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Efficacy evaluation of contemporary and alternative medicine in managing diabetes mellitus: A review

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ABSTRACT

Diabetes mellitus poses a significant global health burden, and achieving optimal glycemic control is crucial in preventing complications. Traditional medicine, rooted in cultural beliefs and practices, has been used for centuries to manage diabetes mellitus. In recent years, contemporary medicine, including pharmaceutical approaches, has gained prominence in diabetes management. This review aims to evaluate the efficacy of contemporary and alternative medicine in managing diabetes mellitus. Evidence-based research is essential to validate the efficacy of alternative medicine and integrate it effectively with contemporary methods for comprehensive diabetes management. This review provides valuable insights into the current diabetes treatment landscape and outlines recommendations for future research and healthcare practices. A total of 107 relevant articles were reviewed, covering studies up to 2024, using search engines and databases such as PubMed, Scopus, Web of Science, and Google Scholar. Both contemporary and alternative medicines show promise in managing diabetes, with an integrated approach potentially offering optimal outcomes. However, further evaluation of the safety of these medicines is necessary, as this remains a limitation and an avenue for future studies.

INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia, abnormal lipid and protein metabolism, and chronic complications affecting the cardiovascular and vascular tissues, such as the arteries, renal glomeruli, myocardium, and the vasculature of the central nervous system (Qureshi et al., 2009; Yu et al., 2024). Diabetes mellitus significantly impacts patients' health, quality of life, and life expectancy while imposing a substantial burden on the healthcare system. It has been recognized as a growing global epidemic by many health advocacy groups, including the World Health Organization (WHO) and the International Diabetes Federation (IDF) (Edwin et al., 2006; Hossain et al., 2024).

According to WHO estimates, diabetes will rank among the world's leading causes of mortality and disability within the next 25 years. The worldwide prevalence of type 2 diabetes mellitus is anticipated to increase to 7,079 persons per 100,000 by 2030, reflecting a rise across all global regions (Khan et al., 2020). In 2021, the International Diabetes Federation (IDF) reported that 537 million adults worldwide had diabetes, and this figure is projected to rise to 643 million by 2030 and 783 million by 2045 (IDF, 2021; Moke et al., 2023a).

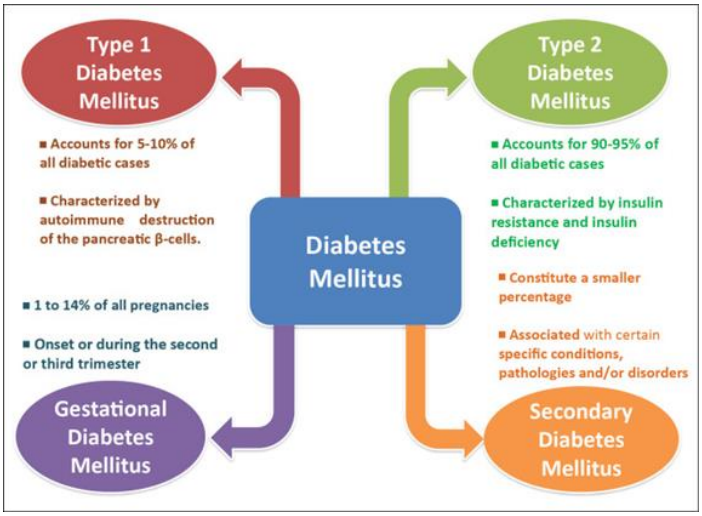
This review evaluates the effectiveness of various contemporary and alternative medicines in managing diabetes mellitus and identifies the strengths of these treatment modalities. A comprehensive online search of relevant published studies in PubMed, Scopus, Embase, and ResearchGate up to 2024 resulted in the selection of 107 articles for inclusion in this review. Keywords used in the search included "*diabetes mellitus,*" "*contemporary medicine in diabetes,*" "*herbal remedies,*" "*hyperglycemia,*" and "*diabetes management.*"

CLASSIFICATION AND PATHOPHYSIOLOGY OF DIABETES MELLITUS

Based on its etiology and pathogenesis, diabetes is classified into four main categories (Banday et al., 2020):

1. Type 1 diabetes mellitus (T1DM)
2. Type 2 diabetes mellitus (T2DM)
3. Gestational diabetes mellitus
4. Secondary diabetes mellitus (linked to specific disease conditions, pathologies, and/or disorders)

Figure 1:
Types of diabetes *(Banday et al., 2020)*



Diabetes is known to have a strong genetic component, with environmental factors contributing to its development (Tremblay & Hamet, 2019). Regardless of the pathogenic cause, the early stage of diabetes is characterized by insulin resistance, primarily affecting the liver, skeletal muscle, and adipocytes (Ortiz-Martínez et al., 2022). Insulin resistance correlates with increased glucose production by the liver and reduced glucose utilization by peripheral tissues, particularly muscles (da Silva Rosa et al., 2020).

The predominant acute complications of diabetes include metabolic disorders such as hyperosmolar hyperglycemic non-ketotic syndrome (HHNS) and infections (Pasquel & Umpierrez, 2014). Long-term complications involve macrovascular problems, microvascular issues, and diabetic ulcers. Understanding the classification and pathophysiology of diabetes is crucial for developing effective remedial actions.

CONVENTIONAL MANAGEMENT OF DIABETES MELLITUS

The conventional management of diabetes mellitus involves a comprehensive approach that includes lifestyle modifications, pharmacotherapy, and regular monitoring to regulate blood glucose levels and prevent complications (García-Molina et al., 2020; Karki et al., 2022). Patients are encouraged to adopt a healthy diet with controlled carbohydrate intake, engage in regular physical activity, and maintain a healthy weight, particularly for type 2

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diabetes. Pharmacotherapy varies between types; type 1 diabetes requires insulin therapy with regimens designed to mimic normal insulin release, while type 2 diabetes typically begins with oral hypoglycemic agents such as metformin, progressing to insulin if necessary. Lifestyle modifications must be integrated with oral hypoglycemic medications for optimal glycemic control.

Pharmacological Management and Its Limitations

Oral therapy is recommended for patients whose glycemic control remains inadequate despite dietary and exercise interventions. There are approximately seven major approved classes of oral hypoglycemic agents currently available, which include biguanides, sulfonylureas, glinides, thiazolidinediones, alpha-glucosidase inhibitors, dipeptidyl peptidase-4 inhibitors, and the most recent sodium-glucose cotransporter-2 inhibitors (Alhadramy, 2016).

Metformin (a biguanide) is considered the first-line pharmacological approach after the diagnosis of type 2 diabetes mellitus (Di Mauro et al., 2022). However, metformin presents several limitations. Its use is contraindicated in patients with significant renal impairment due to the heightened risk of lactic acidosis (Inzucchi et al., 2014). Gastrointestinal disturbances, including nausea, indigestion, flatulence, and diarrhea, are prevalent and may lead to poor adherence (Bonnet et al., 2017). Additionally, long-term use of metformin is associated with vitamin B12 deficiency, necessitating regular monitoring (Infante et al., 2021).

Other classes of oral hypoglycemic agents, while effective, also have notable limitations. Sulfonylureas are linked to an increased risk of ischemic stroke, cardiovascular issues, and mortality (Filion et al., 2019). Thiazolidinediones (TZDs) are commonly associated with a heightened risk of heart failure (Giglio et al., 2022). Dipeptidyl peptidase-4 (DPP-4) inhibitors generally have a favorable safety profile but may demonstrate modest efficacy in lowering blood glucose levels. Although acute pancreatitis has been reported with DPP-4 inhibitors, a definitive connection remains unestablished (Singh et al., 2013; Lai et al., 2015). Sodium-glucose co-transporter-2 (SGLT2) inhibitors, despite their cardiovascular benefits, are associated with genital tract infections, an increased risk of amputation, and diabetic ketoacidosis (Donnan et al., 2019; Pelletier et al., 2021). Alpha-glucosidase inhibitors, such as acarbose, offer cardioprotective effects but are limited by gastrointestinal side effects, including bloating, gas, and diarrhea, which can reduce patient compliance (Hedrington & Davis, 2019). These agents are also less effective at lowering blood glucose levels compared to other medications. Glinides, such as repaglinide, have a shorter duration of action, requiring multiple daily doses and presenting a hypoglycemic risk, particularly if meals are skipped. Weight gain is also associated with these agents, making them less suitable for obese patients.

COMPLEMENTARY AND ALTERNATIVE MEDICINE USE IN DIABETES MELLITUS

Diabetic patients must manage their blood glucose levels through medication and/or by following a structured exercise regimen and dietary plan. The modernization of lifestyle is contributing to the increasing prevalence of type 2 diabetes mellitus in developing countries. Patients with T2DM are typically assigned a restricted diet and advised to engage in exercise, primarily for weight management purposes. When dietary and exercise interventions do not achieve target blood glucose levels, pharmacological therapy is indicated (Umpierrez & Korytkowski, 2016). The development of drug resistance, adverse effects, and lack of responsiveness in a significant portion of the patient population are drawbacks associated with pharmacotherapy. These limitations have led to the increased use of alternative medicine as a potential solution to this global epidemic.

Complementary and alternative medicine (CAM) encompasses a range of medical and health care systems, products, and practices not typically regarded as part of conventional healthcare (Kristoffersen et al., 2018). The National Center for Complementary and Alternative Medicine in the United States defines CAM as "*a group of medical and health care systems, practices, and products that are not presently considered part of conventional medicine.*" Complementary medicine is used alongside conventional therapy, whereas alternative medicine is employed in place of conventional medicine (Kumar et al., 2006; Setiyorini et al., 2022).

The global prevalence of CAM use in diabetes mellitus is rising (Kifle, 2021), with regional variations: Lebanon (38%)

(Naja, 2014), United Arab Emirates (39.3%) (Radwan, 2020), Egypt (41.7%) (Khalil, 2013), United Kingdom (46%) (Thomas et al., 2001), Australia (46%) (Kristoffersen et al., 1996), Taiwan (61%) (Chang et al., 2010), Korea (65%), India (67%) (Kumar et al., 2006), and West Africa (over 80%) (Matheka & Demaio, 2013; Ala et al., 2020; Moke et al., 2021).

A study conducted in Shiraz, Iran, investigated the prevalence and patterns of CAM use among patients with diabetes mellitus. The cross-sectional study, which included 239 patients, found that 75.3% of participants used at least one type of CAM in the preceding year. Herbal preparations were the most popular form of CAM, used by 97.7% of CAM users. Patients who believed that CAM had a synergistic effect with conventional medicine were more likely to use CAM (Hashempur et al., 2015). Folk foods, herbs, natural and spiritual healing, and vitamin and mineral supplements were the most commonly used forms of CAM (Radwan et al., 2020).

Herbal Remedies

Herbal remedies are often preferred, especially in rural areas, due to their easy availability, reduced side effects, and low cost (Arya et al., 2011). Phytochemicals have long been a cornerstone of pharmacological discovery, with a significant proportion of contemporary medicines being derived directly or indirectly from plant sources (Mishra et al., 2018). Several conventional antidiabetic plant treatments are employed worldwide and are considered to have fewer side effects and less toxicity compared to synthetic drug treatments (Bindu & Narendhirakannan, 2019).

The ability of plants to enhance pancreatic tissue function, achieved either by boosting insulin secretion or decreasing intestinal glucose absorption, is frequently the cause of the hypoglycemic effects observed with plant-based therapies (Kooti et al., 2016). Certain herbs are reported to possess antioxidant properties in addition to helping maintain normal blood sugar levels (Parham et al., 2020). Conventional medications have been developed from the active molecules of these medicinal plants, and the hypoglycemic effects of certain herbal extracts have been verified in both human and animal models of type 2 diabetes (Mishra et al., 2018). Metformin, derived from *Galega officinalis*, is a powerful oral glucose-lowering drug and a less harmful biguanide used to treat diabetes (Bailey, 2017). A list of some of the most researched and widely utilized hypoglycemic medicinal plants is summarized below.

Momordica charantia

In diabetes therapy in folk medicine, *Momordica charantia* (bitter melon) has been widely utilized. Both animal experimental models and clinical trials have demonstrated that fresh juice or unripe fruit lowers blood sugar levels (Cortez-Navarrete et al., 2021). It contains many bioactive compounds, such as charantin, polypeptide-p, cucurbitane glycosides, and phenolic compounds. Treatment of alloxan-induced and streptozotocin (STZ)-induced diabetic rats with *Momordica charantia* fruit extract increased the number of β-cells, islet size, and total β-cell area and induced the regeneration of β-cells in pancreatic islets (Singha & Gupta, 2007; Abdollahi et al., 2011). Clinical trials involving several studies on type 2 diabetes mellitus (T2DM) have shown a positive effect of *Momordica charantia* administration on glycemic control parameters (Cortez-Navarrete et al., 2023).

Trigonella foenum-graecum

In Asia, fenugreek (*Trigonella foenum-graecum*) is a common food herb often used to enhance flavours in homes and is well-liked for its strong aromatic qualities. Its seeds have long been used to treat various illnesses, including diabetes (Sarker et al., 2024). With a variety of bioactive compounds in its seeds and leaves, fenugreek has been a folk remedy for diabetes for millennia (Laila & Murtaza, 2015). The pharmacological and biological actions of fenugreek seeds are mainly due to the presence of free amino acids (4-hydroxyisoleucine) and several bioactive components (quercetin, diosgenin, and trigonelline) (Mehrafarin et al., 2011). Reports have shown that *T. foenum-graecum* exhibits hypoglycemic, hypolipidemic, insulinotropic, and antioxidant properties in vivo (Laila et al., 2023). The herb's antidiabetic mechanisms include inhibiting carbohydrate-metabolizing enzymes, restoring glucose-utilizing enzymes, preserving pancreatic β cells, and improving insulin sensitivity (Sarker et al., 2024). The high fibre content, constituting over 50% of seeds, may also contribute to fenugreek's benefits for individuals with diabetes (Fadini, 2017).

During a glucose tolerance test, 15 g of fenugreek seed powder steeped in water significantly reduced postprandial glucose levels in patients with T2DM (Fadini, 2017).

Gymnema sylvestre

Strong antioxidant activity and hypoglycemic effects were demonstrated by the ethanol extract of *Gymnema sylvestre* leaf in a study on diabetic mice (Kang et al., 2012). The primary chemical components of *G. sylvestre* are triterpenoid saponins called gymnemic acids, considered the active compounds responsible for the extracts' antidiabetic properties (Kanetkar et al., 2007). Using liquid chromatography-mass spectrometry (LC/MS) analysis, the antihyperglycemic compounds gymnemagenin and gymnemic acids were identified in *G. sylvestre* extracts (Kang et al., 2012). The woody climber *G. sylvestre* (Asclepiadaceae), found in the tropical forests of India, has been used for generations to treat diabetes (Oh, 2015). People with T2DM who took 400 mg of *Gymnema sylvestre* water-soluble extract daily experienced significant reductions in insulin needs and HbA1c levels (Shanmugasundaram et al., 1990). Aqueous extract of *G. sylvestre* leaves reduced blood glucose levels in diabetic rats by regenerating beta cells and pancreatic islets (Liu et al., 2009; Al-Romaiyan et al., 2012; Oh, 2015).

Azadirachta indica

Azadirachta indica (Neem) is an evergreen tree belonging to the genus *Azadirachta* in the family Meliaceae. The plant is employed in traditional medicine in India, Nigeria, and other nations to treat various illnesses, including diabetes (Subapriya & Nagini, 2005; Afolayan & Sunmonu, 2010; Lawal et al., 2010). According to Ezeigwe et al. (2020), the aqueous extract of *A. indica* significantly induced the regeneration of pancreatic beta cells and reversed the deteriorating effects of diabetes, indicating its potential as an alternative treatment. Other studies have highlighted its ameliorative effects on hyperglycemia (Pingali et al., 2020). Ethanol extracts of *A. indica* stem bark contain bioactive compounds capable of reducing hyperglycemia by improving glucose absorption, inhibiting diabetes-related enzymes, and mitigating oxidative stress (Sanni et al., 2019).

Spondias mombin

Spondias mombin, commonly referred to as hog plum, has demonstrated antidiabetic properties (Gobinath et al., 2022; Moke et al., 2023b; Moke et al., 2024a). In STZ-induced diabetic rats, the methanolic extract of *Spondias mombin* leaves (MESM) significantly lowered blood glucose levels and restored plasma insulin levels following 28 days of therapy with varying doses of MESM (Gobinath et al., 2022). Earlier research reported that methanol and aqueous leaf extracts of *S. mombin* possess antihyperglycemic properties (Adediwura & Kio, 2009; Moke et al., 2015).

Physical Interventions

Acupuncture

Acupuncture, a Chinese therapeutic technique, involves the insertion of very fine needles into specific points on the body to influence the flow of qi, or vital energy. Several randomized controlled trials have examined the effectiveness of acupuncture in diabetes management (Shen & Kong, 2007; Peplow & Baxter, 2012; Kazemi et al., 2019; Cheok et al., 2023). Acupuncture is particularly useful for treating diabetes and its complications, including diabetic neuropathy (Cho & Kim, 2021). Clinical studies suggest that combining acupuncture with conventional antidiabetic drugs significantly improves glycaemic control in type 2 diabetes mellitus (T2DM) by decreasing fasting blood sugar levels and enhancing insulin resistance (Kazemi et al., 2019; Li et al., 2021). While acupuncture is generally considered safe in mild diabetic states, its long-term effects in T2DM remain to be fully established (Li et al., 2021).

Yoga

Research consistently highlights the efficacy of yoga, a traditional Indian practice, in improving glycemic control among individuals with T2DM (Chimkode et al., 2015; Cui et al., 2016; Thind et al., 2018). Yoga combines physical postures (asana) and relaxation techniques (meditation and shavasana), fostering heightened awareness of bodily sensations and present-moment experiences through controlled breathing, postures, and meditation. Several mechanisms have been proposed to explain yoga's biological benefits for diabetes management (Fadini, 2017). Yoga has been shown to enhance insulin sensitivity in target tissues, reducing insulin resistance and increasing

peripheral glucose consumption (Sahay, 2007; Chimkode et al., 2015).

Yoga also modulates the sympatho-adrenal system and hypothalamic-pituitary-adrenal (HPA) axis, potentially enhancing parasympathetic activity and alleviating stress by reducing the release of stress hormones (Padmavathi et al., 2023). By promoting stress resilience, yoga may prevent cortisol-induced elevations in blood glucose levels, thereby aiding glycemic regulation (Else et al., 2010; Thind et al., 2018).

Massage Therapy

Massage therapy, a traditional healing practice, has shown positive effects on blood glucose regulation and relaxation in various studies (Muoio & Newgard, 2008; Umpierrez & Korytkowski, 2016). Massage reduces stress by triggering the relaxation response, which can enhance insulin utilization and reduce counter-regulatory stress hormones. Improved blood circulation associated with massage therapy may also benefit individuals with diabetic neuropathy and other complications (Chatchawan et al., 2015; Sunarmi et al., 2022).

Studies indicate that massage induces skin microcirculation, dilates blood vessels, and improves blood flow, promoting insulin secretion and supporting the function of the nervous and vegetative systems (Wändell et al., 2012; Seiger Cronfalk et al., 2020). Additionally, massage has been found to enhance metabolism and immune function, encouraging muscle tissue to utilize glucose, thus lowering blood sugar levels (Xie et al., 2022).

Dietary Supplements

Vitamins and minerals, essential micronutrients, play critical roles as coenzymes and cofactors in metabolic reactions, supporting fundamental cellular processes (Gombart et al., 2020; Moke et al., 2024b). Research has explored their potential as preventive and therapeutic agents for managing both type 1 and type 2 diabetes and related complications (Dubey et al., 2020; Sumaily, 2022). Trace elements such as chromium (Cr), zinc (Zn), vanadium (V), copper (Cu), selenium (Se), and iron (Fe) are implicated in the onset and progression of T2DM (Siddiqui et al., 2014; Rodríguez-Pérez et al., 2021). Oxidative stress, which contributes to insulin resistance and diabetes, may result from excess or deficiency of these trace elements (Dubey et al., 2020).

Chromium, zinc, copper, iron, and selenium exhibit antioxidant properties, which enhance insulin action by activating insulin receptors or increasing insulin sensitivity (Rodríguez-Pérez et al., 2021). Zinc, in particular, plays a significant role in glycaemic regulation through mechanisms such as promoting glycolysis, reducing gluconeogenesis, and inhibiting intestinal alpha-glucosidase activity (Kant et al., 2021). In pancreatic β-cells, zinc is highly concentrated within insulin secretory granules, and its deficiency has been associated with oxidative stress-induced damage to these cells (Lemaire et al., 2012; Fukunaka & Fujitani, 2018).

Selenium, known for its antioxidant and cytoprotective properties, has been identified as a preventive measure against metabolic disorders, including T2DM (Wei et al., 2015; Steinbrenner et al., 2022). At higher doses, selenium (in the form of selenate) has demonstrated both insulin-mimetic and anti-diabetic effects (Steinbrenner, 2013).

Magnesium, essential for macromolecular metabolism, acts as a rate-limiting factor for enzymes involved in carbohydrate metabolism and energy production (Panel & Nda, 2015). Epidemiological studies have reported a high prevalence of hypomagnesemia among individuals with T2DM, linking magnesium deficiency to an increased risk of developing the condition (Lee & Olefsky, 2021; von Ehrlich et al., 2017).

CONCLUSION

This review provides valuable insights into the efficacy of complementary and alternative medicine (CAM) in diabetes management. The findings highlight the potential of CAM in achieving glycemic control and preventing diabetes-related complications. Traditional medicine, grounded in cultural practices, encompasses a variety of interventions, such as herbal remedies, dietary modifications, and mind-body therapies, with numerous clinical trials and systematic reviews supporting their efficacy. These interventions are becoming widely accepted in diabetes care.

While both traditional and contemporary medicine have unique advantages, evidence suggests that an integrated

approach combining both can yield optimal outcomes in diabetes management. However, future research should prioritize evaluating the safety margins of CAM therapies in clinical settings. Active pharmacovigilance, ethical considerations, and stringent regulatory measures are essential for integrating CAM into conventional healthcare systems.

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