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Canadian Journal of Diabetes

journal homepage:
www.canadianjournalofdiabetes.com

**DIABETES
CANADA**



Review

Natural Health Products and Diabetes: A Practical Review

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ARTICLE INFO

Article history:

Received 2 June 2017

Received in revised form

27 June 2017

Accepted 27 June 2017

Keywords:

Complementary and alternative medicine
diabetes management
efficacy
Herbs
natural health products
Nutriments
safety

Mots clés :

médecine douce
prise en charge du diabète
efficacité
Herbes
produits de santé naturels
Nutriments
innocuité

ABSTRACT

The prevalence of natural health product (NHP) use in Canada is extensive. Patients with chronic diseases, including diabetes, use NHPs at a higher rate than the general population. Many NHPs exert hypoglycemic effects, among other effects relevant to diabetes management. To provide a practical, clinical review of NHPs with such effects targeted to pharmacists, a literature search was performed to collect data on the efficacy and safety profiles of 10 commonly used NHPs that exert antidiabetic properties. The following NHPs are included in this clinical review: alpha-lipoic acid, chromium, magnesium, bitter melon, cinnamon, fenugreek, gymnema, milk thistle, Reishi mushroom and white mulberry. Given the potential of NHPs to additively cause hypoglycemia when used concurrently with conventional medications, pharmacists should be up to date with current evidence around NHPs that may affect diabetes care to prevent adverse reactions and interactions. In addition, effective and respectful communication with patients around NHP use and collaboration with various health-care providers are essential in the patient care process.

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R É S U M É

Au Canada, l'utilisation des produits de santé naturels (PSN) est largement répandue. Les patients atteints de maladies de longue durée, y compris le diabète, ont un taux plus élevé d'utilisation des PSN que la population générale. Plusieurs PSN ont des effets hypoglycémiques, entre autres des effets sur la prise en charge du diabète. Pour offrir aux pharmaciens une revue clinique utile sur les PSN ayant de tels effets, nous avons réalisé une recherche de littérature pour collecter les données sur les profils d'efficacité et d'innocuité de 10 PSN aux propriétés antidiabétiques qui sont fréquemment utilisés. Dans la présente revue clinique, nous présentons les PSN suivants : l'acide alpha-lipoïque, le chrome, le magnésium, la margose, la cannelle, le fenugrec, le Gymnema, le chardon-Marie, le champignon reishi et le mûrier blanc. Étant donné que les PSN ont le potentiel de provoquer par addition l'hypoglycémie lorsqu'ils sont employés en concomitance avec les médicaments traditionnels, les pharmaciens devraient être tenus informés des données récentes sur les PSN qui peuvent nuire aux soins aux diabétiques pour prévenir les effets indésirables et les interactions. De plus, le fait de communiquer de manière efficace et respectueuse avec les patients au sujet de l'utilisation des PSN et de collaborer avec les différents prestataires de soins de santé est essentiel au processus de soins des patients.

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In Canada, natural health products (NHPs) include all vitamins and minerals, herbal remedies, homeopathic medicines, traditional medicines, probiotics, essential fatty acids and amino acids that are considered safe to use without supervision by a health-care professional and do not require a prescription to be sold (1). The prevalence of NHP use is extensive, with a national survey in 2010 indicating that 73% of adult Canadians use at least 1 NHP regularly (2). Reasons for increased use of NHPs by the public include

a growing focus on preventive health care and an increased interest in natural approaches to disease and symptom management (2). Individuals with chronic medical conditions, including diabetes, often turn to NHP use at an even higher rate than members of the general population to manage their conditions (3,4).

NHPs are the second most frequently purchased over-the-counter (OTC) product in Canada and currently account for one-third of all OTC product sales (5); therefore pharmacists remain an important point of contact for patients who wish to discuss safe and appropriate NHP use. It is critical for pharmacists to remain abreast of the current evidence available for NHPs to best advise patients on such use, especially because NHPs are active substances that can exert a profound pharmacological effect.

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With the prevalence of diabetes mellitus in Canada reaching an estimated 6.8% (2.4 million Canadians) (6), pharmacists should be aware of which NHPs are commonly used by patients with diabetes and should be able to recognize NHPs that exert a hypoglycemic effect that may interact with conventional medications used to lower blood glucose levels. Research suggests that certain NHPs can exert hypoglycemic effects; however, literature reviews to date have focused on a small number of herbs (5 or fewer) or just spices (7–9).

The objective of this clinical review is to provide a practical overview of the evidence surrounding 10 commonly used NHPs (nutrients and herbs) that exert an effect in the management of diabetes, with a focus on efficacy and safety.

Nutrients

Alpha-lipoic acid

What is it?

Alpha-lipoic acid (ALA) is a naturally occurring dithiol antioxidant produced in the human body (10). Although most intake of ALA is through oral supplementation, food sources such as spinach, broccoli, brussels sprouts, yams, beets and red meats provide small amounts of intact ALA for utilization (10).

How does it work?

ALA exhibits blood glucose-lowering effects by increasing insulin secretion from the pancreas and thereby increasing the abundance of glucose transporters (glucose transporter 4 receptors) in muscle tissue (11). Given the pathogenesis of oxidative stress contributing to diabetic peripheral neuropathy, ALA has gained popularity in the management of peripheral neuropathy in patients with diabetes by improving nerve blood flow and reducing endothelial dysfunction (12). Oral supplementation with 600, 1200 and 1800 mg of ALA daily significantly decreased the total symptom score of peripheral neuropathy by 4.9, 4.5 and 4.7 points (of 15 total points) ($p < 0.05$), respectively, and significantly improved the patients' global assessment of efficacy ($p < 0.05$) compared with placebo in a randomized, controlled trial (13).

Is it safe?

ALA is safe and generally well tolerated when doses remain within the range of 300 to 600 mg/day (13,14). Higher doses of 1200 to 1800 mg/day are associated with increased adverse effects such as nausea, vomiting and vertigo without a significantly higher rate of efficacy (13,14). A daily dose of 600 mg appears to have the most favourable benefit-to-risk ratio (13,14). ALA has no major drug interactions; however, it may decrease the effectiveness of chemotherapy and levothyroxine, so caution is warranted (15,16). Theoretically, ALA can cause additive hypoglycemic effects with other hypoglycemic agents; however, evidence to date does not support such an interaction (17).

Chromium

What is it?

Chromium is a mineral that is required by the body in small amounts (18). Dietary sources of chromium include grass-fed beef, free range eggs, oats and sweet potatoes (18).

How does it work?

Chromium is essential to various metabolic processes that intricately regulate blood sugar by assisting insulin transport of glucose into somatic cells (19,20). Both chromium picolinate and chromium glucose tolerance factor have shown benefit in the

treatment of diabetes, namely when there is a documented chromium deficiency or when diabetes is poorly controlled (19,20). Without a chromium deficiency, the benefit of chromium in diabetes treatment is unclear, but a systematic review suggests that it may decrease glycated hemoglobin (A1C) by 0.6% and fasting blood glucose by up to 1 mmol/L (21). Although the recommended dose of chromium is the same for both the picolinate and glucose tolerance factor varieties, glucose tolerance factor is more bioavailable and thus should be the favoured choice at 100 to 500 µg twice daily (22).

Is it safe?

Caution is warranted for patients with a history of renal disease or poor renal function because any amount of chromium beyond the adequate intake of 50 to 200 µg/day may result in damage to the kidneys (23). Chromium may increase insulin sensitivity when used concurrently (24) and may bind levothyroxine in the digestive tract, thereby reducing its effectiveness by approximately 20% (25).

Magnesium

What is it?

Magnesium is one of the most important electrolytes in the human body, involved in more than 300 enzymatic reactions that are essential to daily life (26). Common dietary sources of magnesium include seaweed, green leafy vegetables, legumes and nuts (26).

How does it work?

A deficit in magnesium negatively affects insulin signalling, the action of insulin at its receptor sites, and reduces the uptake of glucose from the bloodstream into cells (26). An increased prevalence of magnesium deficiency has been noted in patients with diabetes who have poorly controlled glycemic profiles and those with a longer duration of the disease, as well as those who are displaying chronic microvascular complications (27). Magnesium is one of the most bioavailable and absorbable form of magnesium (28,29) and is, therefore, what is recommended for patients with diabetes at a dose of 300 to 600 mg daily.

Is it safe?

Magnesium bisglycinate is the safest option for correcting a long-term deficiency, such as that seen in some patients with diabetes, and is less likely to induce diarrhea or loose stools than magnesium oxide, which is poorer in quality and bioavailability but more commonly sold in pharmacies (28,29). Magnesium interacts with many drugs, including potassium-sparing diuretics (30), certain antibiotics (31,32) and bisphosphonates (33); caution is warranted to prevent and monitor for such interactions.

Herbs

Bitter melon (Momordica charantia)

What is it?

Bitter melon is a tropical, fruiting plant that has historical medicinal use in Asia, South America, India and East Africa (34).

How does it work?

The active constituents responsible for producing its antidiabetic effects are triterpenes, proteids, steroids, alkaloids, lipids and phenolic compounds—all of which can be extracted from the fruit, seeds and leaves (34). Bitter melon contains Polypeptide-p, an insulin-like plant protein that has been shown to lower blood glucose levels in humans with type 1 diabetes when injected

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