Alternative Therapies for Type 2 Diabetes

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Abstract

Type 2 diabetes is a chronic metabolic disease that has a significant impact on the health, quality of life, and life expectancy of patients, as well as on the health care system. Exercise, diet, and weight control continue to be essential and effective means of improving glucose homeostasis. However, lifestyle management measures may be insufficient or patient compliance difficult, rendering conventional drug therapies (i.e., oral glucose-lowering agents and insulin injection) necessary in many patients. In addition to adverse effects, drug treatments are not always satisfactory in maintaining euglycemia and avoiding late stage diabetic complications. As an alternative approach, medicinal herbs with antihyperglycemic activities are increasingly sought by diabetic patients and health care professionals. Commonly used herbs and other alternative therapies, less likely to have the side effects of conventional approaches for type 2 diabetes, are reviewed.

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Introduction

Diabetes mellitus is a serious chronic metabolic disorder that has a significant impact on the health, quality of life, and life expectancy of patients, as well as on the health care system. In the United States, diabetes is the sixth leading cause of death.[1] Diabetes is divided into two major categories: type 1 diabetes (formerly known as insulin-dependent diabetes mellitus or IDDM) and type 2 diabetes (formerly known as non-insulin dependent diabetes mellitus or NIDDM). The overall prevalence of diabetes is approximately six percent of the population, of which 90 percent is type 2.[2] Treatment and care of diabetes represents a substantial portion of the national health care expenditure, over $105 billion annually. This represents a substantial portion of the health care expenditure – more than one of every 10 U. S. health care dollars and one of four Medicare dollars.[3]

Type 2 diabetes represents a syndrome with disordered metabolism of carbohydrate and fat. The most prominent clinical feature is hyperglycemia (fasting plasma glucose level > 126 mg/dL, or glycosylated hemoglobin A_{1c} (HbA_{1c}) > 6.9%).[4] In most patients with type 2 diabetes, the onset is in adulthood, most commonly in obese people over 40 years of age. Hypertension, hyperlipidemia, hyperinsulinemia, and atherosclerosis are often associated with diabetes.

Pathophysiology and Complications

Type 2 diabetes is known to have a strong genetic component with contributing environmental determinants. Although the disease is genetically heterogeneous, there appears to be a fairly consistent phenotype once the disease is fully manifested. Whatever the pathogenic causes, the

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early stage of type 2 diabetes is characterized by insulin resistance in insulin-targeting tissues, mainly the liver, skeletal muscle, and adipocytes. Insulin resistance in these tissues is associated with excessive glucose production by the liver and impaired glucose utilization by peripheral tissues, especially muscle. These events undermine metabolic homeostasis, but may not directly lead to overt diabetes in the early stage. With increased insulin secretion to compensate for insulin resistance, baseline blood glucose levels can be maintained within normal ranges, but the patients may demonstrate impaired responses to prandial carbohydrate loading and to oral glucose tolerance tests. The chronic over-stimulation of insulin secretion gradually diminishes and eventually exhausts the islet beta-cell reserve. A state of absolute insulin deficiency ensues and overt clinical diabetes becomes fully blown.[5-7] The transition of impaired glucose tolerance to type 2 diabetes can also be influenced by ethnicity, degree of obesity, distribution of body fat, sedentary lifestyle, aging, and other concomitant medical conditions.[8]

The quality of life of type 2 diabetic patients with chronic and severe hypoglycemia is adversely affected. Characteristic symptoms of tiredness and lethargy can become severe and lead to a decrease in work performance in adults and an increase of falls in the elderly.[9] The most common acute complications are metabolic problems (hyperosmolar hyperglycemic nonketotic syndrome or HHNS) and infection. The long-term complications are macrovascular complications (hypertension, dyslipidemia, myocardial infarction, stroke), microvascular complications (retinopathy, nephropathy, diabetic neuropathy, diarrhea, neurogenic bladder, impaired cardiovascular reflexes, sexual dysfunction), and diabetic foot disorders.[9]

Conventional Therapies

The general consensus on treatment of type 2 diabetes is that lifestyle management is at the forefront of therapy options. In addition to exercise, weight control, and medical nutrition therapy, oral glucose-lowering drugs and injections of insulin are the conventional therapies. Since the most important pathological process during the development of diabetes involves three key organs, i.e., pancreatic islets, liver, and skeletal muscle, almost all anti-diabetic therapies are aimed at these organs. Pharmacological treatment is indicated when fasting glucose level exceeds 140 mg/dL, the postprandial glucose level exceeds 160 mg/dL or HbA_{1c} exceeds 8.0 percent.[10]

Pharmacological Treatment and Limitations

Oral Glucose-Lowering Drugs

In the United States, five classes of oral agents are approved for the treatment of type 2 diabetes. By conventional standards, oral therapy is indicated in any patient with type 2 diabetes in whom diet and exercise fail to achieve acceptable glycemic control.[10] Although initial responses may be good, oral hypoglycemic drugs may lose their effectiveness in a significant percentage of patients. The drug categories include sulfonylureas, biguanides, alpha-glucosidase inhibitors, thiazolidinediones, and meglitinides.

Sulfonylureas, including first generation (e.g., tolbutamide) and second generation (e.g., glyburide) sulfonylureas, enhance insulin secretion from the pancreatic beta-cells. A significant side effect is hypoglycemia. Sulfonylurea therapy is also usually associated with weight gain due to hyperinsulinemia,[11,12] which has been implicated as a cause of secondary drug failure.[10-12]

Biguanides include the drug metformin, which was originally derived from a medicinal plant, *Galega officinalis*. Metformin reduces plasma glucose via inhibition of hepatic glucose production and increase of muscle glucose uptake. It also reduces plasma triglyceride and LDL-cholesterol levels. Side effects include weakness, fatigue, shortness of breath, nausea, dizziness, lactic acidosis, and kidney toxicity.

Alpha-glucosidase inhibitors include the drug acarbose. This drug category decreases postprandial glucose levels by interfering with carbohydrate digestion and delaying gastrointestinal absorption of glucose. The major side effects are gas, bloating, and diarrhea.

Thiazolidinediones are represented by troglitazone, rosiglitazone and pioglitazone. These expensive oral agents work by improving insulin sensitivity in muscle and, to a much lesser extent, in the liver. These drugs decrease plasma triglyceride levels, but such decrease may be associated with weight gain and an increase in LDL-cholesterol levels. Liver toxicity is a concern requiring monthly monitoring of liver function. Since troglitazone (Rezulin,) is more toxic to the liver than rosiglitazone and pioglitazone (having resulted in dozens of deaths from liver failure), in March 2000 the FDA asked the manufacturer of Rezulin to remove the product from the market.

Meglitinides (drug name Repaglinide) augment insulin secretion, but weight gain, gastrointestinal disturbances, and hypoglycemia are possible side effects.

Insulin Therapy

Insulin is usually added to an oral agent when glycemic control is suboptimal at maximal doses of oral medications. Some diabetologists prefer to initiate insulin therapy in patients with newly diagnosed type 2 diabetes.[10] Weight gain and hypoglycemia are common side effects of insulin therapy.[13-16] Vigorous insulin treatment may also carry an increased risk of atherogenesis.[14] Table 1 summarizes various limitations of current drug therapies.

Table 1. *Limitations of Hypoglycemic Medications*

Anti-Diabetic Drugs	Limitations/Side Effects
Sulfonylureas	Hypoglycemia, weight gain
Biguanides	Gastrointestinal disturbances
Alpha-glucosidase Inhibitors	Gastrointestinal disturbances
Thiazolidinediones	Liver toxicity, weight gain, high LDL cholesterol, high cost
Meglitinides	Hypoglycemia, weight gain
Insulin	Hypoglycemia, weight gain

Exercise

Any exercise prescription should be individualized to account for patient interests, physical status, capacity, and motivation. Exercising five or six times per week enhances weight reduction. Because many people with diabetes have not been active, exercise should start at a low level and gradually increase to avoid adverse effects such as injury, hypoglycemia, or cardiac problems.[17,18]

Conventional Approach to Diet Therapy

Given the heterogeneous nature of type 2 diabetes, no single dietary approach is appropriate for all patients. Meal plans and diet modifications are generally individualized by a registered dietitian to meet patient needs and lifestyle. A typical conventional approach would recommend a diet composed of 60-65 percent carbohydrate, 25-35 percent fat, and 10-20 percent protein, with limited or no alcohol consumption.[19]

Alternative Approaches

Alternative therapies with anti-diabetic activity have been researched relatively extensively, particularly in India. Ideal therapies should have a similar degree of efficacy without the troublesome side effects associated with

conventional treatments. Alternative treatments for diabetes have become increasingly popular the last several years,[16] including medicinal herbs, nutritional supplementation, acupuncture, and hot tub therapy.

Medicinal Herbs

Many conventional drugs have been derived from prototypic molecules in medicinal plants. Metformin exemplifies an efficacious oral glucose-lowering agent. Its development was based on the use of *Galega officinalis* to treat diabetes.[20] *Galega officinalis* is rich in guanidine, the hypoglycemic component.[21-23] Because guanidine is too toxic for clinical use, the alkyl biguanides synthalin A and synthalin B were introduced as oral anti-diabetic agents in Europe in the 1920s but were discontinued after insulin became more widely available. However, experience with guanidine and biguanides prompted the development of metformin.[24,25]

To date, over 400 traditional plant treatments for diabetes have been reported,[20] although only a small number of these have received scientific and medical evaluation to assess their efficacy. The hypoglycemic effect of some herbal extracts has been confirmed in human and animal models of type 2 diabetes. The World Health Organization Expert Committee on diabetes has recommended that traditional medicinal herbs be further investigated.[20] The following is a summary of several of the most studied and commonly used medicinal herbs.

Ginseng Species

The root of ginseng has been used for over 2,000 years in the Far East for its health-promoting properties. In recent years, it has consistently been one of the top ten selling herbs in the United States. Of the several species of ginseng, *Panax ginseng* (Asian ginseng) and *Panax quinquefolius* (American ginseng) are commonly used. Constituents of all ginseng species include ginsenosides, polysaccharides, peptides, polyacetylenic alcohol, and fatty acids.[26] Most pharmacological actions of ginseng are attributed to ginsenosides, a family of steroids named steroidal saponins.[27,28] The chemical composition of ginseng products and potency may vary with the plant extract derivative, the age of the root, the location where grown, the season when harvested, and the methods of drying.[29,30]

Data from animal studies indicate that both Asian ginseng[31,32] and American ginseng[33,34] have significant hypoglycemic action. This blood glucose-lowering effect appears to be attributed to ginsenoside Rb-2 and more specifically to panaxans I, J, K and L in type 1 diabetic models.[35-39] But whether these constituents have a similar effect on type 2 diabetes is as yet unknown.

There is some clinical evidence on ginseng's hypoglycemic activity. Sotaniemi et al demonstrated a reduction in the levels of fasting blood glucose and HbA_{1c} in type 2 diabetics treated with a small dose (100-200 mg) of ginseng relative to placebo.[40] Ginseng also elevated mood, improved psychophysiological performance and physical activity, and reduced body weight.[40] Vuksan et al also demonstrated that 3 g American ginseng, when given 40 minutes prior to the test meal, significantly lowered the blood glucose in both non-diabetic subjects and type 2 diabetic patients.[41] However, when ginseng was given together with meals, this effect did not persist in non-diabetic subjects. Vuksan proposed several plausible hypotheses regarding ginseng's mechanisms of action: (1) ginseng may slow the digestion of food, decreasing the rate of carbohydrate absorption into portal hepatic circulation;[30,42] (2) ginseng may affect glucose transport, which is mediated by nitric oxide (NO);[32, 43-45] and (3) ginseng may modulate NO-mediated insulin secretion.[46] It was recently shown that NO stimulates glucose-dependent secretion of insulin in rat islet cells.[47]

There are few reports of adverse effects of ginseng, despite the fact that it is estimated six million people ingest it regularly in the United States.[48] The most commonly reported side effects of ginseng are nervousness and excitation, but these diminish with continued use or dosage reduction.[48] Ginseng may exert an estrogen-like effect in postmenopausal women, resulting in diffuse mammary nodularity and vaginal bleeding.[49,50] Ginseng may inhibit the effects of warfarin[51] and interact with the monoamine oxidase

inhibitor phenelzine.[52] Often, such case reports fail to provide sufficient details concerning the type or quality of ginseng used, or whether the preparation actually contained ginseng or ginsenoside.[53,54] Massive overdose can bring about ginseng abuse syndrome, which is characterized by hypertension, insomnia, hypertonia, and edema.[48]

The recommended daily ginseng dosage is 1-3 g of the crude root, or 200-600 mg of a standardized extract.[55] As the possibility of hormone-like or hormone-inducing effects cannot be ruled out, some authors suggest limiting treatment to three months.[55]

Momordica charantia (Bitter Melon)

Momordica charantia, also known as bitter melon, balsam pear, or karela, has been referred to as both a vegetable and a fruit, and is widely cultivated in Asia, Africa, and South America. It has been used extensively in folk medicines as a remedy for diabetes. The blood sugar-lowering action of the fresh juice or unripe fruit has been established in animal experimental models as well as human clinical trials.[56,57]

Bitter melon is composed of several compounds with confirmed anti-diabetic properties. Alcohol-extracted charantin from *Momordica charantia* consists of mixed steroids and was found to be more potent than the oral hypoglycemic agent tolbutamide in an animal study.[58] Bitter melon also contains an insulin-like polypeptide, polypeptide-P, similar in structure to bovine insulin. It was found to decrease blood sugar levels when injected subcutaneously into type 1 diabetic patients.[59] The oral administration of bitter melon preparations has also shown satisfactory results in clinical trials in type 2 diabetic patients.

Welihinda et al showed glucose tolerance was improved in 73 percent of type 2 diabetic patients given 57 g of the juice.[56] In another study, 15 g of the aqueous extract of bitter melon produced a 54-percent decrease in postprandial blood sugar levels and a 17-percent reduction in glycosylated hemoglobin in six patients.[57] The mechanism of bitter melon's activity in lowering blood glucose is unknown, but in diabetic rabbit models it has been proposed to possess a direct action similar to insulin and was found effective in lowering blood glucose in alloxan-treated rabbits.[60] Bailey and Day report the herb appears to inhibit gluconeogenesis.[20]

The recommended dose of bitter melon depends on the form it is being consumed. Dosage for tincture ranges from 5 mL two to three times daily to as high as 50 mL per day.[61] However, bitter melon juice is very difficult to make palatable since, as the name implies, it is quite bitter. To avoid the bitter taste, the Indians and Chinese crush the herbs and form tablets. In Central America, it is prepared as an extract or decoction. Hepatic portal inflammation and testicular lesions in dogs have been reported with excessive administration of cerasee (a component of the wild variety of bitter melon).[62] Dosages of capsulized dried powder range from 3-15 g daily. That is quite a large dose so to avoid the necessity of taking so many capsules, a standardized extract may be used at dosages of 100-200 mg three times daily.

Trigonella foenum graecum (Fenugreek)

Trigonella foenum graecum has been used as a remedy for diabetes, particularly in India.[63] The active principal is in the defatted portion of the seed, which contains the alkaloid trigonelline, nicotinic acid, and coumarin. Administration of the defatted seed (1.5-2.0 g/kg daily) to both normal and diabetic dogs reduced fasting and postprandial blood levels of glucose, glucagon, somatostatin, insulin, total cholesterol, and triglycerides, and increased HDL-cholesterol levels.[64] Human studies have confirmed the glucose- and lipid-lowering effects.[58] At least 50 percent of seeds is fiber and may constitute another potential mechanism of fenugreek's beneficial effect in diabetic patients.[65]

In type 2 diabetic patients, the ingestion of 15 g of powdered fenugreek seed soaked in water significantly reduced postprandial glucose levels during the glucose tolerance test.[65] Dosages of the fiber range from 10-100 g daily in divided dosages. Urine may have a maple syrup smell after fenugreek consumption.[66] No other side effects have been reported to date although, because of

the possibility of it affecting blood sugar by slowing absorption, oral medications should be taken at a different time than fenugreek.

Gymnema sylvestre (Gurmar)

Gymnema sylvestre, a plant native to the tropical forests of India (Figure 1), has long been used as a treatment for diabetes. *Gymnema sylvestre* appeared on the U.S market several years ago, hyped as a "sugar blocker." In a study of type 2 diabetes, 22 patients were given 400 mg *Gymnema sylvestre* extract daily along with their oral hypoglycemic drugs. All patients demonstrated improved blood sugar control. Twenty-one of 22 were able to reduce their oral hypoglycemic drug dosage considerably, and five patients were able to discontinue oral medication and maintain blood sugar control with the Gymnema extract alone.[67] It was postulated that *Gymnema sylvestre* enhances the production of endogenous insulin.[68]

Figure 1. *Gymnema sylvestre*

A typical dosage of *Gymnema sylvestre* extract is 400-600 mg/day. One of its side effects may be a reduction or loss of the taste sensation of sweetness and bitterness, although this occurs only if the plant is directly exposed to the tongue.[61]

Allium cepa and *Allium sativum*

Studies have found both *Allium cepa* (onions) and *Allium sativum* (garlic) have blood sugar lowering effects.[69,70] Volatile oils in raw onion and garlic cloves have been shown to lower fasting glucose concentration in both diabetic animals and human subjects.[71] The active components are believed to be sulfur-containing compounds – allyl propyl disulfide (APDS) in onions and diallyl disulfide (allicin) in garlic. Researchers have postulated that these active ingredients lower glucose levels by competing with insulin (which is also a disulfide) for insulin-inactivating sites in the liver,[70] resulting in an increase of free insulin. Onion extracts reduce blood sugar levels in a dose-dependent manner.[69] A typical dosage of *Allium cepa* is one 400 mg capsule daily. The general daily dosage of garlic is 4 g fresh garlic or 8 mg essential oil.[72]

Pterocarpus marsupium and other Epicatechin-containing Plants

Pterocarpus marsupium has a long history of use in India as a treatment for diabetes. The flavanoid, (-)-epicatechin, extracted from the bark of this plant has been shown to prevent beta-cell damage in rats. In addition, both epicatechin and a crude alcohol extract of *Pterocarpus marsupium* have been shown to regenerate functional pancreatic beta-cells in diabetic animals.[73,74] Epicatechin and catechin consist of glycosides and esters. They are flavan-3-ols, a group of flavanols that have anti-diabetic properties.[75] *Camellia sinensis* (green tea polyphenols) and *Acacia catechu* (Burma cutch) are also good sources of flavan-3-ols. Since Pterocarpus is not very common in the United States, green tea may be a suitable alternative, although further study would be necessary to confirm this.

In an open trial, conducted at four centers in India, Pterocarpus at doses of 2-4 g daily was found to have significant glucose-lowering effects in patients with mild type 2 diabetes.[76] Ninety-seven patients participated in the 12-week trial. By the end of the trial, 67 patients had attained good blood sugar control with 2 g (73%), 3 g (16%), and 4 g (10%).

Vaccinium myrtillus (Bilberry)

Vaccinium myrtillus (bilberry or European blueberry) is a shrubby plant that grows in Europe (Figure 2). Leaves of bilberry were widely used as a treatment for diabetes before the availability of insulin.[20] Oral administration of bilberry leaf tea reduced blood sugar levels in normal and diabetic dogs, even when glucose was concurrently injected intravenously.[77] Bilberry also has a beneficial effect in microvascular abnormalities of diabetes,[78,79] particularly retinopathy. In the case of vascular complications, however, the fruit rather than the leaf is used, with the anthocyanosides being the most important constituent.[80] The standard dose of bilberry fruit extract is based on its anthocyanoside contents and is 80-160 mg three times daily of a 25-percent anthocyanoside extract. The ideal dosage of bilberry leaf for lowering blood sugar has not been elucidated.

Atriplex halimus (Salt Bush)

Atriplex halimus (salt bush) is a plant native to Israel, where much of the clinical data has been collected. Small animals called sand rats develop type 2 diabetes when deprived of this plant.[81] The data on its use for type 2 diabetes in humans is limited to unpublished reports in which 3 g/day decreased blood glucose levels.[82,83]

Aloe vera

The dried sap (fluid) of *Aloe vera* is a traditional remedy used for diabetes in the Arabian peninsula. Ghannam et al reported a hypoglycemic effect of *Aloe vera* in both type 2 diabetic patients and in an animal model.[84] *Aloe vera* juice is prepared from *Aloe vera* gel, a mucilaginous preparation obtained from the leaves of the plant. Oral administration of the juice has been reported to reduce fasting blood glucose and triglyceride levels in type 2 diabetic patients with or without combination of a conventional anti-diabetic agent.[85-87] The amount used was one tablespoon of *Aloe vera* juice twice daily with no significant adverse effects reported.

Figure 2. *Vaccinium myrtillus (Bilberry)*

Mineral Supplementation

The treatment of diabetes requires nutritional supplementation, as these patients have a greatly increased need for many nutrients. Supplying the diabetic with additional key nutrients has been shown to improve blood sugar control as well as help prevent or ameliorate many major complications of diabetes.

Chromium

Chromium is an essential micronutrient for humans. Considerable experimental and epidemiological evidence now indicates that chromium levels are a major determinant of insulin sensitivity, as it functions as a cofactor in all insulin-regulating activities.[88] Chromium facilitates insulin binding and subsequent uptake of glucose into the cell. Supplemental chromium has been shown to decrease fasting glucose levels, improve glucose tolerance, lower insulin levels, and decrease total cholesterol and triglycerides, while increasing HDL cholesterol in normal, elderly, and type 2 diabetic subjects.[89,90] Without chromium, insulin's action is blocked and glucose levels are elevated.[89]

Chromium picolinate, a trivalent chromium (Cr^{3+}), is one of the forms of chromium that exhibits biological activity.[91] A large clinical study on 180 diabetic patients documents the benefit of chromium picolinate for type 2 diabetic patients. In the study, while patients continued their normal medication, they were placed in one of three groups: placebo group, 100 mcg chromium picolinate twice daily, or 500 mcg chromium picolinate twice daily. There were significant dose- and time-dependent decreases in glycosylated hemoglobin, fasting glucose, two-hour postprandial glucose levels, fasting and two-hour postprandial insulin values, and total cholesterol, particularly in the 500 mcg twice daily group.[92] However, not all studies on chromium have yielded positive results. In a controlled six-month study to determine the effect of 200 mcg/day chromium picolinate on individuals with type 2 diabetes, Lee and Reasner reported a decrease in triglycerides but no statistical difference between control and chromium-treated subjects with respect to measured parameters of glucose control.[93] This dosage is considerably smaller than that found effective at lowering glucose in other studies so may explain the disparate findings among studies.

Although no recommended daily allowance (RDA) has been established for chromium, over 200 mcg/day appears necessary for optimal blood sugar regulation. A good supply of chromium is assured by supplemental chromium[94] in addition to dietary sources. Good dietary sources are brewer's yeast[63] and barley flour,[95] while refined sugars, white flour products, and lack of exercise can deplete chromium levels.

Trivalent chromium has long been considered to be a safe nutritional supplement.[96] Although the hexavalent form of chromium is a known human respiratory tract carcinogen when inhaled in high-exposure industrial settings, there is no evidence of any carcinogenesis in humans from the trivalent form of chromium found in chromium supplements.[97,98] Further evaluation of the safety and efficacy of trivalent chromium in diabetes treatment may be warranted.

Vanadium

Prior to the discovery of insulin in 1922, vanadium was used for the control of blood sugar. Two small studies (one with six type 2 diabetic patients, one with seven type 2 diabetic patients) have confirmed the effectiveness of vanadyl sulfate at a dose of 100 mg/day in improving insulin sensitivity.[99,100]

Magnesium

A deficiency of magnesium is significantly more common in type 2 diabetics than in the general population.[101] Magnesium deficiency has been associated with complications of diabetes, retinopathy in particular. One study found patients with the most severe retinopathy were also lowest in magnesium.[102]

Nutrients used in type 2 diabetes are summarized in Table 2.

Physical Interventions: Acupuncture and Hydrotherapy

Acupuncture is best known in the United States as an alternative therapy for chronic pain. However, it has been used for the treatment of diabetes and related complications during the past several decades. There are numerous Chinese publications on the use of acupuncture for diabetes, but only those published in English will be cited here. Acupuncture may be effective in treating not only diabetes, but also in preventing and managing complications of the disease.[103]

Table 2. *Nutrients for the Treatment of Type 2 Diabetes*

NUTRIENT	EFFECTS
Chromium	Improves insulin sensitivity and glucose tolerance
Magnesium	Corrects a deficiency
Zinc	Deficiency causes insulin resistance
Calcium	Improves insulin sensitivity in some populations
Potassium	Deficiency leads to insulin resistance
Vanadyl Sulfate	Improves insulin sensitivity
L-Carnitine	Improves insulin sensitivity after IV infusion
Taurine	May improve insulin sensitivity
L-Arginine	Improves insulin sensitivity after IV infusion
Vitamin E	Reduces glycosylation; provides antioxidant activity
Vitamin C	Reduces glycosylation; provides antioxidant activity
Vitamin B6	Improves glucose metabolism and nerve function
Biotin	Improves glucose metabolism and nerve function
Glutathione	Improves insulin sensitivity after IV infusion
Omega-3 (EFA's)	Improves insulin sensitivity
Coenzyme Q10	Improves insulin sensitivity in some populations
Lipoic acid	Improves insulin sensitivity; antioxidant activity

The effects of acupuncture on diabetes have been observed experimentally and clinically.[104,105] Animal experiments have shown that acupuncture can activate glucose-6-phosphatase (an important enzyme in carbohydrate metabolism) and affect the hypothalamus.[106] Acupuncture can act on the pancreas to enhance insulin synthesis, increase the number of receptors on target cells, and accelerate the utilization of glucose, resulting in lowering of blood sugar.[106] Data from other studies have shown the beneficial anti-obesity effect of acupuncture,[105] which is the most modifiable risk factor for type 2 diabetes. It appears that the therapeutic effect of acupuncture on diabetes is not the result of its action on one single organ, but on multiple systems.

Four commonly used points are: (1) Zusanli point, located three inches below the lateral knee depression, one finger width from the lateral side of the anterior crest of the tibia; (2) Sanyinjiao point, located three inches above the tip of the inner ankle, on the posterior margin of the metatarsal bone; (3) Feishu point, located 1.5 inches lateral and inferior to the spinous process of the third thoracic vertebra in a prone position; and (4) Shenshu point, located 1.5 inches lateral to the posterior midline, lateral and inferior to the spinous process of the second lumbar vertebra in a prone position. These acupuncture points were selected based on traditional Chinese medicine theory. During the treatment, other points can be added according to symptoms and signs.[103] Other methods have also been employed such as point injection with normal saline, small dose insulin, and Chinese herbal medicine extracts. Treatment is generally given once daily or once every other day as a course of 14-21 treatments. It is believed that the longer the course of treatment, the more marked will be the effect.

Acupuncture can be effective in treating complications of diabetes, often with marked improvement in clinical symptoms. Better therapeutic results are obtained in patients with dietary control than in those without it. Physical exercise, breathing exercises, and massage can help improve the therapeutic effect.

Although acupuncture shows some effectiveness in treating diabetes, its mechanisms of action are still obscure.

Since hot-tub therapy can increase blood flow to skeletal muscles, it has been recommended for patients with type 2 diabetes who are unable to exercise.[107] A study reported that eight patients were asked to sit in a hot tub for 30 minutes daily for three weeks. During the study period, patients' weight, mean plasma glucose level, and mean glycosylated hemoglobin decreased.[107] Caution should be taken that the water not be too hot as neuropathy may prevent the patient from noticing they are burning themselves. In addition, poor circulation can result in increased metabolic demands when feet become heated – demands that cannot be met by the diabetic patient. Proper water sanitation and appropriate guidance should be considered when prescribing hot-tub therapy for diabetic patients.[108]

Conclusion

Alternative therapies with antihyperglycemic effects are increasingly sought by patients with diabetes. This comes as no surprise since alternative treatments have been most widely used in chronic diseases, which may be only partially alleviated by conventional treatment. Herbal medications are the most commonly used alternative therapy for blood sugar control; however, their safety and efficacy need to be further evaluated by well-designed, controlled clinical studies. Because various non-standardized forms of the herbs have often been the testing material, the results have been difficult to replicate. Therefore, preparation of standardized medicinal herbs is urgently needed in future studies and therapies. Although herbs used for diabetes are less likely to have the drawbacks of conventional drugs, potential adverse herb-drug interactions should be kept in mind for patients also receiving conventional antidiabetic medications.

Several minerals have been found to benefit people with diabetes, either because of potential deficiencies or because of the beneficial effect on glucose metabolism. Among the most important minerals for supplementation are chromium, magnesium, and vanadium. Other potentially beneficial treatments for type 2 diabetes include acupuncture and hydrotherapy.

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