

Sugar & Spice: CAM Use and Diabetes Mellitus

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At the conclusion of this presentation, participants will be able to:

- Describe complementary/alternative medicine (CAM) use among diabetic individuals from various ethnic groups.
- List commonly used herbal/vitamin/mineral supplements common to diabetic individuals.
- Assess evidence based medicine (EBM) aspects of CAM use including mode of action, effectiveness and areas of concern.
- Integrate CAM use with conventional pharmaco-therapeutics in patient care.

Diabetes Statistics in the United States: Reference graphs available at:

<http://www.cdc.gov/diabetes/pubs/estimates.htm>. Total prevalence of diabetes in people aged 20 years or older, by age group—United States, 2002, Age-adjusted total prevalence of diabetes in people aged 20 years or older, by race/ethnicity—United States, 2002, Number of new cases of diagnosed diabetes in people aged 20 years or older, by age group—United States, 2002

National Center for Complementary and Alternative Medicine (NCCAM): 2007 NCHS's Newly Released CAM Findings

Who was studied? 23,393 adults aged 18 years or older and 9,417 children aged 17 years and under.

How many people use CAM? In the United States, approximately 38 percent of adults (about 4 in 10) and approximately 12 percent of children (about 1 in 9) are using some form of CAM

10 Most Common CAM (%) - 2007

Natural products (18), Deep Breathing (13), Meditation (9), Chiropractic/Osteopathic (9), Massage (8)

Yoga (6), Diet-Based Therapies (4), Progressive Relaxation (3), Guided Imagery (2), Homeopathic (2)

The 10 Most Common Natural Products (%)

Fish Oil/Omega 3 (37), Glucosamine (20), Echinacea (20), Flaxseed Oil/Pills (16), Ginseng (14), Combo Herb Pills (13), Ginkgo (11), Chondroitin (11), Garlic supplements (11), Coenzyme Q 10 (9).

Prevalence of CAM in Diabetes Mellitus (DM)

1996 Medical Expenditure Panel Survey (MEPS): Individuals with DM: 1.6 times more likely to use CAM than those without DM and DM is an independent predictor of CAM use. Increased use with higher education and greater than age 65

MEPS Results of CAM in DM: Nutritional advice and lifestyle diets ranked #1 for CAM use. However, CAM providers offer different nutritional or dietary recommendations than those generally endorsed by Certified Diabetes Educators (CDE) or physicians. Advice included: Ayurvedic diets, Homeopathy, Orthomolecular therapies, Magnesium supplementation, Melatonin, Vitamin megadoses. Diets recommended included Atkins, Ornish, Pritikin, and Weil. Complementary use was more common than alternative use. Of CAM users, 57% told their Health Care Provider (HCP) and 43% were advised to use CAM by their HCP.

What is a Supplement? Biological complementary therapies are classified by the Dietary Supplement Health Education Act (DSHEA) of 1994. There is less stringent approval process vs. drugs. Dietary supplements are not required to prove safety and efficacy to be marketed. They include: a vitamin, mineral, an herb or other botanical, an amino acid, a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or a concentrate, metabolite, constituent, extract, or combination of any ingredient described above.

Dietary Supplement and Nonprescription Drug Consumer Protection Act (2006): Manufacturers and distributors of dietary supplements must submit information to the FDA concerning adverse reactions. Office of Dietary Supplements (ODS), National Institutes of Health (NIH) is seeking to partner with industry and academic institutions to develop a broad and good quality data base.

Polyherbacy: Public health concern due to potential for adverse drug reactions, drug interactions, increased costs, and patterns of use remain hazy.

Dietary supplement sales (2006) >\$21 billion

Obesity: A high incidence of individuals with DM is obese. As clinicians, we instruct them to “lose weight” to be in better control. Changing behaviors is no simple task. Thus, many of our patients choose to use over-the-counter diet aids, which may have untoward effects while providing minimal weight loss advantage.

Dietary Supplements & Weight Loss: Approx. 15% of adults had ever used a weight-loss supplement (n = 9403, telephone survey, 9/02 to 12/02) with 9% in the prior year of which 16% used 2 products. Overall greater use in women especially in woman aged 18-34 years. 10% used for >12 months and 30% who saw a doctor reported their use.

Dietary Supplements & Weight Loss: Top supplements used contained: Ephedra, caffeine and/or bitter orange. Ephedra removed from US markets in 2004 and replaced by synephrine (bitter orange). 19% of stimulant users self-reported history of HTN, heart disease, or diabetes. Meta analysis reports that weight-loss supplement users show slightly higher weight loss over 4-6 months with 2-3 times the risk of adverse effects such as psychiatric, autonomic, gastrointestinal and cardiac issues.

Diuretics and Weight Loss - Recent Concerns: Food and Drug Administration reports that weight-loss capsules called StarCaps™, promoted as natural dietary supplement using papaya, could be hazardous to your health. In violation of the law, the FDA has found that the capsules also contained a potent pharmaceutical drug called bumetanide which can have serious side effects. The FDA in a continuing investigation warns consumers that dozens of weight-loss supplements, most of them imported from China, contain hidden and potentially harmful drugs. FDA tests found that some of the products contained undeclared ingredients including sibutramine, rimonabant, phenytoin, phenolphthalein. In some cases, the amount of active pharmaceutical ingredients in the products far exceeded the FDA-recommended levels, posing a health risk.

Ayurvedic Interventions

Ayurveda is Sanskrit for “knowledge of life” or “knowledge of longevity.” Emphasizes body, mind, and spirit. Began in India 3,000 ago as documented in 4 sacred books from the Indus River civilization. It includes diet, exercise, herbs, meditation, massage, exposure to sunlight, controlled breathing, and detoxification treatments. It emphasizes symptoms over laboratory results. Commonly used herbs for DM treatment follow.

Gymnema sylvestre

Hindu common name is sugar-destroyer. Leaves are chewed whole, taken as powder, or drunk as water decoction. Diminishes taste for sweet and bitter X 1-2 hours.

Natural Medicines Comprehensive Database (NMCD) - Possibly safe for up to 20 months

Mechanism of Action (MOA): Gymnemic acids reduce intestinal absorption of glucose, stimulate beta cell growth, and increase insulin release/increase C-peptide levels. It may decrease weight gain. No specific lab/medication interactions. Not listed on NCCAM “Herbs at a Glance” site (5/10/09)

Coccinia indica – Ivy Gourd

Leaves most medically studied. The juice contains amylase and hypoglycemic alkaloids. May repress key gluconeogenic enzymes. Not listed on NCCAM “Herbs at a Glance” site (5/10/09). NMCD – Possibly safe up to 6 weeks.

MOA: Pectin has hypoglycemic activity. Extracts depress gluconeogenesis by inhibiting glucose-6-phosphatase and extracts may stimulate insulin production. Drug Interactions include additive effect with other anti-diabetic drugs. Recommend D/C 2 weeks prior to surgery

Momordica charnata L. Bitter Melon

The most widely used Ayurvedic traditional remedy for diabetes. Often referred to as “vegetable insulin.” It uses the bitter, unripe fruit or as a juice or extract. Not injected – used orally. Studies use a 17 amino acid peptide by injection. It contains a rapid and slow onset of action. It does not cross-react with bovine insulin. Several cases of vomiting and diarrhea reported in humans. Not found to be toxic when taken as a food in the Indian diet. Not listed on the NCCAM “Herbs at a Glance” site (5/10/09). NMCD – Fruit extracts safe up to 3 month

MOA: Decreases hepatic gluconeogenesis, increases hepatic glycogen synthesis, increases insulin secretion. It contains an insulin-like polypeptide called polypeptide P. It contains a plant “insulin” with pharmacologic effects similar to bovine insulin with an onset of action between 30 and 60 minutes, and a peak effect at about four hours

Two cases of hypoglycemic coma and seizures have occurred in children after drinking bitter melon tea. Recommended to D/C 2 weeks prior to surgery. Bitter melon is used as an ingredient in some kinds of curries. A reduction in blood sugar after eating foods spiced with bitter melon containing curry has been described in a patient taking chlorpropamide (Diabinese).

Trigonella foenum-graecum Linn. Fenugreek

Family of Leguminosae : Potential cross-allergenicity to chickpea, soybeans, peanuts, and green peas

Found in ancient Pharmacopoeia of Egyptian and Greeks. The leaves are eaten as a vegetable and seeds are used to treat diabetes as a gruel or drink, baked in breads or mixed into curry. Possible side effects of fenugreek when taken by mouth include gas, bloating, and diarrhea. Historically used for inducing childbirth – caution during pregnancy.

NCCAM (5/10/09): A few small studies have found that fenugreek may help lower blood sugar levels in people with diabetes. But, there is not enough scientific evidence to support the use of fenugreek for any other health condition.

NMCD – Safe in amounts commonly found in foods. GRAS

MOA : Seeds contain about 50% dietary fiber and pectin and may slow glucose absorption. An amino acid in the seeds may directly stimulate insulin in the presence of moderate to high glucose concentrations.

Drug Interactions: Contains coumarins and may enhance anti-platelet agents. May have additive effect on antidiabetic drugs.

Dosing - For reducing postprandial blood glucose 10 to 15 grams per day, as a single dose or in divided doses with meals has been used.

Traditional Chinese Medicines (TCM)

Earliest known Chinese medical writing, *Huang-ti Nei ching (The Canon of Internal Medicine)*. Two treatises, one a dialogue about living matter and the other a description of medical physiology, anatomy, and acupuncture are known. The “Bible” of traditional Chinese medicine but its true authorship is unknown.

TCM’s Medical Opinion of DM: DM is caused by *Yin* deficiency diathesis, improper diet, emotional disorders, overstrain and excessive sexual activities. Pathogenesis is consumption of *yin* fluids leading to endogenous dryness-heat in the body and presence of blood stasis and phlegm retention. Prolonged *yin* deficiency impairs *yang* with ultimate deficiency of *yin*, *yang* and *qi*. Treatment is more than lowering blood glucose. It is important to promote blood circulation to remove blood stasis, activate vital energy circulation, clear away heat in the body, invigorate liver, kidney to activate *Yang* as well as the spleen and stomach to strengthen the body. Chinese medicine’s classical prescriptions and folk secrets recipes have outstanding curative effect and have been used for hundreds of years. A commonly used herb is Ginseng.

TCM Medicine Cabinet: Radix (Panax) Ginseng

Asian or Korean Ginseng are true ginsengs (American Ginseng is also true). Roots contain ginsenosides shown to improve diabetes. Extracts of roots, stems, leaves and fruits have anti-hyperglycemic effects.

NCCAM: Radix (Panax) Ginseng (5/10/09) indicates: May lower blood sugar levels; this effect may be seen more in people with diabetes. People with diabetes should use extra caution with Asian ginseng, especially if they are using medicines to lower blood sugar or taking other herbs, such as bitter melon and fenugreek that are also thought to lower blood sugar. “NCCAM supports studies to better understand the use of Asian ginseng. Areas of recent NCCAM-funded research include Asian ginseng’s interactions with other herbs and drugs and the herb’s potential to treat chronic lung infection, impaired glucose tolerance, and Alzheimer’s disease.”

NMCD – Possibly safe when used <3 months

MOA – Ginsenosides might reduce tissue insulin resistance and changes in gene expression in Type 2 DM (T2DM) and may directly stimulate insulin release

Dose - Some evidence shows 200 mg po QD can decrease fasting blood glucose levels and hemoglobin A1c (HbA1c) in T2DM

Panax Ginseng: A Study

Improvement in glucose and insulin regulation in 19 well-controlled, type 2 diabetes: results of a randomized, double-blind, placebo-controlled study of efficacy and safety. Treatment group showed decreased 75 g OGTT-PG indices by 8-11% compared with placebo (P<0.05). A small Toronto-based study with future potential.

Other botanical approaches to the treatment of DM exist outside of traditional Ayurvedic or Chinese medical systems. Some of them follow.

Cassia Cinnamon

NMCD – GRAS

MOA - applicable parts are the bark and flower containing polyphenolic polymers such as hydroxychalcone seem to potentiate insulin action, increase insulin and increase glucose uptake. Shown ineffective in the majority of clinical research for T1 and T2DM. An analysis of studies shows no significant reduction in fasting blood glucose, HbA1c, or lipid levels in patients' diabetes

Many types of cinnamon exist: *Cinnamomum verum* (Ceylon cinnamon) is the type used most commonly in the Western world. *Cinnamomum aromaticum* (Cassia cinnamon or Chinese cinnamon) is also commonly used. Food stores' cinnamon often contains a combination. Only cassia cinnamon has been shown to have any effect on blood glucose in humans.

Cassia Cinnamon: Specific Studies show area of controversy

1. "Cinnamon Improves Glucose and Lipids of People With Type 2 Diabetes." ALAM KHAN, MS, PHD, et al.

CONCLUSIONS— The results of this study demonstrate that intake of 1, 3, or 6 g of cinnamon per day reduces serum glucose, triglyceride, LDL cholesterol, and total cholesterol in people with type 2 diabetes and suggest that the inclusion of cinnamon in the diet of people with type 2 diabetes will reduce risk factors associated with diabetes and cardiovascular diseases. *Diabetes Care* 26:3215–3218, 2003

2. Cassia Cinnamon

"Effect of Cinnamon on Glucose Control and Lipid Parameters." William L. Baker, et al.

OBJECTIVE— To perform a meta-analysis of randomized controlled trials of cinnamon to better characterize its impact on glucose and plasma lipids.

Research Design — A systematic meta-analysis of literature through July 2007

Results— Five prospective randomized controlled trials ($n=282$) were identified..

Conclusions— Cinnamon does not appear to improve A1C, FBG, or lipid parameters in patients with Type 1 or Type 2 diabetes. *Diabetes Care* 31:41–43, 2008

Aloe vera: not Aloe latex

Member of Liliaceae family. Aloe leaves contain a clear gel that is often used as a topical ointment. The green part of the leaf that surrounds the gel can be used to produce a juice or a dried substance (called latex) that is taken by mouth. The latex component is not recommended for intake.

MOA : Aloe gel which is obtained from the inner portion of the leaves may have hypoglycemic effects – etiology unknown. Concerns: May have additive effects with other anti-diabetic agents. Shows some promise – not yet proven.

NCCAM (5/10/09): There is not enough scientific evidence to support aloe vera for DM.

Typical dosing: 15ml of aloe gel/day

Aloe latex may discolor alkaline urine red and can interfere with colormetric diagnostic tests. Potent laxative with tolerance potential. FDA (2002) banned its use in laxative products due to the lack of safety data

Chromium – atomic #24

Used safely up to 1000 mcg/day for up to 6 months in studies. The FDA and Institute of Medicine (IOM) evaluations of the safety of chromium suggest that it is safe when used in doses of 200 mcg/day for up to 6 months. However, note insufficient reliable information about the safety of long-term use.

MOA: Valence state dictates activity. CrIII is the form found in foods and supplements. CrVI is used in welding and carcinogenic. Called glucose tolerance factor (GTF) as it plays a part in a complex of glycine, glutamic acid and nicotinic acid. May increase insulin receptor sites

Dietary sources include canned foods, meats, animal fats, brown sugar, coffee, tea, some spices, calf liver, whole grain bread and brewer's yeast

People with DM may have lower chromium levels. Yet, measuring chromium levels – hair, skin and often blood levels do not reflect status. Observing supplementation results in deficient (suspected) patients is best method. Some evidence shows decreased FBG, insulin levels and HbA1c and improved insulin sensitivity in T2DM and may decrease weight gain and fat deposition.

Combining chromium picolinate 1000 mcg/day with levothyroxine 1mg decreases levothyroxine serum levels by 17%. Separate by 30 min. pre and 3-4 hours post.

Typical Dosages for T2DM: 200 – 1000 mcg/day in divided dose. Combining with biotin may improve effect.

Chromium: A Randomly Controlled Double Blinded Placebo Controlled study of 37 T2DM maintained on 5mg/day of glipizide were given daily oral doses of 1000 mcg chromium picolinate (CrPic) for 6mths. Comparison: Placebo = gained 2.2kg, increased abdominal and total body fat. The CrPic group had improved insulin sensitivity, lower GlycoHemoglobin (1.16%) and free fatty acids.

Virgin Mary's Milk - Milk Thistle

Silybum marianum (Latin name): Likely safe with extracts standardized to contain 70-80% of the silymarin constituent for up to 41 months.

MOA: The seed contains silymarin: 4 flavonolignans that are antioxidants. Also known to decrease insulin resistance, reduce blood glucose levels and reduce oxidative damage in DM. Seems to significantly decrease FBG, HbA1c in T2DM when used in conventional therapy. It is being studied by NCCAM for chronic Hepatitis C (5/10/09).

Typical Dosing: 200 mg tid . May inhibit P450 (CYP2C9): i.e. amitriptyline, verapamil, warfarin.

Caution if allergic to plants such as ragweed, marigolds, daisies.

Nopal (Prickly Pear Cactus)- Prickly Pear Cactus

Likely safe when used as a food. Possibly safe when leaves, stems or standardized extracts are used short term.

MOA: Possibly the pectin slows CHO absorption and/or insulin sensitizing effect. Preliminary evidence supports decreased blood glucose levels with some patients having 17-46% drop. Broiled stems 100-500 grams/day is typical divided into 3 doses. Used as a diabetes agent in Mexican and Mexican-American cultures. Nopales added to the usual Mexican breakfast induced a reduction in glucose concentration after the meal, reducing glycemic index and post meal incremental area under the blood glucose response curve (IAUC). Not included on the NCCAM's "Herbs at a Glance" (5/10/09).

Coffee

Safe in low to moderate amounts

MOA: 6 oz brewed coffee = 60-120 mg caffeine. Antioxidants in coffee might improve insulin sensitivity. Caffeine seems to stimulate pancreatic beta cells to secrete insulin. Coffee also contains magnesium and phytoestrogens, both of which have been associated with a beneficial effect on diabetes risk.

Preventing T2DM? Long-term consumption of about 900 mg caffeine per day (6 or more cups of coffee per day) reduces risk of DM. Use filtered coffee to avoid some adverse effects. Darker roasts contain less caffeine due to sublimation during roasting

Coffee may increase bleeding risk. Over stimulation associated with Bitter Orange or Ephedra . Competitively inhibits adenosine and reduces levothyroxine levels along with interacting with other drugs either in theory or principle.

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