

An Overview of Complementary Therapies for Effective Diabetes Management

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ABSTRACT

Diabetes mellitus is a global health concern resulting in significant morbidity and mortality. Till today there is no known cure available for the condition. The extended treatment schedule, unfavorable side effects of commercially available oral hypoglycemic medications, and heavy financial burden, enable patients towards exploring other forms of treatment. The integration of Complementary and Alternative Medicines (CAM) into treatment and management plans for diseases such as diabetes has grown in popularity in recent years. This form of medicine has been used for centuries and has been demonstrated to be effective when used in combination with more traditional therapies. However, there is limited evidence that CAM therapies can be disruptive to the pharmacokinetics and pharmacodynamics of medications or that they are ineffective. In this study primary focus has been given to summarize the effects of some of the common complementary alternative medicines and associated therapies in treatment and management of diabetes along with their possible mechanisms.

Keywords: Alternative medicine, Complementary medicines, Diabetes, Dietary supplements, Herbs, Herbal medicines.

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INTRODUCTION

Complementary and Alternative Medicine (CAM) is a broad term which includes a range of health-care practices, activities, and services which are increasingly accepted by mainstream medicine.¹ According to a medical expenditure panel study, CAM is characterized as a caring approach that includes acupuncture, special diets, massage therapy, use of medicinal plants, biologic feedback, relaxation techniques, etc.² Complementary medicine can also be defined as a group of diagnostic and therapeutic disciplines that are employed in conjugation with the conventional therapy for effective and comprehensive health care. In the 1970s and 1980s, these disciplines were mostly provided as an alternative to traditional medical care; therefore, the term "alternative medicine." was given. As both the conventional and alternative therapy was started using alongside to complement the effect of the other, the term "complementary medicine" was coined.³ Complementary therapies are delivered by a diverse group of professional caregivers, each with their

own set of educational qualifications, professional credentials, and regulatory oversight. Therefore the therapy varies based on geographic location, and cultural ethnicity.⁴ National Center of Complementary and Integrative Health (NCCIH) broadly classified complementary therapies based on their therapeutic input or by the way of administration to the patients namely

Nutritional and natural products based therapy.

- Mind body practices.
- Psychological such as meditation, hypnosis, music therapies, relaxation therapies.
- Physical such as acupuncture, massage, spinal manipulation etc.

Combinations of psychological and physical

The increasing prevalence of diabetes mellitus has become a major global health concern, with serious implications for both mortality and morbidity, with no known cure yet. According to the International Diabetes Federation, there were 463 million people who were diagnosed with diabetes in 2019 and this figure is expected to rise to 700 million by 2045. The use of synthetic anti-diabetic medications has grown in recent years, with thiazolidinediones, meglitinides, biguanides, sulfonylureas,



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glucosidase inhibitors, GLP-1 analogues, and DPP-4 inhibitors all being used to help treat and manage diabetes. Many of these treatments, however, have substantial side effects, and 10-20% of diabetic patients stop taking them as a result of these side effects. Hypoglycemia, weight gain, gastrointestinal side effects (abdominal discomfort, nausea, vomiting, diarrhea, gassiness, and bloating), edema, and a rise in LDL-C are some of the common adverse effects of oral diabetic medications.⁵ Diabetes also comes with a significant financial burden for those who suffer from it. The annual medical expenditures T2DM is worth several billion dollars, including direct costs as well as indirect medical costs.⁶ Thus, there is an urgent requirement for effective substitutions to reduce the complications of diabetes with lower side effects. In recent times, the exploration of additional diabetic therapies has been an area of great interest. Substantial evidence from many research documents has revealed that Complementary and Alternative Medicine (CAM) can be used to treat and manage diabetes around the globe. The utilization CAM in diabetes is on the rise due to the reported drawbacks of conventional synthetic medications and the faith that many people have in traditional treatment.^{6,7} Complementary therapies such as taking nutritional supplements, using herbal medicines, obtaining nutritional guidance, and engaging in spiritual healing and relaxation practices are gaining popularity among diabetic patients.⁸ This review will summarize the research done on the use and limitations of complementary medicine to treat and manage diabetes.

MATERIALS AND METHODS

This study aimed to assess the efficacy of complementary medicine in handling diabetes. To this end, various databases such as PubMed, Google Scholar, Research Gate, Scopus, Medline and Science Direct were searched using keywords like 'diabetes', 'herb-drug combination therapy', 'synergistic action', 'dietary supplements' and 'complementary therapy'. Only English-language articles published after 2010 and relevant to the study's objective were included in the analysis and duplicate articles, abstracts, and articles unrelated to the objective were excluded (Figure 1).

RESULTS AND DISCUSSION

Herbal Complementary Medicine/Therapy

Natural products, particularly those derived from plants are serving as promising lead compounds. Plant-based preparations are the critical contributor in today's field of medicine, due to their ease of use, low cost, and lack of side effects.⁹ As per the recent study by Salehi *et al.* several medicinal plants that have been traditionally utilized in the treatment and management of diabetes.¹⁰ Table 1 outlines the results of recent studies on herbal complementary therapy, which demonstrate significant complementary effects after the co-administration or

simultaneous administration of natural products such as isolated natural compounds and extracts from different parts of plants alongside commercially available drugs.

Recent studies have suggested that polysaccharides derived from natural sources may be beneficial in anti-diabetic therapy, due to their strong antioxidant properties.^{5,11,12} An investigation of anti-diabetic therapy in alloxan-induced diabetic rats found that a combination of polysaccharide isolated from the roots of *Acanthopanax senticosus* (200 mg/kg/BW) and metformin (2 mg/kg/BW) was more effective than metformin alone in relieving diabetes symptoms and healing liver and kidney damage.¹³

One such example of plant namely *Gymnema sylvestre* was reported to have promising hypoglycemic and blood cholesterol-lowering properties.¹⁴ In a study, rats with induced diabetes were given a dose of 400 mg/kg of *Gymnema Sylvestre* leaf extract alongside 0.8 mg/kg of Glimperide for a period of 28 days. The results showed a marked increase in anti-hyperglycemic and anti-hyperlipidemic activity. Further, concomitant administration of the leaf extract in conjunction with glimepiride produces a greater decrease in HbA_{1c} levels in the blood and an increase in serum insulin levels compared to glimepiride taken alone.¹⁵

The use of *Azadirachta indica* (AZI) has been documented since ancient times for its ability to treat a range of illnesses. Recent evidence suggests that extracts from both the leaf and bark of this plant may reduce blood glucose levels and improve the lipid profile.¹⁶ However, when combining Glipizide (GZ) with AZI leaf extract, it is recommended to exercise caution. In a study involving streptozotocin-induced diabetic rats, administering either of two doses of AZI extract (250 mg/kg) or a combination of extract and GZ (5 mg/kg) decreased the bioavailability of GZ and its subsequent hypoglycemic effect.¹⁷

The use of garlic as a nutritional and medicinal supplement has been gaining recognition around the world.¹⁸ The study conducted by R. Kumar *et al.* revealed that a combination of garlic (250 mg) and metformin (500 mg) was more effective at decreasing the blood glucose level of obese diabetic patients than metformin alone. In addition, the participants in the study had a noticeable improvement in their lipid profiles. Additionally, Studies have found that combining garlic and metformin may help to reduce the nephrotoxicity associated with gentamycin.^{19,20}

Further, Gliclazide is a common treatment for type 2 diabetes mellitus, yet it has been demonstrated that its efficacy declines with time. This is attributed to the progressive linear decline in β -cell function that occurs with the disease.²¹ Considering this issue several researches has been carried out to potentiate the efficiency of Gliclazide with combination of herbal drugs. In a study conducted by Vastavai *et al.*, healthy rats and rabbits were co-administered gliclazide (100/200 mg/kg) and curcumin (2/4 mg/kg). Surprisingly, there was a marked decrease in the animals'

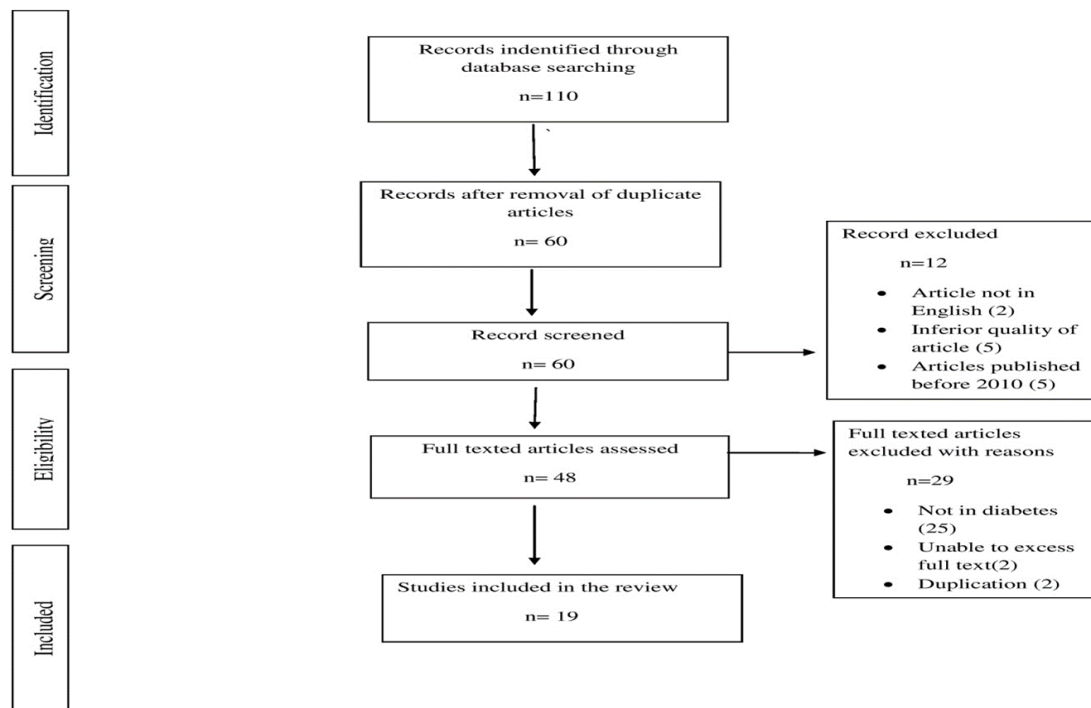


Figure 1: Flow Chart of the study selection process.

blood glucose levels after multiple doses, and the combination proved to be more effective than gliclazide alone in terms of overall therapeutic effects.²² Further a study states that when streptozotocin induced diabetic rats were administered gliclazide and quercetin together, their glucose homeostasis, lipid profile, and inflammatory status were improved. Additionally, insulin immunostaining in their beta cells returned to normal levels.²⁴

Studies have indicated that a combination of *Annona squamosa* leaf extract and various concentrations of Glipizide (300 mg/kg, 3.75 mg/kg, 2.5 mg/kg, 1.25 mg/kg) given to streptozocin-induced diabetic rats on a high-fat diet can lead to a reduction of their blood glucose levels by 25-50%. This could potentially decrease the need for Glipizide.^{24,25} Additionally, co-administering leaf extract of *Brassica rapa* (turnip) with metformin has been reported to improve hypoglycemic activity in diabetic rats.^{26,27}

Limitation of herb drug combination therapy

Herbal medicines or supplements can be used in conjunction with conventional therapy for diabetic patients, but the potential effects of these components should be evaluated. This could have a positive or negative impact on how drugs work in the body.³² The absorption, distribution, metabolism, and/or excretion of conventional medications may be affected when taken with herbs or supplements. This could potentially lead to the inhibition or induction of metabolic enzymes, efflux proteins, and drug transporters.³³ The use of herbs and drugs together can have varying effects, ranging from improved treatment results to the potential for dangerous toxicity and diminished drug efficacy,

and even the possibility of rendering the treatment ineffective.³⁴ Further, The presence of a bioactive component with medicinal activity can be impacted by factors such as the process of cultivation, collection time/season, growth conditions, and parts used. Because of this, the therapeutic potency of herbal medicines or supplements may be affected.³⁵ Therefore, In order to maximize the effectiveness of complementary medicine, it is essential to have a thorough understanding of the patient's clinical condition and the potential benefits and limitations of the therapy.

Dietary Supplement as Complementary Medicine

The use of CAM treatments, including dietary supplements, is growing in popularity for people with diabetes as a way to help manage the condition. Many people are turning to dietary supplements as an additional form of diabetes management. Most common dietary supplements used for diabetes include: herbs, vitamins, minerals, and other dietary components.³⁶ Herbal supplements are the most widely used dietary supplements for diabetes. Herbs such as garlic, ginger, fenugreek, and cinnamon are believed to help manage diabetes symptoms by improving insulin sensitivity, decreasing blood glucose levels, and improving overall glycemic control.³⁷ Table 2 outlines some study that were conducted to highlights the role of dietary supplements in diabetes management. A systematic review of the available literature has revealed that garlic and ginger are the only herbs which have shown a noteworthy reduction in blood glucose levels; however, the effectiveness of these herbs is not unanimous.³⁸ Research has indicated that certain vitamins and minerals are often used

Table 1: A list of some herbal complementary therapies.

Herb/herbal supplement	Dose	Study subject	Study period	Observation	References
<i>Acanthopanax senticosus</i> polysaccharide (ASP)	ASP 200 mg/kg+ metformin 2 mg/kg.	Alloxan-induced diabetic rats.	28 days	↓ Blood glucose, ↓ Blood lipid (TC and TG), TBARS, GSH, AST, ALT, ALP, total bilirubin, creatinine and urea levels ↑ body weight, liver glycogen formation, and antioxidant enzyme (SOD and GPX) levels.	13
Turnip leaf Aqueous extract	Extract 400 mg/kg+50/100 mg/kg metformin.	Streptozotocin-induced diabetic rats.	28 days	Improved hypoglycemic activity ↓ liver enzymes elevation(both AST and ALT) and histological damages.	27
<i>Azadirachta indica</i> aqueous extract of leaves	Extract 250 mg/kg +GZ 5 mg/kg.	Streptozotocin induced diabetic Sprague-Dawley rats.	14 days	↓ hypoglycemic effect ↓ Bioavailability of Glipizide due to the induction of CYP3A activity.	17
<i>Scutellaria baicalensis</i>	Extract 3.52 g/day+ 500 mg metformin.	Human volunteer 20-75 years.	20 weeks	Improve glucose tolerance	28
<i>Gymnema sylvestre</i> Leaf extract	Extract 400 mg/kg+ 0.8 mg/kg glimepiride	Streptozotocin (STZ) induced diabetic rats	28 days	No significant pharmacokinetic interaction. ↓ Blood glucose	15
Curcumin	Curcumin 200 /100mg/kg+ Gliclazide 2/4 mg/kg	Albino rats	21 days	Significant reduction of blood glucose level was observed	22
Quercetin	Quercetin 50 mg/kg+10 mg/kg Gliclazide	Streptozotocin (STZ) induced diabetic rats.	21 days	↓ Blood glucose ↑ c peptide ↑ lipid profile	23
<i>Aloe vera</i> gel	Aloe gel 300 mg/kg+2 mg/kg Metformin.	Male albino rats.	21 days	↓ hyperlipidemia, improve pancreas and kidney integrity ↑ HDL-cholesterol level.	29
Garlic extract	Extract 20 mg/kg+metformin100 mg/kg	Male wistar rats.	20 days	Curative and protective activity against nephrotoxicity.	30
<i>Annona squamosa</i> aqueous leaf extract	Extract 300 mg/kg+3.75 mg,2.5 mg,1.25/kg glipizide	Sprague-Dawley Rats.	25 days	↓ Blood glucose	25

Herb/herbal supplement	Dose	Study subject	Study period	Observation	References
Garlic capsules	Garlic capsule 250 mg+500 mg Metformin.	60 human volunteer of both sex.	12 weeks	Greater fall in cholesterol, triglyceride, and low-density lipoprotein C-reactive protein was observed in combination.	19
<i>Gymnema sylvestre</i> leaf extract.	Extract 500 mg/kg+100 mg metformin.	Wistar rats	21 days	↓ Hypoglycemic effect of Metformin.	31

Table 2: Some common dietary supplements in diabetic patients.

Dietary supplement	Study subject	Doses	Investigation	Observation	References
Chromium picolinate	78 diabetic patients	200 µg of chromium twice a day for 3 weeks.	Fasting blood glucose (FBS), cholesterol, HDL, LDL triglycerides (TG), HbA _{1c} , insulin levels.	↓ FBS ↓ HbA _{1c} ↓ cholesterol.	38
Chromium picolinate	52 diabetic patients	400 µg of chromium in a day for 8 weeks.	FBS, cholesterol, lipoproteins, insulin level and Insulin resistance.	↓ Cholesterol ↓ LDL-C ↓ Insulin resistance No significant improvement in FBS, triglycerides, HDL.	39
Omega-3 fatty acids	344 diabetic patients	1 g/day, 2 g/day, 4 g/day for 1.4 years (median).	Blood glucose, lipid profiles. GFR, ACR.	↓ Cholesterol ↓ Triglycerides ↓ ACR.	44
Magnesium (Mg) supplement	42 diabetic patients	250 mg/day for 3 months.	FBS, HbA _{1c} , insulin levels, C-peptide.	↑ HbA _{1c} , ↑ Insulin levels, ↑ C-peptide ↓ FBS.	45
Oral magnesium	71 diabetic patients	300 mg/day for 3 months.	HbA _{1c} , lipid profile, and serum Mg.	↓ HbA _{1c} ↓ Cholesterol ↓ TG.	46
Zinc supplement	54 diabetic patients	50 mg/day for 12 weeks.	Blood glucose, cholesterol, HDL, LDL triglycerides, HbA _{1c} .	↓ FBS ↓ PPBS ↓ HbA _{1c} ↓ Cholesterol ↓ TG ↑ HDL.	43
Alpha Lipoic Acid	25 diabetic patients	300 mg/day for 3 months.	BMI FBS Cholesterol.	↓ Insulin resistance ↓ TG.	47

as dietary supplements for those with diabetes. For example, Vitamin D and chromium have been studied for their ability to improve glycemic control. An analysis of existing studies demonstrated that the impact of chromium supplementation on glycemic control for individuals with type 2 diabetes was positive,

while the outcomes of Vitamin D supplementation were more inconsistent.³⁹ Further, Research indicates that omega-3 fatty acid supplementation might be useful in treating type 2 diabetes. Research indicates that omega-3 fatty acids may improve insulin sensitivity and reduce inflammation, which can result in better

glycemic control.⁴⁰ Again, probiotics are also thought to improve glycemic control due to their anti-inflammatory properties and ability to reduce body fat. Fiber is another useful supplement for diabetes, as it can help to increase feelings of fullness and slow down glucose absorption.⁴¹ Results from studies suggest that taking particular probiotic strains may help to improve glycemic control in people with type 2 diabetes. Evidence indicates that probiotics may also be beneficial for increasing insulin sensitivity⁴²⁻⁴⁴ Kumar *et al.* revealed that zinc supplementation in combination with oral hypoglycemic drugs could possibly decrease the likelihood of complications associated with diabetes, as evidenced by lower blood glucose, triglyceride, urinary albumin excretion, and inflammation levels in diabetic nephropathy patients.⁴⁵ Finally, studies have shown that dietary supplements, such as Complementary and Alternative Medicine (CAM), may be beneficial in managing type 2 diabetes. However, further research is needed to assess the impact of these supplements on individuals with type 1 diabetes and to evaluate their long-term safety.

Mind-Body Practices

In recent years, mind-body practices have become increasingly popular as an important tool for diabetes management.⁴⁶ Mind-body practices are defined as activities that involve both physical and psychological components. This includes practices such as yoga, tai chi, meditation, and biofeedback. These activities have been found to have a number of benefits for people living with diabetes.⁴⁷ Mind-body practices are a potential solution for managing diabetes, as they can help to maintain a healthy blood sugar level by reduces stress level of person.⁴⁸ Research has revealed that performing yoga and tai chi on a regular basis can lead to an increase in insulin sensitivity and reduced levels of HbA_{1c}, which signifies sustained blood sugar levels. Additionally, engaging in mind-body practices can diminish the chances of developing diabetes-related medical issues, such as heart disease, stroke, and kidney disease.⁴⁹ Further, Meditation is an exercise for the mind and body that has been proven to diminish stress, anxiety, and even help manage high blood pressure and diabetes. An investigation on 12 weeks of Buddhist-based walking meditation exercise on 23 diabetic patients reported a favorable decrease in the fasting blood glucose level.⁵⁰ Finally, mind-body practices can also help to improve overall quality of life among people living with diabetes. These activities can help to reduce symptoms of depression and anxiety, as well as improve physical and emotional well-being and offer positive benefits in diabetic patients, However, the role of this kind of complementary therapy needs to be evaluated further to establish a liner relation in the treatment of diabetes mellitus.

CONCLUSION

The complementary medicine system and its associated therapies becoming popular day by day due to some of its unique features like lesser side effects, low cost, and patient acceptability. Based on the available literature, case study, and clinical application report it may be concluded that the potential of the complementary medicine system to provide an integrative, participatory approach to diabetes care is noteworthy. Yet, comprehensive research is necessary to ascertain the safety and effectiveness of complementary medicine treatments.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

CAM: Complementary and Alternative Medicine; **NCCIH:** National Center of Complementary and Integrative Health; **GLP-1:** Glucagon-like peptide 1; **DPP 4:** Dipeptidyl peptidase 4; **LDL-C:** Low-density lipoprotein-cholesterol; **mg:** Miligram; **kg:** Kilogram; **BW:** Body weight; **TC:** total cholesterol; **TG:** triglycerides; **HDL:** high density lipoprotein; **LDL:** low density lipoprotein; **ALP:** Alkaline phosphatase; **ALT:** Alanine transaminase; **AST:** Aspartate aminotransferase; **TBARS:** Thiobarbituric acid reactive substance; **GSH:** Glutathione; **FBS:** fasting blood sugar; **HbA_{1c}:** Hemoglobin A_{1c}

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