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FILE: ▪ Gymnema (*Gymnema sylvestre*)
▪ Diabetes Mellitus

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RE: Evidence Needed to Support Gymnema's Effect on Diabetes Mellitus

Leach MJ. *Gymnema sylvestre* for diabetes mellitus: a systematic review. *J Altern Complement Med*. 2007;13(9):977-983.

An estimated 150 million people worldwide suffer from diabetes mellitus, and many develop complications from the disease. Among the complications of diabetes are diabetic neuropathy, retinopathy, peripheral neuropathy, autonomic dysfunction, erectile dysfunction, atherosclerosis, hypertension, microvascular disease, and increased susceptibility to infection.[1,2] In the United States in 2002, the cost of managing the disease and its complications was $132 billion.[3] Among the factors responsible for the pathogenesis of diabetes are age, ethnicity, genetics, obesity, autoimmunity, reduced physical activity, pancreatic β-cell defects, insulin resistance, and low-grade inflammation. Some argue that a low-glycemic load diet and increased physical activity, in conjunction with interventions that reduce blood lipids, stimulate the activity of glycogen synthase, improve β-cell activity and insulin secretion, or reduce insulin resistance early in the disease, may prevent or delay the development of type 2 diabetes and reverse the effects of the disease.[4] Existing treatments, such as insulin and oral hypoglycemic agents are associated with some adverse effects. In addition, many patients with diabetes still require ongoing care, monitoring, and treatment for complications.

Gymnema, or gurmar, is a large woody climbing plant found in central and southern India, tropical Africa, and tropical Australia.[5] Both the dried leaf and dried root are used therapeutically. The leaves are used as a digestive, antiviral, diuretic, antiallergic, hypoglycemic, hypolipidemic, and antiobesity agent for the treatment of diabetes, obesity, and dental caries, says the author. Gymnemic acid (actually a mixture of at least 17 different saponins) is thought to be the main constituent of gymnema. Among the other constituents are the gymnemasaponins, the polypeptide Gurmarin, the alkaloid conduritol, gymnamine, gypenoside, and the dammarane-type saponins gymnemasides 1-5 and gymnemasin B, C, and D.

The author conducted a comprehensive search of the literature in April 2006 to identify the best available evidence on gymnema and diabetes mellitus by using a number of databases. The search was limited to randomized controlled trials that used orally administered nonhomeopathic monopreparations of gymnema for glycemic control. He identified only two clinical trials (both of which were open-label comparative studies) as meeting the inclusion criteria though both were nonstandardized. By using the Joanna Briggs Institute critical appraisal of evidence of effectiveness tool, he concluded that the two studies had a high level of bias. Therefore, this article provides only a narrative review of gymnema and diabetes.

According to the author, much of the research on gymnema has examined its hypoglycemic effects and has shown that it may exert an antidiabetic effect through a number of pathways. Experimental studies, for example, have found that many of the constituents in gymnema decrease the uptake of glucose from the small intestine. In rabbits, gymnema has demonstrated improvements in glycogen synthesis, glycolysis, gluconeogenesis, and hepatic and muscle glucose uptake, as well as the reversal of hemoglobin and plasma protein glycosylation.

Some research has suggested that gymnema may improve glycemic control by stimulating insulin release from the pancreatic islets of Langerhans. The author cites a study on the effects of gymnema in rats that reported that the greatest reduction in blood glucose levels and the greatest effect on longevity was observed in moderately diabetic rats given gymnema aqueous extract at a dose of 0.6 g. Also found was that the efficacy of this gymnema extract was inversely related to the severity of the disease. That finding was supported in a similar study cited by the author.

In an open-label trial cited by the author, 65 patients with type 1 and type 2 diabetes were treated with a gymnema leaf extract, 400 mg twice a day for 90 days. This study found that, when compared with baseline the values for preprandial blood glucose level (BGL), postprandial BGL, and HbA1c were decreased by 11%, 13%, and 0.6%, respectively. The evidence for reductions in fasting BGL and postprandial BGL were further supported by two small, nonrandomized, open-label trials of patients with diabetes who took 6-10 g of gymnema leaf extract daily for 15 to 21 days.

Also cited are two controlled, open-label trials, in which the effects of GS_4 (a purified residue of a 50% ethanolic gymnema leaf extract), given at a dose of 400 mg GS_4 daily and conventional therapy were compared to conventional therapy alone. In the first trial with 22 type 2 (noninsulin-dependent) diabetic patients, gymnema significantly reduced blood glucose, glycosylated hemoglobin, and glycosylated plasma proteins compared with baseline data, over the 18 to 20 months; under conventional oral hypoglycemic treatment in 25 patients, those values increased or remained unchanged. In the second trial with type 1 (insulin-dependent) diabetics, gymnema extract given for 6-30 months to 27 patients significantly reduced glycosolated plasma protein in the first 6 to 8 months and serum amylase at 16 to 18 months. Compared with only conventional therapy given to 37 patients, gymnema significantly increased serum C-peptide levels within 16 to 18 months. The conventional treatment group demonstrated no significant improvement in glycemic control during the treatment period, presumably due to no changes in their insulin medication.

Given that gymnema targets several of the etiological factors connected with diabetes, including chronic inflammation, obesity, enzymatic defects, and pancreatic β-cell function, and since no single oral hypoglycemic drug presently exerts such a diverse range of effects, gymnema may be useful in

the management of diabetes and the prevention of associated pathological changes, says the author. Further investigation is needed.

—*Shari Henson*

References

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