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2018 Clinical Practice Guidelines

Complementary and Alternative Medicine for Diabetes

Diabetes Canada Clinical Practice Guidelines Expert Committee

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KEY MESSAGES

- Anywhere from 25% to 57% of people with diabetes report using complementary or alternative medicine.
- Some natural health products have shown a lowering of A1C by $\geq 0.5\%$ in trials lasting at least 3 months in adults with type 2 diabetes, but most are single, small trials that require further large-scale evaluations before they can be recommended for widespread use in diabetes.
- A few more commonly used natural health products for diabetes have been studied in larger randomized controlled trials and/or meta-analyses refuting the popular belief of benefit of these compounds.
- Health-care providers should always ask about the use of complementary and alternative medicine as some may result in unexpected side effects and/or interactions with traditional pharmacotherapies.

KEY MESSAGES FOR PEOPLE WITH DIABETES

- Many people with diabetes use complementary medicine (along with) or alternative medicine (instead of) with conventional medications for diabetes.
- Although some of these therapies may have the potential to be effective, they have not been sufficiently studied and others can be ineffective or even harmful.
- It is important to let your health-care providers know if you are using complementary and/or alternative medicine for your diabetes.

Introduction

Despite advances in the management of type 1 and type 2 diabetes, therapeutic targets are often not met. People dissatisfied with conventional medicine often turn to nontraditional alternatives. Complementary and alternative medicine (CAM) can be loosely defined as health-care approaches developed outside of mainstream Western, or conventional medicine, with “complementary” meaning used together with, and “alternative” meaning used in place of conventional medicine (1). According to a report from the Fraser Institute, 50% to 79% of Canadians had used at least 1 CAM sometime in their lives, based on surveys from 1997, 2006 and 2016 (2). The most common types used in 2016 were massage (44%), chiropractic care (42%), yoga (27%), relaxation techniques (25%) and acupuncture (22%). According to the United States 2012 National Health Interview Survey (NHIS), 17.7% of American adults

used a dietary supplement other than vitamins and minerals (3). A few surveys have sought to characterize the use of CAM in persons with diabetes. In a Canadian study of 502 people with diabetes, 44% were taking over-the-counter supplements with 31% taking alternative medications (4). A United States national survey reported 57% of those with diabetes using CAM in the previous year (5). The Medical Expenditure Panel Surveys (MEPS) showed that those with diabetes were 1.6 times more likely to use CAM than those without diabetes, with older age (≥ 65 years) and higher educational attainment (high school education or higher) independently associated with CAM use (6). An Australian study reported 25% of people with diabetes stated they had used CAM within the previous 5 years (7).

This chapter will review CAM, including natural health products (NHP) and others, such as yoga, acupuncture, tai chi and reflexology, that have been studied for the prevention and treatment of diabetes and its complications.

NHP for the Prevention and Treatment of Diabetes and Its Complications

In Canada, NHP are defined as vitamins and minerals, herbal remedies, homeopathic medicines, traditional medicines, such as traditional Chinese medicines, probiotics, and other products like amino acids and essential fatty acids (8). They are regulated under the Natural Health Products Regulations, which came into effect in 2004. In general, the current level of evidence for the efficacy and safety of NHP in people with diabetes is lower than that for pharmaceutical agents. Trials tend to be of shorter duration and involve smaller sample sizes. Concerns remain about standardization and purity of available compounds, including their contamination with regular medications and, in some cases, toxic substances (9–11). Various NHP have been studied to evaluate their impact on the development of both type 1 and type 2 diabetes, glycemic control in people with diabetes, and on the various complications of diabetes.

NHP for the Prevention and Treatment of Diabetes

A number of immune modulators have been studied in an attempt to prevent or arrest beta cell decline in type 1 diabetes, most with limited success. A few NHP have also been studied in this

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regard. A randomized controlled trial of people with new-onset type 1 diabetes assessed the effect of vitamin D supplementation on regulatory T (Treg) cells (12). After 12 months, Treg suppressive capacity was improved, although there was no significant reduction in C-peptide decline. Observational studies have suggested an inverse relationship between vitamin D levels and the development of type 2 diabetes (13), although randomized controlled trials are lacking (14). In the large, prospective cohort study, The Environmental Determinants of Diabetes in the Young (TEDDY), early probiotic supplementation may reduce the risk of islet autoimmunity in children at the highest genetic risk of type 1 diabetes (15).

A number of NHP have been evaluated to assess their effect on the progression from impaired glucose tolerance (IGT) to diabetes. Tianqi is a traditional Chinese medicine consisting of 10 different herbs. In a double-blind, placebo-controlled trial of 12 months duration, Tianqi was shown to reduce the progression from IGT to type 2 diabetes by 32% (16). A systematic review and meta-analysis of observational studies of omega-3 fatty acids or fish intake showed that an increased intake of alpha linoleic acid (ALA) and fatty fish reduced the risk of type 2 diabetes significantly with ALA, only in Asians (17). In a randomized controlled trial, the traditional Chinese medicine Shenzhu Tiaopi granule (SZTP) significantly reduced the conversion from IGT to type 2 diabetes to 8.52% from 15.28% with placebo, with a significantly higher number of people with IGT reverting to normal blood glucose levels as well (42.15% vs. 32.87% for placebo) (18).

In adults with type 2 diabetes, the following NHP have been shown to lower glycated hemoglobin (A1C) by at least 0.5% in randomized controlled trials lasting at least 3 months:

- Ayurveda polyherbal formulation (19)
- *Citrullus colocynthis* (20)
- *Coccinia cordifolia* (21)
- Eicosapentaenoic acid (22)
- *Ganoderma lucidum* (23)
- Ginger (*Zingiber officinale*) (24)
- *Gynostemma pentaphyllum* (25)
- *Hintonia latiflora* (26)
- Lichen genus *Cladonia* BAFS “Yagel-Detox” (27)
- Marine collagen peptides (28)
- Nettle (*Urtica dioica*) (29)
- Oral aloe vera (10)
- *Pterocarpus marsupium* (vijayasar) (30)
- *Salacia reticulata* (31)
- *Scoparia dulcis* porridge (32)
- Silymarin (33,34)
- Soybean-derived pinitol extract (35)
- Touchi soybean extract (36)
- Traditional Chinese medicine herbs:
 - Berberine (37)
 - Fructus Mume (38)
 - Gegen Qinlian Decoction (GQD) (39)
 - Jianyutangtang (JYTK) with metformin (40)
 - Jinlida with metformin (41)
 - Sancaijiangtang (42)
 - Shen-Qi-Formula (SQF) with insulin (43)
 - Tang-Min-Ling-Wan (TM81) (44)
 - Xiaoke (contains glyburide) (11)
 - Zishentongluo (ZSTL) (45)
- *Trigonella foenum-graecum* (fenugreek) (46,47)

These products are promising and merit consideration and further research, but, as they are mostly single, small trials or meta-analyses of such, it is premature to recommend their widespread use.

The following NHP either failed to lower A1C by 0.5% in trials lasting at least 3 months in adults with type 2 diabetes, or

were studied in trials of shorter duration, nonrandomized or uncontrolled:

- *Agaricus blazei* (48)
- American ginseng (*Panax quinquefolius* L.) (49)
- Antioxidants: (fruit/vegetable extract) (50), (pomegranate extract) (51)
- *Camellia sinensis* (52)
- Flaxseed oil (53)
- French maritime pine bark (54)
- Ginseng (55,56)
- *Juglans regia* extract (57)
- Liuwei Dihuang Pills (LDP) (58)
- *Momordica charantia* (bitter melon or bitter gourd) (59,60)
- *Rosa canina* L. (rose hip) (61)
- *Salvia officinalis* (62)
- Soy phytoestrogens (63)
- *Tinospora cordifolia* (64)
- *Tinospora crispa* (65)
- Vitamin C (66–68)
- Vitamin E (69–73)

The following NHP have demonstrated conflicting effects on A1C in trials lasting at least 3 months in adults with type 2 diabetes:

- Cinnamon (74–79)
- Coenzyme Q10 (80–83,85,86)
- *Ipomoea batatas* (caiaipo) (87,88)
- L-carnitine (89–92)
- Magnesium (93–99)
- Omega 3 fatty acids (100,101)
- Probiotics (102,103)
- Zinc (104,105)

A few products, such as chromium, vitamin D and vanadium, have been the subjects of special interest in diabetes.

Chromium is an essential trace element involved in glucose and lipid metabolism. Early studies revealed that chromium deficiency could lead to IGT, which was reversible with chromium repletion. This led to a hypothesis that chromium supplementation, in those with both adequate and deficient chromium stores, could lead to improved glucose control in people with diabetes (106,107). Indeed, an analysis of the large NHANES database showed that, in those in the general population who reported consuming a chromium supplement, the odds of developing diabetes was 19% to 27% lower than those not taking a chromium supplement (108). However, randomized controlled studies of chromium supplementation have had conflicting results, with most showing no benefit on improving A1C (109–121), although some showed an improved fasting glucose level (120,121). Most were small studies, of short duration, and some not double-blinded. More recent meta-analyses have also reported conflicting results, with some concluding no benefit of chromium on reducing A1C, lipids or body weight in people with diabetes (122), and others reporting some benefit depending upon the dose and formulation consumed (84). The later meta-analysis reported marked heterogeneity and publication bias in the included studies.

Vitamin D has received much interest recently with purported benefits on cardiovascular disease (CVD), cancer and diabetes. Randomized controlled trials have not demonstrated a benefit of vitamin D supplementation on glycemic control in diabetes (123–138), further confirmed by meta-analyses (139,140).

Vanadium, a trace element that is commonly used to treat type 2 diabetes, has not been studied in randomized controlled trials evaluating glycemic control by A1C over a period of 3 months or longer.

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