CNI608 5/98
CLINICAL NUTRITION INSIGHTS

Vol. 6, No. 8

Herbal Support for Diabetes Management

BY TIM KACZMAR, M.D.

An estimated 16 million people in America have diabetes. Approximately 10% of the diabetic population is composed of Type I or insulin-dependent diabetes, whereas the remainder of diabetics are Type II or non-insulin dependent. It is estimated that a third of the non-insulin dependent diabetics are unaware of their disease.[1]

Type I diabetes is characterized by an immune-mediated, selective destruction of >90% of insulin-secreting beta cells. Individuals with Type I diabetes therefore require regular insulin injections to control blood sugar levels. The hyperglycemia that is associated with Type II diabetes results from both an impaired insulin secretory response to glucose and decreased insulin effectiveness (insulin resistance).[2] A third, less common form of diabetes is gestational diabetes. Although this form usually disappears following delivery, 40% of women with gestational diabetes will go on to develop Type II diabetes later in life.[1] The major symptoms of diabetes include excessive thirst, frequent urination, increased appetite, weakness and fatigue, and weight loss (in Type I). Other symptoms may include muscle cramps, impaired vision, poor wound healing, and, in women, itching due to vaginal yeast infection.

While the tendency to develop diabetes is strongly hereditary, there is believed to be an environmental component yet to be fully identified that triggers its development in susceptible individuals. Lack of exercise and obesity are considered major contributors to Type II diabetes; roughly 90% of individuals with type II are obese. These conditions can predispose one to the condition of insulin resistance, which is characterized by the hyper-secretion of insulin (hyperinsulinemia). Increased insulin resistance results in increased fasting and postprandial beta cell synthesis, which leads to "beta cell burnout" and, eventually, diabetes. The condition of insulin resistance may exist for many years before pancreatic beta cell function actually becomes impaired. In addition to diabetes, insulin resistance and the resultant hyperinsulinemia are associated with an increased risk for coronary artery disease, hypertension, and high blood pressure.

COMPLICATIONS OF DIABETES

Diabetes is the seventh leading cause of death in the United States.[1] Unfortunately, it can go undiagnosed until one of its life-threatening complications develops. The major chronic complications associated with diabetes include retinopathy, neuropathy, nephropathy, and atherosclerotic coronary artery disease and peripheral atherosclerotic vascular disease. About 85% of all diabetics develop retinopathy, 25-50% develop kidney disease, and 60-70% have mild to severe forms of nerve damage. Diabetics are also 2-4 times more likely to develop cardiovascular disease and 2-4 times more likely to suffer a stroke.[1,2]

The increased risk to developing pathological complications associated with diabetes is directly related to conditions of hyperglycemia. Chronic elevations in blood sugar levels contribute to the formation of advanced glycation end products (AGEs), which result from the nonenzymatic glycosylation of proteins, and to the formation of sugar alcohols. The formation of both AGEs and sugar alcohols is associated with long-term pathology of the nerves, blood vessels, kidney, lens, and pancreas, and in general contribute to the aging process.[3] Sugar alcohol formation in particular is directly involved in cataract development and loss of nervous function. Maintaining blood glucose homeostasis is therefore critical for preserving the health of the patient and reducing the risk of associated pathological disease.

DIABETES MANAGEMENT

The primary goal in the management of diabetes is to control blood sugar levels. In the Type I diabetic, this requires regular insulin injections. When blood homeostasis is not maintained, pathological complications begin to manifest. Because diabetics are also at a greater risk of developing cardiovascular disease compared to non-diabetics, preventive measures that include dietary and lifestyle modifications are also important.

Fundamental to the successful management of Type II diabetes is dietary modification including the strict control of simple carbohydrate intake and increasing the percentage of complex carbohydrates, as well as fiber. Also important is regular exercise and weight reduction (in overweight individuals). While some cases of Type II diabetes can be controlled by weight loss and diet alone, in some instances the use of insulin or oral hypoglycemic drugs, such as sulphonylureas and biguanidines, are necessary to help keep blood glucose at a normal level. Additionally, dietary supplements such as chromium, may provide benefit to diabetic individuals.[4-6] The benefits of vitamin E, magnesium, and other nutrients are still being elucidated.[4-6]

In recent years, several plant extracts have been examined for antidiabetic activity in an effort to identify alternative treatment strategies that pose less of a risk for diabetics. Although herbs can be very effective in helping to manage elevated blood glucose, they should not be used in place of insulin in persons with Type I or Type II diabetes requiring insulin.

HERBAL SUPPORT FOR DIABETES MANAGEMENT

Before the advent of insulin injections and other pharmaceutical preparations, healers relied heavily upon herbs to treat diabetes. Although numerous herbs are reported to possess some degree of antidiabetic activity,[7] a significant amount of research, as well as traditional usage, suggests that gurmar leaf (*Gymnema sylvestre*), bitter gourd fruit (*Momordica charantia*), and fenugreek seeds (*Trigonella foenum graecum*) may be among the best in terms of efficacy and safety. These, as well as several other valuable herbs such as garlic and ginseng represent safe, useful adjuncts to conventional therapeutic approaches to diabetes management. Also, it is plausible that the insulin and glucose normalizing effects of some of these herbs may benefit the non-diabetic with insulin resistance; however, research in this area is needed.

It is important to note that as with any change of diet, medication, or lifestyle with the diabetic, the administration of herbal supplements requires close monitoring of blood glucose levels, as these agents may reduce requirement for insulin or oral hypoglycemic drugs, and may cause hypoglycemia in some individuals.

Gymnema

Gymnema sylvestre is an herb that has a long history of use in India for controlling diabetes. The common name, gurmar, meaning "sugar-destroying," was given because of the plant's antisacharogenic property (suppresses the taste of sugar). Chewing the leaves actually deadens the sense of sweet tastes and also the bitterness of bitter substances.[8] This property is believed to be due to a glycoside known as gymnemic acid. While several compounds have been isolated from the leaves of gurmar, the precise antidiabetic principles remain unknown. Nonetheless, administration of the whole leaf extract has been shown to exert a hypoglycemic effect in both experimentally induced diabetic animals and diabetic humans, which suggests that the plant may have several active components that work synergistically.[9-12]

In the diabetic rabbit model, administration of *G. sylvestre* was shown to not only bring about blood glucose homeostasis, but also increase the activities of enzymes involved in glucose utilization.[9] The investigators reported an increase in the activity of certain insulin-dependent enzymes that are normally lowered in diabetic tissues, suggesting that the herb may act to increase insulin availability. Also in a manner similar to insulin, *G. sylvestre* caused a reduction in the activities of enzymes that are normally increased in the diabetic, such as glycogen phosphorylase, gluconeogenic enzymes, and sorbitol dehydrogenase. Additionally, the investigators reported that glycogen depletion in the liver and lipid accumulation in the diabetic animals was reversed as a result of *G. sylvestre* therapy.

Recently it has been reported that the oral administration of *G. sylvestre* to diabetic rats increased the number of pancreatic islet and beta cells, as well as insulin levels, suggesting a possible repair or regeneration of the endocrine pancreas. The investigators speculate that some residual pancreatic function is necessary for this effect to occur, as the extract showed no hypoglycemic effect in pancreatectomised animals.[10]

CLINICAL STUDIES

Extracts of gymnema have been shown to effectively lower blood glucose levels in both Type I and Type II diabetic patients.[11,12] In some cases, administration of the herb eliminated the need for oral hypoglycemic drugs.

In one study, 22 Type II diabetic patients receiving oral hypoglycemic drugs were administered an aqueous extract of *G. sylvestre* (400 mg/day) for a period of 18-20 months.[11] During the course of the study, patients treated with *G. sylvestre* demonstrated a significant reduction in blood glucose, glycosylated hemoglobin, and glyosylated plasma proteins. Five of the 22 diabetic patients were able to discontinue the use of their oral hypoglycemic drugs and maintain their blood glucose levels with the extract alone. In the remaining patients, the dose levels of conventional drugs could be reduced as the treatment progressed. The investigators speculate that *G. sylvestre* may help to increase levels of insulin and infer from animal studies that this mechanism may be as a result of the repair or regeneration of the residual beta cells in the islets of Langerhans in diabetic patients.

This assumption is supported by the appearance of raised insulin levels in the serum of patients following the administration of *G. sylvestre.* Gymnema extract did not produce any lowering of blood glucose in healthy volunteers.[11]

In another study, administration of 400 mg/day of a water-soluble extract of the leaves of *G. sylvestre* was shown to reduce fasting blood glucose and insulin requirements in patients with insulin-dependent diabetes undergoing insulin therapy.[12] A reduction in glycosylated hemoglobin and glycosylated plasma protein levels as well as serum lipids was also noted.

Fenugreek

Fenugreek seeds *(Trigonella foenum graecum)* have long been described in the Greek and Latin pharmacopoeias for the treatment of diabetes. More recently, several studies have demonstrated hypoglycemic properties of fenugreek seeds in both animal and human studies, thus, lending support to its traditional use.[13-19] Research further suggests that fenugreek has a lowering effect on plasma cholesterol and triglyceride levels.[16-18,20]

The hypoglycemic effect of fenugreek is thought to be largely due to its high content of soluble fiber, which acts to decrease the rate

of gastric emptying thereby delaying the absorption of glucose from the small intestine. Also, fiber in general (except for cellulose) enhances fecal excretion of bile acids and cholesterol, which would explain in part fenugreek's hypocholesterolemic properties.

The defatted fraction of fenugreek in particular has been shown to lower basal blood glucose levels, plasma glucagon and somatostatin levels, and reduces orally induced hyperglycemia in normal dogs.[13] While it is believed that the soluble fiber portion of fenugreek is largely responsible for its effects on lowering postprandial blood glucose levels, it is likely that other factors contribute to fenugreek's antidiabetic properties as well. For instance, it has been suggested that a specific amino acid, hydroxyisoleucine, which represents 80% of the free amino acids in fenugreek seeds, may possess insulin-stimulating properties.[21] Fenugreek also contains compounds like trigonelline and coumarin with reported hypoglycemic properties.[22]

Clinical Studies

Fenugreek seeds have been shown to be useful in the management of both Type I and Type II diabetes.[16-19] Administration of 5 g of powdered fenugreek seed (2.5 g capsules twice daily) resulted in significant lowering of blood glucose (fasting and postprandial) in non-insulin dependent diabetics with and without coronary artery disease (CAD). In the diabetic patients with CAD, fenugreek also significantly lowered total cholesterol and triglyceride levels.[16]

In another study, the administration of defatted fenugreek seed powder (100 g divided into two equal doses for 10 days) to insulin-dependent diabetics, resulted in significantly reduced fasting blood sugar and improved glucose tolerance test results.[17] Additionally, there was a 54% reduction in 24 hour urinary glucose excretion as well as a significant reduction in cholesterol and triglyceride levels.

Similar improvements in glucose tolerance were reported in both normal and Type II diabetics following fenugreek therapy.[18-19] In patients with Type II diabetes, fasting blood glucose, 24 hour urinary glucose output, and serum cholesterol were significantly reduced following continued therapy (25g per day for 21 days). In addition, the authors noted that insulin requirements for two Type II patients on insulin were reduced from 56 units/day to 20 units/day. The investigators speculate that the fenugreek seeds may help to improve insulin sensitivity, which is presumed to be due to the effects of fiber, which slows carbohydrate metabolism resulting in reduced insulin levels and lowered blood glucose. Interestingly, dietary fiber does not have to be concurrently administered with a meal in order to produce a beneficial effect on glucose tolerance. It appears that individuals may develop improved insulin sensitivity with the regular consumption of fiber.

Bitter Gourd

Bitter Gourd (*Momordica charantia*), also known as balsam pear, is a tropical vegetable widely cultivated in parts of Asia, Africa, and South America, which has been extensively used in folk medicine as a remedy for diabetes.[23] In recent years, the antidiabetic action of the fresh juice or extract of the unripe fruit has been established in both animal and human studies.[24-30]

Although the precise mechanism of action remains to be fully elucidated, preliminary evidence suggests that *M. charantia* may help to stimulate insulin release or possibly glycogen synthesis in the liver.[23] Additionally, the plant is believed to contain several antidiabetic principles. For instance, an insulin-like protein, known as insulin-P or polypeptide-P, has been extracted from *M. charantia* fruit and has demonstrated hypoglycemic effects when injected subcutaneously into Type I diabetics.[23,31] Also, *M. charantia* contains charantin, a mixed steroid compound isolated through alcohol extraction, which was found to be a more potent hypoglycemic agent than tolbutamide.[28]

Clinical Studies

An aqueous extract of *M. charantia* (100 g reduced to a 100 ml volume dose) given once per day was found to be highly effective in lowering blood sugar levels in Type II diabetics over a period of 7 weeks. In addition to hypoglycemic effects, the subjects showed a significant delay in the appearance of cataracts compared to the control group.[28]

Administration of *M. charantia* has also been shown to improve the outcome of the oral glucose tolerance test in Type II diabetics. In one study, the administration of 100 ml of *M. charantia* fruit juice improved glucose tolerance in 73% of test subjects following an oral glucose tolerance test.[29] Similar improvements in glucose tolerance were observed following the administration of 50 ml of *M. charantia* fruit juice.[30]

Garlic and Onions

Garlic and onions contain sulfur compounds, which are believed to be responsible for many of the plants' reported health benefits, including antidiabetic properties. S-allyl cysteine sulphoxide (SACS) is one such compound present in garlic, which has demonstrated antidiabetic effects in experimentally induced diabetic rats. SACS was reported to decrease fasting blood glucose and lower serum cholesterol levels in diabetic rats in a manner similar to the effects of glibenclamide and insulin.[32] In one human study, onion extract was shown to reduce hyperglycemia in a dose-dependent manner following a glucose tolerance test.[33]

CHINESE HERBS: AN INTEGRATED APPROACH TO DIABETES

In Chinese herbal medicine, herbs are traditionally combined based on their ability to balance those organ systems associated with a patient's presenting complaints. A Chinese herbal formula designed to balance sugar metabolism, will typically provide plants traditionally observed to effectively control the loss of fluids due to excessive urination, curb appetite by improving the digestion and assimilation of food, moisten or rehydrate tissues, and support the central nervous and cardiovascular systems.

An antidiabetic formula might contain rehmannia root (*Rhemannia glutinosa*), trichosanthes root (*Tricosanthes kirilowee*) and pueraria root (*Peuraria lobata*), herbs traditionally used to relieve excessive thirst and replenish fluids lost through excessive urination.[34] Ophiopogon root (*Ophiopogon japonicus*), poria (*Poria cocos*) and licorice root (*Glycyrrhiza uralensis*) might be included for their ability to promote healthy digestion, assimilation, and detoxification. Schizandra berry (*Schizandra chinensis*), an herb traditionally used to tonify the heart and kidneys, replenish vital energy and arrest fluid loss might also be added to counteract the fatigue, excessive thirst, dehydration, nervousness, irritability, forgetfulness, neuropathy and erratic blood pressure associated with diabetes.[37]

Research in the area of Chinese herbology has focused on both the individual activity of specific herbs and on traditional Chinese formulas. Miura et al. recently reported a significant lowering of blood glucose and insulin levels in Type II mice treated with a Chinese formula containing the following herbs: ophiopogon, pueraria, rhemmania, tricosanthes, poria, schisandara, licorice, and others.[38] Interestingly, these herbs on an individual basis are reported to possess a variety of healthful properties, including blood glucose regulating, immuno-modulating, liver detoxifying, and antiinflammatory properties.[35,36] These properties are significant to the diabetic as autoimmune processes are believed to play a role in the destruction of beta cells, and inflammation mediated by free radicals is also characteristic of the diabetic condition.

References

1. American Diabetes Association, 1997.
2. Berkow R. The Merck Manual. Rathway, NJ: Merck & Co., Inc., 1992.
3. Linder, M. Nutritional Biochemistry and Metabolism with Clinical Applications 2nd ed. Appleton & Lange: Norwalk, CT, 1991.
4. Anderson, R et al. Elevated intakes of supplemental chromium improve glucose and insulin variables in individuals with type 2 diabetes. *Diabetes* 1997;46:1786-1791.
5. Paolisso G et al. Daily magnesium supplements improve glucose handling in elderly subjects. *Am J Clin Nutr* 1992;55:1161-1167.
6. Paolisso G et al. Pharmacologic doses of vitamin E improve insulin action in healthy subjects and non-insulin-dependent diabetic patients. *Am J Clin Nutr* 1993;57:650-656.
7. Marles FJ, Farnsworth NR. Antidiabetic plants and their active constituents: an update. *Protocol J Nat Med* Winter 1996:85-111.
8. Nadkarni AK. *Indian Materia Medica Popular Prakashan Private Ltd:* Bombay, 1976.
9. Shanmugasundaram KR, et al. Enzyme changes and glucose utilization in diabetic rabbits: the effect of Gymnema sylvestre, R.Br. *J Ethnopharmacol* 1983;7:205-234.
10. Shanmugasundaram ERB, et al. Possible regeneration of the islets of langerhans in streptozotocin-diabetic rats given gymnea sylvestere leaf extracts. *J Ethnopharmacol* 1990;30:265-279.
11. Baskaran K, et al. Antidiabetic effect of a leaf extract form Gymnema sylvestre in non-insulin-dependent diabetes mellitus patients. *J Ethnopharmacol* 1990;30:295-305.
12. Shanmugasundaram ERB, et al. Use of Gymnema sylvestre leaf extract in the control of blood glucose in insulin-dependent diabetes mellitus. *J Ethnopharmacol* 1990;30:281-294.
13. Ribes G, et al. Antidiabetic effects of subractions from fenugreek seeds in diabetic dogs. *Proceedings Soc Exper Biol Med* 1986;182:159-166.
14. Ajabnoor MA, Tilmisany AK. Effect of Trigonella foenum graecum on blood glucose levels in normal and alloxan-diabetic mice. *J Ethnopharmacol* 1988;22:45-49.
15. Khosla P, et al. Effect of Trigonella foenum graecum (fenugreek) on blood glucose in normal and diabetic rats. *Indian J Physiol Pharmacol* 1995;39:173-174.
16. Bordia A, et al. Effect of ginger (*Zingiber officinale Rosc.*) and fenugreek (*Trigonella foenum graecum L.*) on blood lipids, blood sugar and platelet aggregation in patients with coronary artery disease. *Prost Leuko EFA* 1997;56:379-384.
17. Sharma RD, et al. Effect of fenugreek seeds on blood glucose and serum lipids in Type I diabetes. *Eur J Clin Nutr* 1990;44:301-306.
18. Sharma RD. Effect of fenugreek seeds and leaves on blood glucose and serum insulin responses in human subjects. *Nutr Res* 1986;6:1353-1364.
19. Madar Z, et al. Glucose-lowering effect of fenugreek in non-insulin dependent diabetics. *Eur J Clin Nutr* 1988;42:51-54.
20. Valette G, et al. Hypocholesterolemic effect of fenugreek seeds in dogs. *Atherosclerosis* 1984;50:105-111.
21. Haefele C. et al. Characterization of a dioxygenase from Trigonella foenum graecum involved in 4-hydroxyisoleucine biosynthesis. *Phytochem* 1997;44:563-566.
22. Ali L, et al. Characterization of the hypoglycemic effects of Trigonella foenum graecum seed. *Planta Med* 1995;61:358-360.
23. Welihinda J, et al. The insulin-releasing activity of the tropical plant Momordica charantia. *Acta Biol Med Germ* 1982;41:1229-1240.
24. Karunanayake EH, et al. Effect of Momordica charantia fruit juice on streptozotocin-induced diabetes in rats. *J Ethnopharmacol* 1990;30:199-204.
25. Singh N, et al. Effects of long term feeding of acetone extract of Momordica charantia (whole fruit powder) on alloxan diabetic albino rats. *Ind J Physiol Pharmac* 1989;33:97-100.
26. Ali L, et al. Studies on hypoglycemic effects of fruit pulp, seed, and whole plant of Momordia charantia on normal and diabetic model rats. *Planta Med* 1993;59:408-411.
27. Srivastava Y, et al. Effect of Momordica charantia Linn. Pomous aqueous extract on cataractogenesis in murine alloxan diabetics. *Pharmacol Res Comm* 1988;20:201-209.
28. Srivastava Y, et al. Antidiabetic and adaptogenic properties of Momordica charantia extract: an experimental and clinical evaluation. *Phytotherapy Res* 1993;7:285-289.
29. Welihinda J. et al. Effect of Momordica charantia on the glucose tolerance in maturity onset diabetes. *J Ethnopharmacol* 1986;17:277-282.
30. Leatherdale BA, et al. Improvement in glucose tolerance due to Momordia charantia (Karela). *Br Med J* 1981;282:1823-1824.
31. NG TB, et al. Insulin-like molecules in Momordica charantia seeds. *J Ethnopharmacol* 1986;15:107-117.
32. Sheela CG, Augusti KT. Antidiabetic effects of S-allyl cysteine sulphoxide isolated form garlic Allium sativum Linn. *Ind J Exper Biol* 1992;30:523-526.
33. Sharma KK et al. Antihyperglycemic effect on onion: effect on fasting blood sugar and induced hyperglycemia in man. *Ind J Med Res* 1977;65:422-429.
34. Brown D. *Encyclopedia of Herbs and Their Uses*. Dorling Kindersley: New York, 1995.
35. Hikino H et al. Isolation and hypogycemic activity of trichosans A, B, C, D, and E: glycans of Trichosanthes kirilowii roots. *Planta Med* 1989;55:349-350.
36. Miura T et al. Antidiabetic effect of seishin-knaro-to in KK-Ay mice. *Plant Med* 1997;63:320-322.
37. Yeung, H. Handbook of Chinese Herbs and Formulas, vol. 1, Institute of Chinese Medicine: California, 1983, pages 529-530, 475, 504, 378-79, 223-225, 214.
38. Miura, T. et al, Hypoglyemic activity of To-Kai-San (Chinese medicines) in normal and KK-Ay mice. *J. Nutr. Sci Vitaminol.* 1997; 43:11-17