Natural Approaches to the Prevention and Management of Diabetes Mellitus

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According to facts and figures provided by the American Diabetes Association, there are an estimated 15.7 million people in the United States with diabetes. Approximately 5.4 million of these people have not yet been diagnosed.[1] The hyperglycemia resulting from types I and II diabetes mellitus can lead to multiple challenges for the person with diabetes. Patients who are struggling to compensate for a lack of insulin secretion and/or a lack of insulin efficiency face possible complications, such as retinopathy, nephropathy, neuropathy, and atherosclerosis. At the core of preventing and dealing with diabetes mellitus is an understanding of how the body regulates the metabolism of its principal energy source, glucose, and how specific nutrients, diet modifications, and supportive botanical medicines can be utilized to optimize glucose metabolism.

Specific Nutrients for Glucose Metabolism

Chromium

Trivalent chromium is one of the most studied nutrients in glucose metabolism. In one study that highlights the need for chromium supplementation in patients with type II diabetes, researchers compared fasting blood and second-morning urine samples between 93 patients with type II diabetes and 33 healthy controls. The researchers found that mean serum chromium levels were approximately 33 percent lower and urine levels were almost 100 percent higher in the patients with diabetes versus the controls.[2] In addition, while subjects who did not have diabetes showed a negative correlation between fasting levels of plasma chromium and insulin, no such correlation existed in the subjects with diabetes. Moreover, the authors noted, based on their work over several years, that, in the early stages of diabetes, an inverse relationship between plasma chromium and glucose levels has been observed, which disappears after 2 years. The authors suggested that chromium loss over years may worsen an already existing chromium deficiency in patients with type II diabetes and contribute to their insulin resistance.

In a recent review,[3] more than a dozen clinical trials in patients with type II diabetes have shown positive results from supplementation with chromium. The multiple benefits reported include improved fasting glucose, improved glucose tolerance, decreased insulin levels 60 minutes after eating, decreased glycosylated hemoglobin levels, and an increase in high-density lipoprotein (HDL). These metabolic improvements seem to be caused by several mechanisms, including an increase in the number of insulin receptors in insulin-dependent cells, such as adipocytes and hepatocytes, and an increase in phosphorylation of the insulin receptor, which results in increased sensitivity of receptors to insulin.

With regard to this second mechanism of action, an increased phosphorylation of insulin receptors, there is now some elucidation of how chromium might act at a very basic molecular level. According to one recently proposed model,[4] four chromium ions are needed to bind to a low–molecular-weight oligopeptide so that the resulting complex of the oligopeptide and chromium can assume the correct geometrical shape needed to bind to the phosphorylating portion of the insulin receptor. A potentially important suggestion made in this model is that, in order for the bioactive form of chromium picolinate to release its chromium ion to enter a cell, the chromium must first undergo a reduction reaction, which may generate hydroxyl radicals. Perhaps, in the future, it will be most efficient to give patients who take chromium adjuvant antioxidant support.

While there are occasional studies that do not report benefits of chromium supplementation in glucose metabolism,[5] these studies typically use a dose of chromium that is less than 200 µg/day or use a form of chromium, such as chromium chloride, which seems not to be as bioavailable as chromium picolinate. A reasonable dosage range for chromium supplementation, suggested in the literature, would be 200–1000 µg/day, with greater benefit expected from the dose larger dose. It is also important to educate patients about research demonstrating that simple sugar consumption increases the amount of chromium excreted in the urine.[6]

Some patients with newly diagnosed type I diabetes have experienced complete reversal of their diabetes with niacinamide.

Vanadium

Vanadium, which is positioned next to chromium as a transition metal on the periodic table, has also been studied for its effects on glucose metabolism. In one recently published study of subjects who received 150 mg per day or 300 mg per day of vanadyl sulfate for 6 weeks, there was improvement in three of five subjects who received 150 mg and in four of eight of the subjects who received 300 mg.[7] Reductions in fasting glucose and glycosylated hemoglobin were enough to be significant, although not dramatically so. In addition, this work demonstrated that, in skeletal muscle, vanadium also appears to modulate the number of insulin receptors and their phosphorylation. Two other small studies also demonstrated improvement in glycemic control using only 100 mg/day* of vanadyl sulfate for 3 or 4 weeks, and, in both studies, the improvement in blood glucose control continued for periods of 2 or 4 weeks after supplementation had ended.[8,9] It is important to note that that even the lower doses of vanadyl sulfate (100 mg per day) caused some gastrointestinal intolerance (see chart entitled Key Nutrients for Controlling Glucose Metabolism.

A different, organic form of vanadium, bis(maltolato)oxovanadium (BMOV), has also been shown to be effective in lowering glucose levels, at least in rat models. The dosage of BMOV needed, however, to lower glucose levels effectively, was only half of the dose of vanadyl sulfate required to obtain the same effect.

B Vitamins

The water-soluble B vitamins are required cofactors for many of the enzymes required for metabolizing glucose via glycolysis and the Kreb's cycle, and a growing body of literature suggests their importance in diabetes. For example, in the case of vitamin B_6, a study of the serum levels of 518 patients with diabetes revealed that pyridoxal levels were significantly lower compared to levels in 371 controls, with 25 percent of the patients with diabetes having levels below the lower limit of the normal range.[10] In another study comparing 50 patients with diabetic neuropathy to patients with diabetes but without without neuropathy, serum pyridoxal levels were significantly lower in the patients with diabetic neuropathy.[11]

There are also several studies demonstrating the clinical effects of B vitamins supplementation on diabetes. One study of 24 patients with diabetic neuropathy utilized a treatment with a complex of vitamins B_6, B_{12}, and a form of B_1 modified to be more lipid soluble. After 12 weeks, there was significant improvement in the nerve conduction velocity of the peroneal nerve and a trend toward improvement in the threshold level of vibration perception.[12]

One informative study of a B vitamin in diabetes research was done some years ago by researchers who took a small group of patients with type I diabetes off insulin treatment and gave them either 16 mg/day of biotin or a placebo.[13] Compared to the control group, the mean blood glucose level of the biotin-treated group was significantly lower after 1 week of treatment (126 mg per dL in the biotin group versus 266 mg per dL in the control group). In examining the levels of tissue biotin compared to plasma biotin among patients with type I diabetes and controls without diabetes, it was found that an increasing ratio of tissue biotin to plasma biotin was associated with increasing fasting blood sugar levels in the subjects with diabetes, but not in subjects without the disorder. Perhaps future work will help to confirm that biotin can control blood glucose levels and elucidate the differences in how biotin is utilized in people with or without diabetes.

Niacinamide is also worth specific mention because it has been shown to help prevent type I diabetes in laboratory animals. These observations have been noted in at least ten clinical trials of which six were double-blinded. These studies involved patients with type I diabetes who had been diagnosed with the disorder 5 years or less prior to the study. Of the positive studies, some patients with newly diagnosed type I diabetes have experienced complete reversal of their diabetes with niaci-

*See box entitled Key Nutrients for Controlling Glucose Metabolism.

There is research showing that magnesium levels tend to be low in subjects with diabetes and that 3 months of supplementation is adequate for reversing the problem.

Select Botanical Considerations for Treating Diabetes

Herb	Amount	Notes
Bitter melon *(Momordica charantia)*	15–50 g per day	Start low and work up to higher doses.
Fenugreek (*Trigonella foenumgracum*)	15–50 g per day	Administer in divided doses.
Gymnema (*Gymnema sylvestre*)	400 mg of extract	Monitor glucose levels closely.
Corosolic acid (*Lagerstroemia speciosa*)	32–48 mg	Adjustment of medicines often needs close attention.
Pterocarpus (*Pterocarpus marsupium*)	Varied	Dose varies depending widely depending upon extraction process.

namide. Other positive findings included prolonged remissions, lower insulin requirements, increased beta-cell function, and enhanced metabolic control.[14,15]

Caveat

Whenever supplementation with nutrients that are key to glucose metabolism is undertaken with the objective of reducing hyperglycemia significantly, it is important to monitor blood glucose levels adequately in order to avoid severe hypoglycemia during treatment. See box entitled Key Nutrients for Controlling Glucose Metabolism for more detailed caveats.

Dietary Interventions in Diabetes Mellitus

Dietary modifications can be a powerful tool for preventing and treating diabetes. If, for example, a clinician is treating a patient who is at a high risk of developing type II diabetes before symptoms of hyperinsulinemia and/or hyperglycemia become acute, this is an excellent opportunity to emphasize the potential benefit of cereal fiber. In a large prospective study of 65,173 females over 6 years, researchers looked for associations between the glycemic index of subjects' diets and their risk of developing type II diabetes.[16] A glycemic index is an indication of a food's potential to raise blood glucose and the demand the food creates for insulin. Foods with a high glycemic index generally include items such as white bread, mashed potatoes, white rice, and cola beverages. More intermediate-range glycemic foods are items such as apples and orange juice. Low-glycemic foods are generally those that maintain their natural unprocessed fibers, such as broccoli and peanut butter.

In this prospective study, women in the quintile with the highest average glycemic index had a significantly higher risk of developing type II diabetes (Relative risk [RR], 0.72; confidence interval [CI], 0.58–0.90; $P = 0.001$) compared to women with the lowest average glycemic index. One of the strongest associations for an individual food type was seen in the analysis of cereal fiber intakes and the risk for developing diabetes. Women in the study quintile with the highest median cereal fiber intake (7.5 g/day) had an RR of 0.72 (CI, 0.58–0.90; $P = 0.001$) of developing type II diabetes compared to the women in the quintile with the lowest median intake of cereal fiber (2.0 g/day). In contrast, women with a diet characterized by a high glycemic load and a low cereal fiber intake had an RR of 2.50 (CI, 1.14–5.51) for developing type II diabetes compared to women eating a diet with a low glycemic load and high cereal fiber. Results from the same research team following a sample of more than 42,000 men prospectively were similar.[17]

An additional association in this work that was significant was the risk of diabetes and magnesium intake. In the women's study, subjects with a median intake of 338 mg/day had an RR of 0.62 (CI, 0.58–0.90; $P < 0.001$) compared to women with a median intake of 222 mg/day. This is especially important to keep in mind because a lack of sufficient magnesium is so easily remedied by magnesium supplementation. In fact, although supplementation did not seem to improve glycemic control in subjects who were already diagnosed with type II diabetes, there is research showing that magnesium levels tend to be low in

Substituting soy for animal protein might protect patients who have diabetes from nephropathy.

subjects with diabetes and that 3 months of supplementation is adequate for reversing the problem.[18]

One form of fiber that may be particularly useful for treating patients once they are diagnosed with either type I or type II diabetes is the fiber from legumes. In one study of 9 patients with type I diabetes and 18 with type II diabetes, subjects were placed for 6 weeks on a high carbohydrate diet that was rich in legumes and then also a low-carbohydrate diet for 6 weeks.[19] In subjects with diabetes of either types, the mean preprandial and 2-hour postprandial blood glucose levels were significantly lower when the subjects were on the diet that was rich in legumes. The amount of glucose passed in the subjects' urine was also significantly less when they were on the high-legume diet.

An additional consideration in the diet of patients with diabetes is the amount of protein they consume in relation to the health of their kidneys. One commonly referred to hypothesis suggests that too much protein intake causes hyperfiltration and glomerular hypertension, which leads to reduced kidney function and eventual nephropathy in some patients with diabetes.[20] Clinical data that seem to support this hypothesis come from trials that have utilized limited protein intake and have shown subsequent, significant drops in glomerular filtration rate (GFR) and/or the amount of albumin excretion in subjects with diabetes.[21,22]

The complete relationship between protein consumption and kidney health in patients who have diabetes is a complex one and is beyond the scope of this article. One interesting hypothesis, however, is that, while some forms of protein, especially beef, increase postprandial renal plasma flow and GFR, soy does not seem to alter postprandial renal function, suggesting that substituting soy for animal protein might protect patients who have diabetes from nephropathy.[23] Unfortunately, a small pilot study designed to test this hypothesis, in which 8 men with type II diabetes replaced half of their protein intake with soy protein, failed to show reduction in proteinuria. However, the study is important because it helps us to consider the concept that effects of protein intake on kidney health in patients with diabetes may be dependent on the type of protein being consumed. While we are still a long way from understanding the perfect diet for patients with diabetes, understanding which types of proteins will spare kidney

Key Nutrients for Controlling Glucose Metabolism

Supplement	Dosage	Notes
Chromium (as picolinate)	200–1000 µg/day of actual chromium	Response time varies from <10 days to >3 months.
Vanadium (as sulfate)	150 µg–50+ mg per day of combined vanadium–sulfate salt	Watch closely for signs of GI intolerance. Smaller doses in µg noted here because these doses are often helpful. If using larger doses (in mg as cited in the text), monitor intake very closely; may also require concurrent supplementation with coenzyme Q10.
Niacinamide (vitamin B_3)	25 mg/kg	Monitor liver enzymes and glucose levels.
Vitamin B complex (including B_1, B_6, and B_{12})	100-mg complex	Taken with food to lessen GI upset.
Manganese	10–30 mg/day	Gradual dosing is recommended.
Magnesium (aspartate/citrate)	350–500 mg/day	Divided doses may be necessary if loose stool occurs.
Biotin	16 mg/day	Conduct a trial of 1 week while monitoring blood glucose levels closely.

GI = gastrointestinal.

Five of 22 study subjects were able to discontinue their use of conventional medications and manage their conditions solely with a gymnema extract.

function most effectively, and thus delay the onset of nephropathy, could certainly be a fruitful field for future research.

Botanicals for Diabetes

The many botanicals useful in the treatment of diabetes could themselves occupy a lengthy review. Here a few are discussed briefly.

Pterocarpus

Rich in the flavanoid (-)-epicatechin, pterocarpus (*Pterocarpus marsupium*), an Ayurvedic herb, may be helpful for patients with both type I and type II diabetes. In an animal study, rats whose beta-islet cells were first destroyed with the toxin alloxan and then given large intravenous doses of (-)-epicatechin experienced a return of normal blood glucose levels.[24] Histologic examination of pancreas samples showed regeneration of the beta-islet cells. In a human trial in India, among subjects who had been recently diagnosed with type II diabetes, 67 of 97 patients studied were able to control blood glucose levels (measured both for fasting and postprandial levels) after 12 weeks of treatment. Doses needed for control ranged between 2–4 g of extract and there were no side-effects reported.[25]

Fenugreek

In a study of patients with type I diabetes given 50 g of defatted fenugreek (*Trigonella foenumgracum*) seed powder with both lunch and dinner for 10 days, there was a 54 percent decrease in 24-hour urine glucose excretion. Other benefits from this high source of fiber included decreases in total serum cholesterol, low-density lipoprotein, and very–low-density cholesterol and triglycerides, while levels of HDL remained unchanged.[26]

Bitter Melon

In a small study of nine patients with type II diabetes, a simple water extract of the fruit of bitter melon *(Momordica charantia)* was enough to lower blood glucose levels significantly during a 50-g oral glucose tolerance test. This improvement was not associated with an increase in serum insulin.[27]

Gymnema

A simple water extract from the leaf of gymnema (*Gymnema sylvestre*) may hold promise for patients who have either type I or type II diabetes. Twenty-seven subjects with type I diabetes who received 400 mg of such an extract per day showed a reduction in the need for insulin as well as decreases in fasting blood glucose and glycosylated hemoglobin and glycosylated plasma protein levels.[28] When a water extract was given to 22 patients with type II diabetes for 18–20 months, there were, again, significant decreases in the same biomarkers used in the study with patients who have type I diabetes.[29] One promising aspect of the study with subjects who have type II diabetes is that the extract was given safely in conjunction with other conventional medications that the subjects were already using. Five of the 22 subjects were able to discontinue their use of conventional medications and manage their conditions solely with the gymnema extract. What is more, the reduction of insulin needs in the type I diabetes study combined with an observation of higher insulin levels in the type II diabetes study suggest that this extract is stimulating or even regenerating for beta-islet cells.

Corosolic Acid

Corosolic acid (*Lagerstroemia speciosa*), a plant extract, has been shown to help maintain normal transport of involved 12 patients with type II diabetes. When given 48 mg of Glucosol,™ (Soft Gel Technologies, Inc., Los Angeles, California) these subjects experienced improved glucose metabolism.[†,30,31] Although larger clinical trials are needed, the initial results have proven promising. Clinically, I have noted meaningful results often in patients with type II diabetes that have not responded fully to other approaches.

Conclusions

There is still much to learn about maximizing the benefits of nutrient supplementation, diet modification, and botanical medicines in preventing and treating diabetes. What information is available, however, provides many potential complementary approaches that are worth trying to enable patients with this disorder to live longer and healthier lives. ⊓

[†]Judy, W.V. Balancing blood sugar with Glucosol: Basic and clinical Glucosol studies. Unpublished research; and (no author) Glucosol hypoglycemia dose response relationship in type I diabetics: Study number one. Research, sponsored by Soft Gel Technologies, Inc., Los Angeles. Research was conducted at Southeastern Institute of Biomedicine, Bradenton, Florida.

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