Complementary and Alternative Medicine Therapies for Diabetes: A Clinical Review

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Complementary and alternative medicine (CAM) refers to a wide range of clinical therapies outside of conventional medicine.[1] The term "complementary" refers to therapies that are used in conjunction with conventional medicine, whereas "alternative" medicine includes therapies that are used in place of conventional medicine. The term "integrative" medicine has been advocated by some CAM providers and researchers as representing a combination of conventional medicine, CAM, and evidence-based medicine.[2]

The National Center for Complementary and Alternative Medicine, a federal scientific agency for CAM research, categorizes CAM into five domains: biologically based practices, mind-body medicine, manipulation and body-based practices, energy medicine, and whole-medical systems (Table 1). Biologically based practices and mind-body medicine are the most common CAM modalities used and studied for the treatment of diabetes in the West and are the focus of this review.

In the United States, CAM is frequently used by adults, with 40% reporting use in the past 12 months.[3] An estimated 34% of adults with diabetes use some type of CAM therapy.[4] The estimated out-of-pocket expense in 2007 on CAM therapies was $44 billion.[5]

Although some CAM therapies have been shown to affect glycemic control, the clinical efficacy and mechanism of many CAM therapies for diabetes is controversial, and safety issues are a concern. Adverse effects of many CAM therapies are not well documented. Because patients with diabetes often take multiple prescription medications, there exists the potential for herb-drug and herb-dietary supplement interactions, leading to adverse events.[6,7] At least 63% of the general population do not disclose use of CAM therapies to their physicians.[8]

The purpose of this clinical review is to discuss selected CAM therapies frequently used for patients with diabetes and to provide a framework to advise patients on CAM use.

Biologically Based Practices: Herbs and Supplements

IN BRIEF

More than one-third of patients with diabetes in the United States use some type of complementary and alternative medicine (CAM). Herbs, dietary supplements, and mind-body medicine are the most commonly used and studied CAM modalities to treat diabetes. This article provides an overview of CAM for diabetes, including proposed mechanisms, a summary of evidence, and adverse effects. It also offers recommendations for counseling patients regarding CAM use.

Definition, regulation, and safety

In 1994, the Dietary Supplement Health and Education Act (DSHEA), approved by the U.S. Congress, defined dietary supplements as products taken by mouth that contain vitamins, minerals, herbs, or other botanicals, amino acids, and substances such as enzymes, organ tissues, glandular substances, and metabolites. Supplements can take different forms, including tablets, capsules, soft gels, gel capsules, liquids, or powders.

Importantly, DSHEA treats dietary supplements as a type of food rather than as drugs. Under this bill, dietary supplements do not need U.S. Food and Drug Administration (FDA) approval before marketing, and manufacturers are not mandated to establish the quality, efficacy, or safety of products. Manufacturers cannot make specific clinical claims that supplements can treat or cure a specific condition. However, nonspecific statements are allowed, such as proclamations that the product "supports," "promotes," or "enhances" specific organ systems. For example, a supplement manufacturer cannot state on the product label that the substance "reduces blood glucose in patients with diabetes," but may state that the product "supports glucose tolerance."

After marketing, the FDA is responsible for determining whether dietary supplements are "unsafe." In 2007, the FDA established a new set of regulations called Good

Table 1. Types of Complementary and Alternative Medicine[1]

CAM Therapy	Description	Examples
Biologically based practices	Therapies involving substances found in nature that have purported medicinal properties	Herbs and dietary supplements such as vitamins and foods
Mind-body medicine	Practices that use the relationship of mind and body to achieve improved health or treat disease	Yoga, tai chi, and meditation
Manipulation and body-based practices	Practices that manipulate or move specific body parts or the whole body	Chiropractic therapy, osteopathic manipulation, and massage
Energy medicine	Practices involving belief in energy fields around and inside the human body that are altered by providers for health benefit	Reiki, external qi gong, and therapeutic touch
Whole medical systems	Complete medical systems that often evolved separately from or earlier than conventional medicine	Homeopathy, naturopathy, *Ayurveda* (traditional medicine from India), and traditional Chinese medicine

Manufacturing Practices to improve the quality of dietary supplements by requiring the industry to appropriately label and ensure the purity, strength, and composition of all dietary supplements. These regulations are scheduled to be phased in by this year. Therefore, their successful implementation cannot yet be evaluated.

The high consumer demand, large supplement industry, and current regulatory framework yield a wide range of products with different compositions and uncertain safety and efficacy. In a 2008 position statement, the American Diabetes Association (ADA) stated that there is insufficient evidence to demonstrate the efficacy of supplements in diabetes management and recognized the lack of standardization among preparations.[9] In the following discussion, we summarize selected herbs and dietary supplements that are commonly used for patients with diabetes and that clinicians may encounter in practice (Table 2).

Botanical products for diabetes treatment

Allium sativum *(garlic)*. Found in many kitchens, *allium sativum* (garlic), has also been used for medicinal purposes around the world. A majority of contemporary medical use and research for garlic has focused on treatment of cardiovascular-related diseases.

In clinical trials, garlic supplementation among patients with dyslipidemia produced modest reduction in total cholesterol with no significant changes in LDL or HDL cholesterol levels.[10,11] Pooled data from clinical trials of patients with hypertension have shown significant decreases in systolic (8.4 ± 2.8mmHg) and diastolic (7.3 ± 1.5mmHg) blood pressure levels in patients using garlic treatment compared to control groups.[12] Less research has been conducted among patients with diabetes. Limited animal studies have suggested that the chemical components of garlic may increase insulin secretion or decrease degradation.[10,11] Clinical trials of oral garlic in patients with type 2 diabetes have not demonstrated significant changes in blood glucose or insulin levels.[12,13]

Aloe vera. This desert plant is the source of the common gel used topically for dermatological conditions. In the Arabian peninsula, parts of the aloe plant have been used orally as a traditional treatment for diabetes. The gel derived from the meaty pulp of the leaf, taken orally, may produce hypoglycemic effects through β-cell stimulation.[13,14]

Two controlled, nonrandomized trials in patients with type 2 diabetes who were given aloe gel juice reported decreases in fasting blood glucose during 6 weeks.[15,16] However, these studies lacked sufficient details in reporting, including study design and results, leading to inconclusive evidence. In contrast to the gel, aloe latex from the inner lining of the leaf contains a harsh anthroquinone laxative that may be unsafe.[17]

Coccinia indica *(ivy gourd)*. *Ayurveda* is a traditional medical system from the Indian subcontinent that often uses herbs for treatment. The creeper plant *coccinia indica* is prescribed in *Ayurveda* for the treatment of diabetes. *Coccinia* may produce hypoglycemia in a mechanism similar to

Table 2. Selected Biologically Based Practices Used for Diabetes

Name	Hypothesized Effect(s) on Glucose Metabolism	Potential Adverse Effects*
Botanicals		
Allium sativum (garlic)	• Insulin secretagogue	• Blood thinning (use caution with anti-coagulation or anti-platelet medications)
Aloe vera	• Insulin secretagogue	• Abdominal pain, diarrhea from laxative component, with subsequent electrolyte depletion
Coccinia indica (ivy gourd)	• Insulin mimetic	• None reported
Gymnema sylvestre (gymnema)	• Insulin secretagogue	• Suppression of sweet taste
Momordica charantia (bitter melon)	• Insulin mimetic • Decreased hepatic glucose production	• Glucose-6-phosphate deficiency • Contraindicated in pregnancy
Opuntia streptacantha (prickly pear cactus, nopal)	• Decreased carbohydrate absorption	• Diarrhea, nausea, abdominal fullness
Panex ginseng, P. quinquefolius (ginseng)	• Insulin mimetic • Alters hepatic glucose metabolism	• May interfere with effect of anti-coagulation and anti-platelet medications • Estrogenic effect with breast tenderness, amenorrhea, vaginal bleeding, impotence • Hypertension • Insomnia
Trigonella foenum graecum (fenugreek)	• Insulin secretagogue • Decreased carbohydrate absorption	• Gas, bloating, diarrhea • Contraindicated in pregnancy
Supplements		
Alpha-lipoic acid	• Increased insulin sensitivity	• Monitor thyroid function in patients with thyroid disease
Chromium	• Increased insulin sensitivity	• Minimal
Coenzyme Q10	• No effect on blood glucose	• Few reported in clinical trials
Magnesium	• Insulin secretagogue • Increased insulin sensitivity	• Diarrhea, abdominal cramping • Magnesium toxicity in individuals with renal failure
Omega-3 fatty acids	• Slight increase in blood glucose	• Intake > 3 g may increase risk of bleeding • Fish meat may have high levels of methylmercury; to be eaten with caution by children and pregnant/breastfeeding women • May increase LDL; caution in patients with very high LDL
Vanadium	• Insulin mimetic	• Prolonged high doses may cause renal toxicity

**All biologically based practices that may reduce blood glucose have the potential for interacting with conventional diabetes medications, producing hypoglycemia. This is not a comprehensive list of potential adverse effects.*

insulin.[18] Two randomized, controlled trials (RCTs)[19,20] and one controlled, nonrandomized trial[18] have suggested decreases in fasting blood glucose without adverse effects among type 2 diabetes patients after administration of *coccinia*. In one of these studies,[20] 60 subjects were randomized to *coccinia* or placebo. Patients who received the herb had a 16% decrease in fasting blood glucose.

Although data are suggestive of a therapeutic effect for *coccinia*, further research is necessary to determine optimal preparations, dose, mechanisms, and safety.

Gymnema sylvestre *(gymnema)*. This botanical has also been used for two centuries in *Ayurveda* for the treatment of diabetes. Traditionally, the leaves of the plant are chewed, which can suppress the sweet taste sensation, giving rise to its Hindi name *gurmar*, or "sugar destroyer." In addition to affecting taste, the herb has demonstrated hypoglycemic effects in animal and human studies, perhaps functioning as an insulin secretagogue.[21,22]

An extract of *gymnema* leaf, called GS4, has been studied as an adjuvant therapy to conventional care in two controlled, nonrandomized trials of patients with type 1 and type 2 diabetes, respectively.[23,24] Both studies reported significant before-to-after improvements in fasting blood glucose and A1C levels among patients receiving GS4. No significant before-to-after changes were reported in the control groups. These studies lacked between-group comparisons and randomization, precluding definitive evidence for *gymnema* for the treatment of diabetes.

Momordica charantia *(bitter melon)*. This tropical vegetable, grown in Africa, Asia, and South America, is known as bitter melon, or "vegetable insulin." It may reduce blood glucose in patients with diabetes.[25,26] Potential mechanisms of action for bitter melon are decreased hepatic glucose production, increased hepatic glycogen synthesis,[27] and insulin-mimetic activity.[28,29] Most clinical trials of bitter melon among patients with diabetes have lacked adequate design to determine clinical effectiveness.[26,30]

Opuntia streptacantha *(prickly pear cactus, nopal)*. Found in desert regions of North America, nopal is used in Mexican cuisine and indigenous medicine. Mexican-American patients with diabetes have reported using nopal for glucose control.[31] Few studies of nopal have been published in English, and these have explored acute metabolic effects rather than clinical outcomes.[32,33]

Panex ginseng, P. quiquefolius *(ginseng)*. The panex genus contains multiple species described as ginseng, with two varieties most frequently used and studied: panex ginseng (Asian ginseng, Chinese ginseng, Korean ginseng) and panex quinquefolius (American ginseng). The root of this herb traditionally has been used in Asia and is one of the most popular botanicals in the United States.[3]

Ginseng has many proposed health benefits, including improved general well-being, increased concentration, and treatment of cardiovascular disease and diabetes (*panex* is cognate to panacea). Ginseng can cause hypoglycemia, perhaps through activity similar to insulin or by altering hepatic glucose metabolism.[34]

Buettner et al., in a systematic review,[35] found conflicting clinical data of ginseng's effect on blood glucose in diabetic and nondiabetic populations. Variations in response may reflect chemical heterogeneity of different ginseng batches used in studies.[36,37]

Trigonella foenum graecum *(fenugreek)*. Fenugreek is grown in North America and Asia and often flavors Indian food. It has been used as medicine for diabetes in India and China. Mechanisms proposed for fenugreek in diabetes are decreased carbohydrate absorption and increased insulin secretion.

Several clinical trials among patients with type 1 or type 2 diabetes suggest a potential effect, but studies thus far have lacked sufficient quality.[38,39]

Dietary supplements for diabetes

***Alpha-lipoic acid (ALA)*.** ALA is a chemical compound that is found in food (especially high in spinach, broccoli, and tomatoes), produced endogenously, and sold as a nutritional supplement. As an antioxidant, ALA may mitigate high levels of oxidative stress, which in patients with diabetes contributes to insulin resistance and secondary complications such as diabetic neuropathy.[40]

Acute intravenous ALA therapy (1–10 days) has been reported to improve insulin sensitivity.[41,42] A randomized, placebo-controlled trial of ALA supplementation in patients with type 2 diabetes[43] showed a 25% increase in insulin sensitivity after 4 weeks of ALA therapy at doses of 600–1,800 mg. The long-term effects of ALA have yet to be determined, although one study of patients with type 2 diabetes showed improved glycemic control after 12 weeks of therapy.[44]

Chromium. As an essential mineral, chromium plays an important role in facilitating glucose metabolism. Whole grains, egg yolks, broccoli, and brewer's yeast have high quantities of chromium.[45] Although rare, severe states of chromium deficiency are associated with reversible diabetes because of insulin resistance.[46,47] These observations have fueled marketing of chromium for individuals with diabetes who are not necessarily deficient in chromium to increase insulin sensitivity.

A meta-analysis of 14 RCTs[48] of patients with type 2 diabetes (n = 381) concluded that there were significant changes in glucose metabolism after supplementation with chromium. Overall, the authors emphasized the poor quality of studies and the need for further research. Reports suggest that response to chromium may be dependent on individual patient phenotypes with those with high insulin resistance being most responsive.[49–51]

Coenzyme Q10. Coenzyme Q10 is a cofactor used in oxidative respiration and is produced endogenously. Supplementation of coenzyme Q10 is especially popular for cardiovascular diseases. Two RCTs of patients with type 2 diabetes and a single RCT of patients with type 1 diabetes produced no strong evidence for glycemic control with coenzyme Q10 supplementation.[52,53]

Magnesium. Magnesium is an abundant mineral in the human body involved in numerous biochemical processes, including glucose metabolism. Dietary sources of magnesium include whole grains, beans, nuts, and green, leafy vegetables. Magnesium deficiency is associated with poor glucose control in patients with diabetes.[54] However, in clinical trials, supplementation of magnesium has not yielded clear long-term positive benefits in type 2 diabetes.

Song et al.[55] conducted a meta-analysis compiling data from nine RCTs with a total of 370 subjects with type 2 diabetes. The duration of the studies ranged from 4 to 16 weeks and the studies administered a median magnesium dose of 15 mmol/day (360 mg/day) to active-treatment groups. The mean post-intervention fasting glucose after 12 weeks of treatment was significantly lower among active-treatment compared to placebo groups: –0.56 mmol/l (95% CI –1.10 to –0.01). The difference in post-intervention A1C was not significant.

Observational data suggest that magnesium supplementation may decrease the risk of type 2 diabetes. A meta-analysis in 2007[56] included seven prospective cohort studies that collected dietary and supplementary magnesium intake and incidence of type 2 diabetes. The relative risk for the development of type 2 diabetes with a 100 mg/day increase in magnesium was 0.85 (95% CI 0.79–0.92).

Omega-3 fatty acid. Omega-3 polyunsaturated fatty acids (PUFAs) are one of the most common dietary supplements taken in the United States.[3] Major sources of omega-3 PUFAs include fish, marine-derived supplements, and prescription formulations (sold under the trade names Omacor and Lovaza).

In the general population, observational studies and RCTs indicate reductions in coronary artery disease and sudden cardiac death based on omega-3 PUFA intake.[57,58] In patients with type 2 diabetes, a meta-analysis of omega-3 PUFA supplementation[59] that pooled data from 23 RCTs with a total of 1,075 patients did not show any significant changes in fasting glucose, A1C, or fasting insulin.

With a mean intake of 3.5 g/day of omega-3 PUFAs, significant decreases in triglycerides (–0.45 mmol/l, 95% CI –0.58 to –0.32) and VLDL cholesterol (–0.07 mmol/l, 95% CI –0.13 to 0.00) and increases in LDL cholesterol (0.11 mmol/l, 95% CI 0.00–0.22) were noted. Subanalysis of patients with hypertriglyceridemia demonstrated no significant increase in LDL. Based on multiple studies, high omega-3 PUFA intake does not prevent the onset of type 2 diabetes.[60]

Vanadium. Vanadium is a mineral with no known biological importance or deficiency-associated disease.[39,61] Although three controlled studies of vanadium for type 2 diabetes reported significant decreases in fasting blood glucose levels, small sample sizes and lack of randomization limit these results.[62–64]

Mind-Body Medicine

Mind-body medicine is based on the concept that the physical body and mind influence each other. It uses specific techniques to affect this connection for the benefit of health. Mind-body techniques have arisen in various cultures and contexts. Some mind-body techniques, such as cognitive-behavioral therapy, bio-feedback, and hypnosis, have been adapted into mainstream medical culture and usually are not considered CAM.

Within CAM, most mind-body therapies have derived from Eastern traditions, such as yoga, tai chi, and meditation. Yoga, a mind-body practice from India, has become increasingly popular in the West to promote health. The practice of yoga may include techniques of movement, breathing, meditation, chanting, and lifestyle change. Tai chi is a mind-body practice from China with roots in martial arts and ancient healing traditions. Tai chi consists of coordinated gentle movements with mental focus, breathing, and relaxation.[65] Meditation consists of various techniques that regulate the mind to produce a desired mental state. Examples of meditative techniques are mantra-based meditation, relaxation response, mindfulness meditation, Transcendental Meditation, Vipassana meditation, and Zen meditation.

For therapies that include movement, such as yoga and tai chi, mind-body therapies can be a form of exercise for patients with diabetes. According to ADA, patients with diabetes should be advised to perform at least 150 minutes/week of moderate-

intensity aerobic physical activity.[66] The exercise intensity of yoga and tai chi has been categorized as low- to moderate-intensity.[67–70] However, in controlled clinical trials, neither yoga[71,72] nor tai chi[73–77] has consistently demonstrated significant long-term improvements in glycemic control or A1C.

Chronic diseases such as diabetes are associated with diminished quality of life and psychological depression and anxiety. Mind-body therapies have behavioral and psychological effects that may help patients cope with disease and improve mood and quality of life.[78] Among patients with diabetes, clinical trials have shown improvement in measures of quality of life and stress with yoga and tai chi practice.[73,79–81] Very few studies of meditation have been conducted in patients with type 2 diabetes.[78,82]

The risks of practicing mind-body medicine are minimal, and movement-based practices such as tai chi and yoga probably have equivalent risk to conventional exercise. Overall, the quality of published research for mind-body interventions for patients with diabetes is poor, and more rigorous study is necessary.

Advising Patients With Diabetes About CAM Therapies

Health care providers treating patients with diabetes should ask patients about their use of CAM therapies. Given the low disclosure of CAM use by patients to physicians, clinicians need to actively inquire about such therapies.

When collecting information about medications in a patient history, clinicians should also ask about the use of herbs and dietary supplements. Mind-body practices can be reviewed in the context of social history when evaluating physical activity and assessing strategies to deal with stress.

Because patients often self-select CAM modalities, providers should ask patients why they chose a particular therapy. This will help providers understand patients' knowledge and beliefs about the therapy and foster communication between providers and patients.

After identifying CAM use, physicians can access resources to evaluate further clinical efficacy and safety. Table 3 outlines both public and proprietary resources for clinicians and patients. Checking resources for potential interactions with chronic medications is important to avoid adverse effects. Dietary supplements reviewed in Table 1 may augment the effect of conventional glucose-lowering medications, producing hypoglycemia.

In advising patients on CAM use for diabetes, physicians need to weigh the evidence of efficacy and safety (Table 4).[83] For CAM modalities that are clearly ineffective and may be unsafe, discouraging patients is most appropriate. In contrast, when there is convincing information for efficacy and safety, providers may recommend use. Many CAM therapies for diabetes have inconclusive data on efficacy but are probably safe. In such cases, patient counseling and monitored use is reasonable.

Patients taking herbs or supplements concurrent with medications may require more frequent evaluation to identify potential interactions. Providers can also highlight the cost of CAM therapies to patients, especially when efficacy is doubtful. Because of limited

Table 3. Resources for Information on CAM

Resource	Content
Public	
National Center for Complementary and Alternative Medicine (nccam.nih.gov)	• Definitions of CAM modalities, general recommendations, and current clinical trials
Office of Dietary Supplements (www.ods.od.nih.gov/index.aspx)	• Description of dietary supplements, including scientific evidence on botanicals
Medline Plus Drugs and Supplement Directory (www.mlm.nih.gov/medlineplus/druginformation.html)	• Description of dietary supplements, including monographs
Proprietary	
Natural Medicines Comprehensive Database (www.naturaldatabase.com)	• Description of dietary supplements, including monographs, scientific evidence, and interaction checker
Natural Standard (www.naturalstandard.com)	• Description of dietary supplements, including monographs, scientific evidence, and interaction checker
Consumerlab.com (www.consumerlab.com)	• Independently evaluates manufactured botanicals for ingredients and contaminants

Table 4. Advising Patients on CAM Use		
Evidence of Efficacy	**Evidence of Safety**	**Advice**
High	High	Recommend
Inconclusive	High	Counsel and monitor
High	Inconclusive	Counsel and monitor
Inconclusive or low	Low/unsafe	Discourage
Adapted from Ref. 83.		

data, women who are pregnant or lactating and children should be cautioned about the unknown potential adverse effects of dietary supplements.

When patients choose to take a botanical or dietary supplement, providers may be asked to recommend specific products. Given the manufacturing and regulatory framework, there is high variability in the content and quality of products sold. Consumers may use a third-party resource such as Consumer Labs (www.ConsumberLabs.com) to identify dietary supplements with higher integrity. Another option is to use formulations already shown to be safe and effective in clinical trials.

Conclusion

A high prevalence of patients with diabetes use CAM therapies, and health care providers need to be prepared to counsel such patients. Frequently, CAM modalities used for diabetes are biologically based therapies and mind-body medicine. Biologically based practices, including herbs and dietary supplements, can affect glucose metabolism, but evidence for their clinical use in patients with diabetes is scarce. Mind-body practices may offer a healthy lifestyle change for patients with diabetes, but long-term improvements in glycemic control have not been shown in clinical trials.

Regulation of botanical products in the United States allows for marketing without established efficacy or safety. Physicians need to specifically ask about supplement use and monitor patients for potential adverse effects, especially hypoglycemia in patients with diabetes.

When counseling patients on CAM use, physicians should respect patients' choices regarding self-management, while providing evidence-based information about efficacy and safety or the lack thereof. Despite unclear data, a large number of patients will continue using CAM in the future. As research grows in this field, physicians have an opportunity to help patients make decisions about the most safe and effective CAM therapies to consider.

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