M. R., Guerrero-Quiroz, L. A., & Nuño, K. (2018). Effect of *Moringa oleifera* consumption on diabetic rats. *BMC Complementary and Alternative Medicine*, *18*, 1-10.
Vyas, P., Binawara, B.K., & Narnolia, P.K. (2024). Effect of Gurmar (Gymnema sylvestre) Leaf Powder on Glycemic Control in Type 2 Diabetes Mellitus. *International Journal of Pharmaceutical and Clinical Research*, 16(7), 724-728.
Wang, Z., Mu, W., Li, P., Liu, G., & Yang, J. (2021). Anti-inflammatory activity of ortho-trifluoromethoxy-substituted 4-piperidione-containing mono-carbonyl curcumin derivatives in vitro and in vivo. *European Journal of Pharmaceutical Sciences*, *160*, 105756.
Wlosinska, M., Nilsson, A. C., Hlebowicz, J., Hauggaard, A., Kjellin, M., Fakhro, M., & Lindstedt, S. (2020). The effect of aged garlic extract on the atherosclerotic process–a randomized double-blind placebo-controlled trial. *BMC Complementary Medicine and Therapies*, *20*, 1-10.
Xie, W., Zhao, Y., & Zhang, Y. (2011). Traditional Chinese medicines in treatment of patients with type 2 diabetes mellitus. *Evidence-based Complementary and Alternative Medicine*, *2011*(1), 726723.
Zhang, M., Zhao, R., Wang, D., Wang, L., Zhang, Q., Wei, S., & Wu, C. (2021). Ginger *(Zingiber officinale Rosc.)* and its bioactive components are potential resources for health beneficial agents. *Phytotherapy Research*, *35*(2), 711-742.
Zheng, Y., Ley, S. H., & Hu, F. B. (2018). Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nature Reviews Endocrinology*, *14*(2), 88-98.