Patients with diabetes are not alone in their increasing interest in using herbal preparations and nutritional supplements. The use of these products has increased exponentially over the past 10 years. The plethora of information available through sources, such as the Internet, may be conflicting and confusing for the consumer and health-care provider. It is a challenge for physicians and other health-care professionals to be aware of the products being used to help improve the symptoms experienced by patients with diabetes. It is also difficult to help educate the patient regarding the benefits and/or potential risks of these products. The steps in the decision-making process physicians may need to work through with patients are outlined in Table 1.
Assessment of the Patient's Motivation

Patients with chronic conditions, such as diabetes, may be frustrated with poor control of symptoms, and are searching for an easy solution to their discomfort. The increased interest in alternative therapies often stems from a general misperception that a natural source product, such as a herbal preparation or a nutritional supplement, is relatively safe and free of side effects, compared to its prescription counterpart. This highlights the important role of family physicians in educating and informing patients of the risks and benefits of these products.

The concept of cultural relativism is important to understand. A patient’s family background or culture may have a strong influence on his/her decision to use a herbal or nutritional supplement.

We need to acknowledge that these products may have therapeutic merit, either pharmacologically, or because of a culture-based belief system, despite a lack of evidence to support their use. A naïve acceptance that these products are clinically benign, however, denies our professional responsibility as health-care providers, to fully inform the patient.

An additional patient motivator is the simple desire for autonomy and the ability to have some input into the decisions regarding their own health care.

Assessment of Product Source

Government regulation of herbal products and nutritional supplements has developed slowly over the past 15 years. Traditionally, all products in the current Canadian health-care market were classified either as foods or drugs.

The current regulation, Schedule A (to the Food and Drugs Act), prohibits any claims regarding prevention, treatment or cure of the 46 listed conditions.

Summary

**Nutritional Supplements and Herbal Medicine in Diabetes**

- Government regulation of herbal products and nutritional supplements has developed slowly over the past 15 years. Traditionally, all products in the current Canadian health-care market were classified either as foods or drugs.
- An ongoing review of the primary literature is important to maintain an up-to-date perspective on the efficacy of natural health products. This includes databases, such as MEDLINE, Embase and the Cochrane Database of Systematic Reviews.
- Current data do not support routine supplementation of chromium in patients with diabetes. Vanadium is currently not recommended as a supplement for individuals with diabetes, because a safe dose to produce the desired therapeutic effect is not yet known. There is no evidence demonstrating toxicity of vitamin E, even at high doses of 3,200 IU daily for several months, although the effects of such doses on other nutrients in the body are unknown. Current data also do not support routine supplementation of vitamin E in diabetics.
- It is important to consider the benefit patients may receive through the autonomy they feel by making the decision to self-medicate. Ensuring that the patient has an opportunity for follow-up with the physician or another member of the health-care team will help monitor for changes in blood sugar control and screen for adverse effects.
including diabetes. As a result of this legislation, there are many products on the market that do not have adequate labeling to provide the consumer with direction regarding indications for use and dosage. There is a high risk that patients may misuse products, and a corresponding high potential for adverse effects.

More recently, the 1999 report of the Canadian Standing Committee on Health recommended the establishment of an Office of Natural Health Products (ONHP). An expert advisory committee to the ONHP has been given a mandate to set the course for the regulation of natural health products in a separate category from drugs and foods. This mandate includes the development of standard monographs for each product, so that they may reach the market with evidence supporting safety and risks for adverse effects, without having to meet the rigorous Health Protection Branch (HPB) requirements for designation as a drug.

An assessment of product source is also important to address problems, such as identification

Table 1

**Decision Making Steps Regarding the Use of Nutritional Supplements and Herbal Products in Diabetes**

- Assessment of the patient's motivation (understanding the patient's perspective).
- Assessment of the product source (understanding government regulation).
- Review of the evidence in the literature (knowing and using well-referenced drug information resources).
- Risk/benefit assessment (evidence of adverse effects).
- Consider the impact of other medical conditions, current medical therapy and over-the-counter (OTC) product use.
- Confirm access to health-care professional for follow-up and monitoring.
and product consistency. Herbs, in particular, may have many common names, which make it difficult for consumers to ensure they are purchasing the correct product. Herbal products and nutritional supplements may be purchased in many locations, including pharmacies, health food stores, herbal shops and grocery stores, in addition to their availability through mail order supply via the Internet and door-to-door flyers. The lack of regulation raises several concerns. Lack of product standardization and inadequate labeling means that the concentration of the active ingredient from batch to batch cannot be guaranteed. For those products that do exert a pharmacologic action, the inconsistency in daily dosage may adversely affect blood sugar control and put patients at risk of hypoglycemic episodes.

Some products on the Canadian market have a Drug Identification Number (DIN) displayed on the package. The DIN number, at a minimum, assures that the product has met the Canadian Goods Manufacturing process and contains a set amount of active ingredient from which a dose can be determined. In addition, an independent research lab, Consumer Lab, has developed out of consumers’ and health-care professionals’ growing need for an independent evaluation of health and nutritional products on the market. This organization may aid in distinguishing products that meet recognized standards of quality.

Individuals with diabetes may be at risk of excessive oxygen radical production from the auto-oxidation of glucose and hyperketonemia.

Review of Evidence and Efficacy

An ongoing review of the primary literature is important to maintain an up-to-date perspective on the efficacy of natural health products. This includes databases, such as MEDLINE, Embase and the Cochrane Database of Systematic Reviews. A summary of some of the most common nutritional supplements and herbal products used by patients with diabetes is found in Tables 2 and 3 respectively.

It is also important for physicians to be aware of the information that is available to patients from such sources as the Internet. The amount of misinformation available on the Web, and the risk for misunderstanding by the consumer, highlights the importance of the role of the physician in educating patients.

Nutritional Supplements

Chromium. Chromium is an essential trace mineral, and, next to calcium, it is the second most frequently purchased nutritional supplement. The proposed mechanism of action involves chromium linking with a low-molecular-weight chromium-binding substance to increase insulin sensitivity at receptor sites. The product form of chromium is an important consideration. Trivalent chromium is the biologically active form of chromium and is linked with ligands and salts to improve bioavailability. Chromium chloride appears to be less effective than the polynicotinate and the picolinate salts.

Human trials have suggested that chromium supplementation may have therapeutic benefit for individuals with Type 2 diabetes, glucose intolerance and gestational diabetes. These data provide some evidence for chromium efficacy through reductions in fasting and two-hour glucose and insulin levels, improvement in hemoglobin A1c serum concentrations, improved glucose tolerance, reversal of ele-
## Table 2
### Nutritional Supplements Used in Diabetes

<table>
<thead>
<tr>
<th>Supplement</th>
<th>Rating</th>
<th>Mechanism</th>
<th>Adverse Effects/Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trace Elements</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chromium picolinate</td>
<td>E1(+-)</td>
<td>Mechanism of action at molecular level unknown. Possibly promotes insulin-receptor complex. Improves glucose tolerance.</td>
<td>Case reports: Contact dermatitis, Renal failure.</td>
</tr>
<tr>
<td>Magnesium</td>
<td>E2</td>
<td>Deficiency worsens blood sugar control in Type 2 diabetes.</td>
<td>None reported.</td>
</tr>
<tr>
<td>Vanadium</td>
<td>E3(-)</td>
<td>Possible increase in insulin sensitivity. Decreased insulin requirements.</td>
<td>Cellular damage to DNA, blockage of protein synthesis, May increase oxidative stress.</td>
</tr>
<tr>
<td>Zinc</td>
<td>E2, E3</td>
<td>Zinc deficient state impairs synthesis and secretion of insulin.</td>
<td>Vomiting, diarrhea. Interferes with copper metabolism.</td>
</tr>
<tr>
<td><strong>Antioxidants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alpha lipoic-acid</td>
<td>E1(+-)</td>
<td>Antioxidant. Inhibits lipid peroxidation of nerve membranes.</td>
<td>None reported.</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>E1(+-)</td>
<td>Improves endothelial vasodilator function.</td>
<td>None reported.</td>
</tr>
</tbody>
</table>

**Evidence-Based Rating Legend:**

- **E1** Randomized Control Trials (RCTs) supporting efficacy
- **E2** RCTs but poor study design/small numbers/equivocal results.
- **E3** Non-RCTs/Human case reports.
- **E4** Animal studies suggesting therapeutic benefit.
- **E4** Historical/anecdotal use.
### Table 3
Herbal Medicine Used in Common Conditions in Diabetes

<table>
<thead>
<tr>
<th>Herb</th>
<th>Rating</th>
<th>Mechanism</th>
<th>Adverse Effects /Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood Sugar Control</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>American ginseng (Panax quinquefolium)</td>
<td>E1 (+/-)</td>
<td>Reduction in postprandial glycemia.</td>
<td>None reported.</td>
</tr>
<tr>
<td>Asian ginseng (Panax ginseng)</td>
<td>E1 (+/-)</td>
<td></td>
<td>Changes INR with warfarin treatment.</td>
</tr>
<tr>
<td>Alfalfa</td>
<td>E3</td>
<td>Dietary fibre.</td>
<td>None reported.</td>
</tr>
<tr>
<td>Gymnema (Gymnema sylvestre)</td>
<td>E2</td>
<td>Blood glucose-lowering activity unknown. Inhibits ability to taste sweet compounds.</td>
<td>Hypoglycemia.</td>
</tr>
<tr>
<td>Guar gum (Cyamopsis tetragonolobus)</td>
<td>E2, E3</td>
<td>Delayed absorption of glucose from intestine.</td>
<td></td>
</tr>
<tr>
<td>Bitter melon (Momordica charantia)</td>
<td>E2, E3</td>
<td>Hypoglycins deplete liver glycogen.</td>
<td>Vomiting sickness causing death.</td>
</tr>
<tr>
<td>Ackee Fruit (Blighia sapida)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hawthorn (Crataegus sp.)</td>
<td>E2, E3</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hyperlipidemia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Garlic (Allium sativum)</td>
<td>E1 (+/-)</td>
<td>Unknown.</td>
<td></td>
</tr>
</tbody>
</table>
vated insulin and glucagon blood levels and the reduction in the requirement of oral hypoglycemic medications. Doses studied ranged from 200 mcg daily to 1,000 mcg daily. Researchers have questioned the ability to reproduce these encouraging study results in a North American population. The inability to accurately measure chromium status in the body makes it difficult to determine if the beneficial effects of chromium are due to replacement of a chromium deficit or to the pharmacologic nature of the supplement itself. Trivalent chromium is reportedly free of toxicity, even at extremely high doses. Current data do not support routine supplementation of chromium in patients with diabetes.

### Table 3 Cont’d

<table>
<thead>
<tr>
<th><strong>Herb</strong></th>
<th><strong>Herb Rating</strong></th>
<th><strong>Mechanism</strong></th>
<th><strong>Adverse Effects/Interactions</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neuropathy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Neuralgia (assoc. with Neuropathy)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cayenne pepper (Capsaicin)</td>
<td>E1 (+/-)</td>
<td>Depletion of substance P from nociceptors.</td>
<td>Burning sensation initially. Concern with use on extremities.</td>
</tr>
<tr>
<td><strong>Intermittent Claudication</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Urinary Tract Infection</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Evidence Based Rating Legend:**

- E1 Randomized Control Trials (RCTs) supporting efficacy RCTs, but poor study design/small numbers/equivocal results.
- E2 non-RCTs/human case reports.
- E3 Animal studies suggesting therapeutic benefit.
- E4 Historical/anecdotal use.
Vanadium (vanadyl sulfate). Vanadium is another trace element that has been shown to have a blood-glucose-lowering effect. Whether vanadium’s mechanism of action is insulin mimetic, or if it increases insulin sensitivity, has yet to be determined. Small, non-randomized studies in humans have shown promising results in Type 2 diabetes, but no effect in Type 1 individuals, suggesting that the glucose-lowering effect is dependent on the presence of endogenous insulin. At a dose of 1mg/kg/day, the small sample of human studies report gastrointestinal upset as the only observed adverse effect. In vitro studies, however, have demonstrated toxicity at the cellular level, due to the blockage of protein synthesis. Vanadium currently is not recommended as a supplement for individuals with diabetes, because a safe dose to produce the desired therapeutic effect has not yet been determined.

Antioxidants. There is increased interest in oxidative stress and the role it may play in the development of long-term complications of diabetes, such as neuropathy, retinopathy, nephropathy and micro and macroangiopathy. Individuals with diabetes may be at risk of excessive oxygen radical production from the auto-oxidation of glucose and hyperketonemia. In addition, they may have a decreased oxidation defense capacity, due to glycation of antioxidative enzymes.

Alpha-lipoic acid (thioctic acid). Alpha-lipoic acid is classified as an aqueous scavenger antioxidant. It is often used in the self-treatment of diabetic neuropathy. At the cellular level, in animal and human studies, there is evidence that alpha-lipoic acid improves oxidative stress, even in the presence of poor glycemic control. Its mechanism of action includes inhibition of lipid peroxidation of nerve membranes and improvement in nerve conduction rates. Alpha-lipoic acid has been studied in doses of 600 mg orally three times daily. No adverse effects have been reported. The series of Alpha-lipoic Acid in Diabetic Neuropathy (ALADIN) II studies have shown a strong trend towards efficacy by measuring outcomes of neurological deficit through nerve conduction tests and perception to touch and pain. Outcomes using a patient reported symptomatic scale, however, have failed to show improvement in pain, burning and numbness. Further study is required to confirm these findings. Current data do not support routine supplementation of alpha-lipoic acid in patients with diabetes.

Vitamin E. Vitamin E is classified as a lipid scavenger antioxidant. Studies in diabetic animals provide support for the use of vitamin E to reduce the level of oxidative stress and to slow or prevent the long-term complications of diabetes. Research conducted on individuals with diabetes has shown various results to date. Some studies have examined the blood levels of biochemical markers of oxidative stress, such as lipid peroxides, and the oxidative susceptibility of low density lipoprotein (LDL), showing significant improvements. Other studies, however, were inconclusive or had conflicting results. The influence of vitamin E supplementation on factors, such as glycated hemoglobin and triglyceride levels, also has been evaluated, but further studies are required. Recent small trials investigating biophysical parameters, such as improvement of retinal blood flow, show promis-
ing results. Doses of vitamin E studied range from moderate doses of 100 international units (IU) to 3,200 IU daily. There is no evidence demonstrating toxicity of vitamin E, even at high doses of 3,200 IU daily for several months, although the effects of such doses on other nutrients in the body are unknown. Current data do not support routine supplementation use of vitamin E for patients with diabetes.

**Herbal Medicine**

**Gymnema sylvestre (GS4).** Gymnema sylvestre is a herbal preparation that has been used for years in East Indian culture, and has its roots in Ayurvedic medicine. *In vitro* studies on animal beta cells demonstrate a stimulation of insulin release by an increase in cell permeability. Small, non-randomized studies in humans suggest an anti-hyperglycemic effect. Doses of 400 mg daily have been studied with no reports of toxicity. The risk of hypoglycemia, however, should be acknowledged, especially in patients using other therapy to control blood sugar. Randomized controlled trials need to be conducted to further identify its therapeutic effect and determine a safe and effective dose. The routine use of gymnema to help control blood sugar cannot be recommended at this time.

**Ginkgo biloba.** Although ginkgo biloba is actually a tree, the leaf extract has been grouped with other herbs that have a potential pharmacological action derived from a plant source. Researchers have isolated specific terpenes, called ginkgolides, that have been shown in animal models to inhibit the platelet-activating factor, improve blood flow and decrease vascular resistance. These effects have encouraged its use in diabetes for the self-treatment of symptoms, due to peripheral vascular disease, including intermittent claudication and retinopathy.

The majority of research studies to date examine the effects of Ginkgo on cerebral insufficiency and Alzheimer’s Disease. The few randomized controlled trials that have investigated its use in peripheral vascular disease have shown promise. The clinical outcomes measured showed improvement in the distance patients walked before the onset of pain, as well as the total distance walked. The studies, however, were criticized for poor methodology. Study participants were smokers prior to the study and stopped for the duration of the study, which may have influenced the beneficial outcomes.

The usual dose studied was 40 mg three times daily. The product has received approval for marketing as a drug in Europe. Adverse effects are mild and include headache, gastrointestinal upset and allergic reactions. Current data do not support routine supplementation of Ginkgo biloba in patients with diabetes.

**Garlic (allium sativum).** Individuals with diabetes have an increased risk of cardiovascular complications, such as atherosclerosis. Garlic has been used for many years because of its suspected beneficial effects on blood pressure, cholesterol, triglyceride levels and platelet aggregation. It is believed that the active constituent of garlic is allicin and its derivatives. It is important to recognize that allicin is enzymatically converted from the amino acid allinin when fresh garlic is crushed or chewed. Commercial preparations of dried garlic need to be enteric-coated to pass into the bowel in order for the enzymatic conversion to occur. Products on the market may fluctuate in their yield of allicin.

Research in human populations have produced conflicting results. More tightly controlled studies are required to determine garlic’s efficacy in atherosclerosis.

There are few adverse effects reported from the use of garlic. Because it has been shown to possess anti-platelet activity, caution is advised if there is concurrent use with a blood thinner, such as warfarin. A small percentage of individuals
Alternative Therapies in Diabetes

have experienced gastrointestinal discomfort, such as heartburn and flatulence, in addition to the expected garlic odor on the breath and body. The routine use of garlic for cardiovascular benefits in diabetes cannot be recommended at this time.

Ginseng. Ginseng products and their proposed use for symptomatic relief in diabetes continue to confuse consumers and health-care professionals. Two ginseng preparations have been studied in patients with diabetes. The mechanism of action is not yet clearly identified, however, it is suspected that the active components are steroidal saponins called ginsenosides. These compounds appear to have an effect on many different receptors at the cellular level.

American ginseng (Panax quinquefolium). Small, randomized trials in individuals with Type 2 diabetes have shown promise. Vuksan et al demonstrated a reduction in postprandial glycemia compared to controls. American ginseng doses of 3 g before meals have been studied, however, this glucose-lowering effect does not appear to be dose-related. Adverse effects have not been reported.

Asiatic ginseng (Panax ginseng). One small trial in humans showed an improvement in fasting blood glucose and Hb A1C after using doses on 100 mg to 200 mg daily. In vitro studies have shown an effect on platelet aggregation, therefore, its use in patients taking blood thinners, such as warfarin, is of concern.

The routine use of any type of ginseng for diabetic symptoms cannot be recommended at this time.

Fenugreek (Trigonella foenum graecum). Fenugreek seeds have long been known in traditional medicine to have a glucose-lowering effect. Animal studies have shown promising results in a Type 2 diabetes model demonstrating a decrease in postprandial glucose and plasma glucagon. These beneficial effects have been attributed to the high fiber content of fenugreek seeds (54%). More recently, the amino acid 4-hydroxyisoleucine has been isolated from fenugreek seeds and shown, in vitro, to increase glucose-induced insulin release from islets of Langerhans. A therapeutic dose of fenugreek has not yet been determined. Adverse effects reported in the human studies to date include gastrointestinal symptoms, such as diarrhea and gas. Cases of gastroenteritis and hypoglycemia also have been reported. Due to the lack of data supporting a therapeutic dose and the subsequent risk of adversely influencing blood glu-

The concept of cultural relativism is important to understand. A patient’s family background or culture may have a strong influence on his/her decision to use a herb or nutritional supplement.

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Cose control, the routine use of fenugreek cannot be recommended at this time.

Patient Follow-Up

Although there may be insufficient research to confirm efficacy of these products from the western medical model perspective, patients may still choose to self-medicate with nutritional supplements and herbs. This situation poses a challenge for health-care providers who follow evidence-based decision-making.

It is important to consider the benefit patients may receive through the autonomy they feel by making the decision to self-medicate. There may be an improvement in overall compliance with a diabetes health regimen, or an increased motivation to work on improving lifestyle choices to benefit diabetes.

It is important to ensure the patient has an opportunity for follow-up with the physician, or another member of the health-care team, in order to monitor for changes in blood sugar control and to screen for adverse effects from these products.

Conclusion

The role of the physician is to educate patients, in order that they may make informed decisions regarding the use of nutritional supplements and herbal products. This is very important. Open communication with patients in a nonjudgmental fashion will help increase the awareness of the physician regarding the types of products used by patients, and facilitate appropriate monitoring. This effort will help minimize the risk of adverse effects due to the concomitant use of herbs and nutritional supplements with a patient’s current diabetes therapy.

References