The Role of Complementary and Alternative Medicine in Diabetes

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Complementary and alternative medicine (CAM) describes a diverse group of medical and health care systems, practices, and products not currently considered to be part of conventional medicine. Inadequacies in current treatments for diabetes have led 2 to 3.6 million Americans to use CAM for diabetes treatment, despite limited studies of safety and efficacy of CAM methods. CAM is used mostly by West Indians, Africans, Indians, Latin Americans, or Asians. Prayer, acupuncture, massage, hot tub therapy, biofeedback, and yoga have been used as well as various plant remedies for treating diabetes. Several CAM practices and herbal remedies are promising for diabetes treatment, but further rigorous study is needed in order to establish safety, efficacy, and mechanism of action. In the meantime, it is important to be aware that many patients with diabetes may be using CAM and to consider potential interactions with conventional medicines being used.

Introduction

Diabetes affects approximately 16 million people in the United States and has significant medical, economic, and psychological ramifications. Inadequacies in current approaches to treatment have led many patients to consider alternatives. Complementary and alternative medicine (CAM) is defined by the National Center for Complementary and Alternative Medicine as a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine [1••,2]. In 1997, the out-of-pocket expenditures on CAM were comparable to that of all US physician services [3].

Despite the limited evidence of safety and efficacy, an estimated 2 to 3.6 million Americans use CAM specifically for diabetes [3–5]. One study found that the most commonly used CAM is solitary prayer and spiritual practices; other studies report nutritional and lifestyle advice to be most commonly used, followed by spiritual healing, herbal remedies, massage, and medication. Among CAM users, 60.6% found at least one of the therapies to be "very helpful." Other methods include herbal remedies and practices such as acupuncture, yoga, biofeedback, and relaxation treatment. In traditional Chinese medicine, diabetes is viewed as an imbalance of opposing forces of yin (negative energy) and yang (positive energy) and acupuncture restores the resultant disruption in the flow of qi.

Worldwide, nearly 400 herbs and plant preparations are reported to have beneficial effects in the treatment of diabetes mellitus [6••]. In traditional Chinese, Indian, Tibetan, and Native American medicine these natural preparations may be used exclusively. Among people of West Indian, African, Indian, South American, or Asian origin in the United States, up to 37% use CAM to complement Western pharmacologic treatment. Increasingly patients ask about "something I bought at the health food store for diabetes" or simply use "natural remedies" covertly. It is important to be aware of CAM, and its efficacy and safety, to ensure integration with current medical management. The American Diabetes Association recognizes its use and cautions patients against side effects and against stopping the use of conventional medicine [2]. This review focuses on the increasing awareness of commonly used CAM practices and provides background on relevant human studies.

Complementary and Alternative Practices

Acupuncture

Acupuncture, developed in China over 2000 years ago, involves penetrating the skin at defined points with thin, solid, metallic needles that are manipulated manually or electrically [1••,7–12]. Acupuncture is an accepted form of treatment for chronic pain; one mechanism of action is an increase in endorphins, which may be modulated by the frequency of electrical stimulation [12]. An extensive Chinese-language literature exists that is beyond the scope of this review [9].

In diabetes, the effects of acupuncture may be seen after 25 treatments and therapy generally lasts 2 to 3 months; patients with type 2 diabetes appear to have a better response than those with type 1 diabetes. Acupuncture has been reported to reduce both hyperglycemia and improve insulin resistance. One study reported that 1 month of acupuncture at the Quihai point followed by an xiaoke plaster of traditional Chinese herbs was associated with significant glycemic improvement; 71% of 309 patients had fasting plasma glucose levels less than 130 mg/dL from a baseline of 238 mg/dL [10]. Another study compared three courses of 10 daily acupuncture treatments to herbal pills and found similar and significant improvements in fasting plasma glucose, which decreased from 224 to 145 mg/dL [11]. The mechanism whereby acupuncture is effective for diabetes is unclear in the context of Western medicine. Anecdotally, acupuncture has been used for diabetic neuropathy, gastroparesis, and bladder neural dysfunction [12]. A single case report from China, using magnets on the ear (a variation of ear acupuncture because electrical and magnetic energies are closely related), reported complete control of blood glucose and eye disease [13].

Massage

Massage, or manipulation of muscle and connective tissue to improve their function and to promote relaxation and well-being, has been promoted as a treatment for diabetes [14]. It is supposed to improve blood circulation, metabolism, and pancreatic function. Dillon [15] demonstrated that massaging the site of insulin injection can increase the short-term absorption and blood levels of insulin in type 1 diabetes (compared with no massage) and lower the blood glucose. Eight patients were treated in this manner for 18 months and showed improved long-term glycemic control (A_{1c} 10.5% to 8.4%).

Hot tub therapy

Hot tub therapy was reported in eight patients with type 2 diabetes treated with hot water immersion for 3 weeks while other factors such as diet, exercise, medications, and insulin remained stable [16]. There was a decrease in body weight, fasting plasma glucose (182 ± 37 to 159 ± 42 mg/dL), and hemoglobin A_{1c} (HbA_{1c}) (11.3% ± 3.1% to 10.3% ± 2.6%). The putative principle is that partial immersion in hot water simulates the effects of exercise with benefits resulting from increased muscle blood flow and glucose uptake.

Biofeedback

Biofeedback has been used to train people to relax and thereby reduce stress. Components include guided imagery in which positive images are evoked, including peaceful mental images or images of controlling a chronic disease such as diabetes. Another component is progressive muscle relaxation; it involves tensing and relaxing a specific muscle group combined with deep breathing and mental imagery. Randomized controlled studies of the effects of biofeedback on diabetes types 1 and 2 show varied results [17,18••,19–21]. Most are small studies. In patients with type 2 diabetes, 12 months of biofeedback did not result in any additional glycemic improvement beyond conventional intensified treatment (diet, education, and medications) [17]. The authors suggested that relaxation training may improve glucose tolerance in a subset of anxious patients. In a subsequent short-term 4-week study of 20 patients, biofeedback decreased anxiety but had no effect on fasting or postprandial blood glucoses or fructosamine [21]. In contrast, in a longer-term, 12-month randomized control study of 108 patients, Surwit et al. [18••] showed that stress management training practiced at home significantly reduced HbA_{1c} by 0.5%; however, anxiety did not predict response to treatment. Reasons for conflicting results in type 1 diabetes are also not apparent [19,20].

Yoga

Yoga, which is of Indian origin, is practiced worldwide for its health benefits, including physical fitness, relaxation, and awareness of self. It is based on the principle that the mind and body are intimately related. Stress produces a state of physical and mental tension. In yoga, physical postures and breathing exercises improve muscle strength, flexibility, blood circulation, and oxygen uptake as well as hormonal functions. Although there is a vast literature on the health benefits of yoga, only a small section is devoted to its effects on diabetes. However, a few clinical trials done in India suggest that yoga can improve glycemic control [22–24].

Overall, most studies of CAM have not been performed under rigorous scientific conditions, including standardizing the intervention and the use of a randomized control design. Although studies of biofeedback were randomized and controlled, most had small numbers of patients. Many questions can be raised, including the duration of treatment and what might constitute an appropriate control group. Benefits from stress reduction may be due to the well-known association of acute and chronic stress with the development of obesity and insulin resistance through activation of the hypothalamic-pituitary-adrenal (HPA) axis [25,26]. Inflammatory cytokines may also be involved, translating the stress response into pathologic states [27]. Complexities in interpreting any form of stress reduction are apparent from studies in bonnet macaques, where obesity may be due to increased HPA activity developed in early infancy due to maternal stress. Subsequent reversal of stress later in life in this model appears not to modify heightened HPA activity or reverse the consequent metabolic disorders [28]. Benefits of acupuncture may be due to neural stimulation, whereas yoga may tap into as yet unchartered neural regions.

Complementary and Alternative Herbal Remedies

Plants have been a rich source of new drugs and play a key role in CAM [29••]. Metformin, the most commonly used antidiabetic drug, derives from the French lilac or *Galega officinalis*. It has been known as an antidiabetic agent since the Middle Ages and is rich in guanidine, which lowers the blood glucose. Guanidine's toxicity led to the development of alkyl diguanides, and later biguanides including metformin [30].

Some traditionally used herbs and plants have been more rigorously tested in double-blind controlled trials than others and the following appear promising: *Coccinia indica*, *Momordica charantia*, *Gymnema sylvestre*, *Panax quinquefolius*, *Opuntia streptacantha*, and *Aloe vera* (Table 1) [31–48]. Nevertheless, further testing is necessary within the scientific context to assess efficacy, safety, and mechanism of action. Other agents that are used include *Ocimum sanctum* or holy basil, *Trigonella foenum-graecum* or fenugreek, curry leaf, fig leaf, *Pterocarpus marsupium* (vijayasar), French maritime pine bark extract, hops with peroxisome proliferator-activated receptor-α and -γ agonist action [37], and Konjac mannan. Finally, herbal combinations are commonly used in Chinese and Tibetan medicine [49].

Coccinia indica

C. indica is also known as ivy gourd. This native Indian plant is part of the Ayurvedic pharmacopeia [31,50–53]. Several randomized controlled studies suggest effectiveness with little toxicity. A study of 70 patients with type 2 diabetes compared *C. indica* (dried leaf pellets) with no drug or chlorpropramide for 12 weeks and found it was as effective as chlorpropramide [50], whereas another study showed the crushed dried leaves to be effective in a 6-week study of 32 patients with poorly controlled type 2 diabetes [31]. The mechanism of action appears to be by insulin-mimetic properties.

Momordica charantia

M. charantia is a cultivated fruit often known by as bitter melon, balsam pear, or karela (karolla); it is widely used in India, South America, Africa, and Asia. Patients from these regions living in the United States are very likely to use this agent. The fruit is cooked (often fried) or raw juice extracted and consumed as part of the diet. The leaves of the wild variety are known as cerasee, and when dried are used to prepare a tea, especially by South American or West Indian patients. There is evidence that *M. charantia* decreases gluconeogenesis and increases insulin secretion as well as glucose uptake.

Welhinda et al. [54] reported acute lowering of blood glucose using the juice of the fruit. Leatherdale et al. [42] found that a 50-mL aqueous extract of karela reduced the glycemic excursion of a 50-g oral glucose tolerance test by approximately 20% within 1 hour. The glucose-lowering effect appears to persist for 2 to 3 months [55]. No randomized placebo-controlled trials have been done. The active ingredients are not known but may include charantin (a mixture of glycosides), vicine, and an insulin-like peptide. Bailey and Day [30] report two hypoglycemic "principles": one rapid acting and uncharacterized, and the other slow acting and present in the alkaloid fraction. There has been one report of testicular lesions in dogs given large amounts of the extract and one report of hepatic portal inflammation from excess cerasee tea [30]. The juice and the fruit are both exceedingly bitter and this may be a common element relevant to its mechanism of action.

Gymnema sylvestre

G. sylvestre is another native of the Indian subcontinent. This woody climber was prescribed for diabetes by the 6th century physician Sushruta. Like *Momordica*, the active ingredient may also be a glycoside. The leaves are reputed to cause a loss of taste for sweetness and bitterness and are known as "gurmar" or "killer of sweet." In patients with both type 1 and type 2 diabetes, it is reported to improve glycemic control when added to conventional treatment [45,56] (A_{1c}, 11.9% to 8.34%, fasting blood glucose, 174 to 124 mg/dL) after 18 to 20 months. Its mechanism of action has been hypothesized to include increased insulin secretion and β-cell function as well as increased peripheral glucose uptake apparently based on approximately 50% improvement in fasting blood glucose [56].

Panax quinquefolius

P. quinquefolius is better known as ginseng. There are several types, including American or *P. quinquefolius*, Japanese or *Panax japonicus*, and Chinese or *Panax ginseng*; the root or the leaves may be used. Ginseng is reported to have many beneficial effects, including increasing overall energy and concentration and the treatment of diabetes [5]. In type 2 diabetes, two 8-week trials using American ginseng reported decreased fasting plasma glucose as well as A_{1c} (8.3% ± 1.3% to 7.7% ± 0.9% mmol/L and 6.5% ± 1.7% to 6.0% ± 0.3%, with 100 mg of ginseng) [32,33,57]. However, a recent acute short-term study comparing the effect of eight different types of ginseng on the effect of an oral glucose tolerance test in healthy controls compared with placebo showed very little effect [57]. The authors note the variable potency of different batches of ginseng, and that the response may vary depending upon the clinical characteristics of the patients (eg, obese or not). Ginseng appears to stimulate the nervous system and to contain hypoglycemic peptidoglycans. The mechanism of action is multifactorial and based on animal studies includes increased glucose transport and uptake and modulation of insulin secretion [58].

Opuntia streptacantha

O. streptacantha is also known as nopal or prickly pear cactus. This native of South America is used by people from the southwestern part of the United States, especially

Table 1. Clinical trials on herbs in the treatment of diabetes

Study	Herb	Scientific name	Type of study	Patient, *n, type*	Outcome	Comment
Azad Khan et al. [31]	Ivy gourd	*Coccinia indica*	R, PCT, DB, 6 wk	32 T2DM	Sig. ↓ in GT, FPG	Freeze-dried leaves of *C. Indica* compared with chlorophyll tablets
Vuksan et al. [32,33]	Ginseng	*Panax quinquefolius/ ginseng/japonicus*	R, PCT, DB, 8 wk	36 newly diagnosed T2DM	Sig. imp. in FBG and HbA_{1c}	Psychophysical performance imp.
Frati-Munari et al. [34]	Aloe vera	*Aloe vera*	PCT, 42 d	72 T2DM	Sig. ↓ in BS and serum triglycerides	No change in weight and appetite
Ludvik et al. [35]	Caiapo, Japanese sweet potato	*Ipomoea batatas*	R, PCT, DB, 12 wk	61 T2DM	Sig. ↓ in HbA_{1c}, glucose, and body weight	Caiapo could be a useful neutriceutical (food additive)
Gupta et al. [36]	Fenugreek, methi	*Trigonella foenum-graecum*	R, active control trial, DB, 2 mo	25 newly diagnosed diabetes	No sig. diffs. between 2 groups	Fenugreek seed extract and diet/exercise are equally effective
Yajima et al. [37]	Hops	*Humulus lupulus*	R, PCT, DB, 8 wk	20 newly diagnosed T2DM	Imp. in HbA_{1c}, blood glucose, and SBP	Possible mechanism: transactivator of PPAR-α and -γ receptor without weight gain
Hsia et al. [38]	Pancreas tonic or AntiBetic*	Mixture of ingredients†	R, PCT, DB, 3 mo	63 T2DM	Sig. ↓ in patients with higher HbA_{1c}	Higher (46%) dropout rate in active treatment group
Khan et al. [39]	Cinnamon	*Cinnamomum cassia*	R, PCT, 5 wk	60 diabetes	Sig. ↓ in FPG and imp. in lipid profile	Daily consumption of cinnamon may be beneficial for diabetes and cardiovascular risk reduction
Namdul et al. [40]	Tibetan medicine	*Kyura-6, Aru-18, Yungwa-4, Sugmel-19*	R, PCT, NB, 24 wk	200 newly diagnosed T2DM	Sig. ↓ in FBG, PPBG, and HbA_{1c} (22%). Treatment group had worse symptoms	Treatment based on patients' age, sex, personality, pulse and urine characteristics; higher dropout rate
Frati et al. [41]	Nopal	*Opuntia streptacantha Lemaire*	R, PCT, NB, single dose	14 type 2 vs 14 healthy subjects	Sig. ↓ in PPBG and serum insulin levels	Potential mechanism: cellular enhancement of insulin sensitivity
Leatherdale et al. [42]	Bitter gourd, bitter melon, karela	*Momordica charantia*	NR, nonPCT, single dose	9 Asian T2DM	Sig. imp. in GT	Juice of raw *M. Charantia*, possible mechanism: improved peripheral glucose use
Fujita et al. [43]	Touchi extract	*Soyabean or Aspergillus sp.*	NR, nonPCT, single dose	8 borderline and 4 diabetes	Sig. ↓ in PPBG and serum insulin	Possible mechanism: inhibits α-glucosidase

*Gero Vita International, Marina del Rey, CA.
†*Aegle marmelos*, *P. marsupium*, and small amount of *M. charantia*, *G. sylvestre*, *T. foenum-graecum*, and *Azadirachta indica.*
‡*A. indica*, *Phyllanthus emblica*, *Curcuma longa*, *T. foenum-graecum*, *Syzygium cumini*, *Tribulus terrestris*, *Terminalia belerica*, *Terminalia chebula*, and *Routula aquatica.*
BS—blood sugar; DB—double-blinded; diffs.—differences; DM—diabetes mellitus; FPG—fasting plasma glucose; GT—glucose tolerance; HbA_{1c}—hemoglobin A_{1c}; imp.—improvement; NA—not available; NB—nonblinded; nonPCT—non–placebo-controlled trial; NR—nonrandomized; PCT—placebo-controlled trial; PPAR—peroxisome proliferator-activated receptor; PPBG—postprandial blood glucose; R—randomized; SBP—systolic blood pressure; sig.—significant; T1DM—type 1 diabetes mellitus; T2DM—type 2 diabetes mellitus.

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Study	Herb	Scientific name	Type of study	Patient, n, type	Outcome	Comment
Shekhar et al. [44]	Cogent db	Mixture of ingredients‡	R, nonPCT, open label, 3 mo	60 T2DM	Sig. ↓ in HbA_{1c}, FPG, PPBG, lipid profile, and symptoms	Cogent db was an add-on to conventional therapy
Baskaran et al. [45]	Periploca of woods, ram's horn or gurmar	*Gymnema sylvestre*	Open trial, controlled trial, 18–20 mo	47 T2DM	Sig. ↓ in FPG, HbA_{1c}, lipid profile, and serum insulin levels (fasting and postprandial)	23% stopped their oral hypoglycemic agents, used as a supplement
Indian Council of Medical Research [46]	Indian Malabar vijayasar or false teak	*Pterocarpus marsupium*	Flexible dose, open trial, multi-center, 12 wk	97 T2DM	69% attained control of their FBG and PPBG	No effect on HbA_{1c}
Hosoda et al. [47]	Oolong tea	NA	R, crossover, 30 d	20 T2DM	Sig. ↓ in glucose and fructosamine	Oolong tea can be an effective therapeutic adjunct
Serraclara et al. [48]	Fig leaf	*Ficus carica*	R, crossover, 60 d	10 T1DM	Sig. ↓ in insulin dose and PPBG	Fig leaf compared with bitter tea

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BS—blood sugar; DB—double-blinded; diffs.—differences; DM—diabetes mellitus; FPG—fasting plasma glucose; GT—glucose tolerance; HbA_{1c}—hemoglobin A_{1c}; imp.—improvement; NA—not available; NB—nonblinded; nonPCT—non–placebo-controlled trial; NR—nonrandomized; PCT—placebo-controlled trial; PPAR—peroxisome proliferator-activated receptor; PPBG—postprandial blood glucose; R—randomized; SBP—systolic blood pressure; sig.—significant; T1DM—type 1 diabetes mellitus; T2DM—type 2 diabetes mellitus.

among Mexicans. Among patients with type 2 diabetes, following a single dose of 500 mg of stem extract there was a decrease in the blood glucose in two patients with diabetes [34,41]. Because both the blood glucose and the insulin decreased, it has been assumed that insulin action was enhanced by this intervention. Nopal has a high fiber and pectin content, which may alter intestinal glucose uptake thereby improving glycemia. In one study the serum glucose levels improved significantly among patients with type 2 diabetes receiving nopal compared with those not receiving nopal [34]; this effect was not seen in the healthy population.

Aloe vera

Aloe vera is a member of the Liliaceae family. It is used for many medicinal purposes, including wound healing and various skin lesions. It may have anti-inflammatory properties. The sap or the gelatinous part of the stem is used for diabetes. It contains glucomannan, which may be the active principle. There are two studies showing improved fasting glucose among diabetes patients treated with juice from the gel for 6 weeks [59,60]. There have been no reported toxicities. The aloe gel is also bitter.

Other plants and herbs

A recent report of 63 patients with type 2 diabetes treated for 12 weeks in a randomized double-bind placebo-controlled trial with 4 g/d of caiapo, a Japanese sweet potato, showed significantly reduced A_{1c} (7.21% ± 0.15% to 6.7% ± 0.14%), fasting blood glucose (143.7 ± 1.9 to 128.5 ± 1.7 mg/dL), and body weight [35]. An acidic glycoprotein has been identified and thought to be responsible for increased insulin sensitivity. Another report on oolong tea, popular in China, is made from withered, partially oxidized, and dried tea leaves. It is different from black tea, which is fully fermented and green tea, which is not, in the number of polymerized polyphenols. In one study on patients with type 2 diabetes, daily tea consumed for 30 days showed significant reductions in random blood sugars (229 ± 54 to 162 ± 30 mg/dL) and fructosamine (410 ± 96 to 323 ± 63 μmol/L). The mechanism was presumed to be insulin-like activity of tea phenols and caffeine [47]. Cinnamon decreased blood glucose in a 5-week randomized placebo-controlled study of 60 men and women with diabetes [39]. Cinnamon capsules consumed by patients reduced fasting blood glucose significantly, from 11.6 to 8.7 mmol/L, in patients with type 2 diabetes.

Herbal combinations

There are several combinations of herbs used in traditional Chinese medicine that complement acupuncture. Often these include ginseng in combination with other polysaccharides. A multicenter trial in Northeast China with 328 patients with type 2 diabetes used Yi-jin and showed a clinical improvement in 85.8% [49].

A unique feature of Tibetan medicine is that the prescription is individualized based upon age, sex, personality, and pulse and urine characteristics [40]. After 24 weeks of prescribed Tibetan medicine, there was an approximately 20% reduction in fasting and postprandial glucose and A_{1c} levels.

Pancreas tonic is a mixture of *Aegle marmelos* and *P. marsupium*, with small amounts of *M. charantia*, *G. sylvestre*, *T. foenum-graecum*, and *Azadirachta indica*. In a single-center, randomized, double-blind, placebo-controlled 3-month trial there was an improvement in glycemic control in patients with type 2 diabetes (A_{1c}, 10.1% ± 1.2% to 8.8% ± 1.9%) [38].

Cogent db was first used in Indian Ayurvedic medicine to treat diabetes. This mixture contains *A. indica*, *Phyllanthus emblica*, *Curcuma longa*, *T. foenum-graecum*, *Syzygium cumini*, *Tribulus terrestris*, *Terminalia belerica*, *Terminalia chebula*, and *Routula aquatica* [44]. One controlled study treated patients with type 2 diabetes with cogent db for 3 months and showed significant improvements in fasting plasma glucose and A_{1c} levels (220 to 158 mg/dL and HbA_{1c} 10.2% to 8.3%, $P < 0.001$). This study also showed a decrease in cholesterol and an absence of toxicity.

Conclusions and Practice Considerations

CAM is increasingly used by patients with chronic diseases such as diabetes. Spiritual prayer, nutritional advice, herbal remedies, relaxation, meditation, yoga, and acupuncture are some of the known practices. Although many CAM practices are ancient remedies and may be beneficial, few have been rigorously tested for efficacy and safety with appropriately powered studies. Many patients use CAM but may or may not volunteer this information. The covert use of CAM may confound therapeutic strategies with unexpected outcomes and side effects.

Although some practices may be neutral, others may raise the blood sugar (if an ineffective CAM is used exclusively) or excessively lower it (if an effective CAM is added to conventional treatment). Alternatively, patients ask about the use of CAM and patients from certain groups may use these frequently, especially West Indians, Asians, and Africans, although CAM is certainly not limited to these groups. The increasing prevalence of obesity and consequent diabetes has increased the use of CAM with its simple and compelling appeal of "natural," "healthy," and "successful."

Thus, an awareness of the widespread use of CAM is important in overall diabetes management. CAM is out of the closet and it is essential that practitioners directly ask about its use. In the absence of evidenced-based guidelines, one must put the use of CAM into a therapeutic context for each patient, bearing in mind the need not to discontinue conventional proven treatments and an awareness of side effects of CAM and potential interactions with proven treatments.

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