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■ **Hyperglycemia**

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RE: A Review of the Hypoglycemic Effects of Five Commonly Used Herbs

Deng R. A review of the hypoglycemic effects of five commonly used herbal food supplements. *Recent Pat Food Nutr Agric.* April 1, 2012;4(1):50-60.

Glucose is the major energy source for the human body and plays a vital role in maintaining health. Glucose is circulated throughout the body in the blood and is maintained at a relatively constant level to ensure a steady source of energy for cells to function. The inability to regulate glucose in the blood results in hypoglycemia (low blood glucose) or hyperglycemia (high blood glucose). Hyperglycemia is associated with prediabetes and diabetes mellitus, which are conditions that increase the risk of cardiovascular disease and other complications. Although there are many drugs on the market that help control hyperglycemia, many of these pharmaceutical therapies have adverse effects or do not work effectively.

This review provides clinical trial information on 5 commonly used food supplements that are reported to have hypoglycemic effects: amla (Indian gooseberry; *Phyllanthus emblica* syn. *Embllica officinalis*), fenugreek (*Trigonella foenum-graecum*), green tea (*Camellia sinensis*), bitter melon (*Momordica charantia*), and cinnamon (*Cinnamomum* spp.). The Jadad scoring system was used to assess the methodological quality of these clinical trials (higher numbers=higher quality) and the quality of evidence was also provided (A=strongest evidence).

Amla (*Phyllanthus emblica* syn. *Embllica officinalis*)

Amla is an edible fruit from trees in the Phyllanthaceae and Euphorbiaceae families. The fruit is used to treat a variety of disease conditions, including hyperlipidemia and diabetes. Two recent patents made claims that amla could be used for managing hyperglycemia. These claims were made based on the results of 4 clinical trials conducted with patients who had diabetes.

In the first trial, fasting blood sugar (FBS) levels and glycated hemoglobin (HbA1c) were significantly decreased in patients receiving the composite supplement, whereas the control group remained unchanged. The second trial indicated a significant reduction in both FBS

and HbA1c levels in all 3 age groups of the diabetics. The third trial showed no significant reduction in FBS or HbA1c; however, patients with high FBS levels had a significant reduction in FBS, and a non-significant reduction in HbA1c levels. In a fourth clinical study, results indicated a significant reduction of FBS compared to patient baseline levels, but no significant effect for HbA1c levels was observed.

Based on the Jadad scale, the quality of the amla trials ranged from 0 to 4. Thus, there is strong scientific evidence (Level B1) to support that the composite supplements with amla are effective for lowering blood glucose levels in diabetics, although there is not enough evidence to support that amla was effective by itself.

Fenugreek (*Trigonella foenum-graecum*)

Fenugreek grows throughout the world with major production in Asia, Europe, and the Americas. Four patents or patent applications describe the value of using this herb for managing metabolic diseases, including hyperglycemia and diabetes.

Many of these health effects are supported by clinical trials, including 4 trials before 2000. In the first trial, there was a significant reduction in glucose levels in patients with non-insulin dependent diabetes. A second trial indicated the treatment significantly reduced FBS and improved the glucose tolerance test. In a third trial, results showed that supplementation with fenugreek reduced plasma glucose and improved glucose tolerance. In the fourth trial, patients with mild hyperglycemia exhibited a significant decrease in FBS and postprandial glucose levels, whereas there were no significant changes for healthy subjects or patients with severe hyperglycemia.

In a 2001 double-blind, controlled study, no significant differences were detected in FBS or the glucose tolerance test between active and control groups, but there were significant differences in the area under the curve of blood glucose and insulin sensitivity. In a larger trial in 2005, the results indicated a reduction in FBS and postprandial glucose levels in both groups. In 2008, another trial showed the treatment group had significantly decreased FBS, postprandial glucose, and HbA1c levels and improved clinical symptoms. In a 2009 trial, type 2 diabetics were divided into 2 groups with 1 group receiving a daily dose of 10 g of fenugreek powder in hot water and the other group consuming the same amount in yogurt for 8 weeks. Interestingly, only the group consuming the fenugreek in hot water had significantly decreased FBS.

The hypoglycemic effect of fenugreek was also examined in a healthy or healthy obese population. In one trial, postprandial glucose levels were significantly reduced in the treatment group. In a single-blind, randomized, crossover study and in a double-blind, randomized, and placebo-controlled trial, no significant results were found.

The quality of the fenugreek trials conducted on patients with diabetes and on healthy, obese, or overweight individuals ranged from 0 to 3 on the Jadad scale. It was found that there was good scientific evidence (Level B2) to suggest that fenugreek was effective in reducing blood glucose levels in patients with diabetes; however, fenugreek did not lower blood glucose in healthy, obese, or overweight individuals.

Green Tea (*Camellia sinensis*)

Several recent patents and patent applications claim that green tea, catechins from green tea, or green tea in combination with other natural products have hypoglycemic activity. There were 4 clinical trials that assessed the hypoglycemic effects of green tea. In one randomized, controlled study, no significant differences were found between the placebo and treatment groups in FBS and HbA1c levels. In a double-blind, placebo-controlled,

randomized, multiple-dose study, results showed no significant differences in HbA1c. Similarly, no significant differences in blood glucose and HbA1c levels were found in a double-blind study in patients with diabetes. In a 2011 randomized, double-blind, placebo-controlled trial, no significant differences were seen in FBS and HbA1c levels.

There were also 4 clinical trials that evaluated the hypoglycemic activity of green tea in healthy subjects or healthy obese individuals. In the first trial, HbA1c levels were significantly decreased following the intervention, but no changes in FBS levels were detected. The second trial assessed the effect of acute ingestion of green tea on healthy subjects during moderate-intensity exercise. The results indicated that the insulin area under the curve decreased in both treatment groups with a concurrent increase in insulin sensitivity. A third trial in overweight or obese males (n=8) revealed that there were no significant effects on FBS and HbA1c levels, insulin sensitivity, insulin secretion, or glucose tolerance. The fourth trial, a randomized, crossover study, showed that plasma glucose levels increased in the treatment group compared to the control group, and no significant differences were found in serum insulin levels or the area under the curve for glucose or insulin.

Altogether, the quality of the clinical trials using green tea ranged from 0 to 4 on the Jadad scale, with the majority having negative results as far as reducing blood glucose levels. Thus, there is strong evidence (Level B1) that green tea is not effective in controlling hyperglycemia.

Bitter Melon (*Momordica charantia*)

Bitter melon is often used for bitter flavoring in cooking. Consumption of bitter melon has been linked to a variety of health benefits, including the ability to help control hyperglycemia. There are 5 patent applications describing the use of bitter melon for the treatment of hyperglycemia. In the first study, a significant reduction in FBS (21.5% to 49.2%) was found in the treatment group, whereas the untreated diabetics and healthy subjects had only a slight reduction at 12 hours post-treatment. In another trial, patients had significant improvements in glucose tolerance. In addition, drinking 50 ml of fresh bitter melon fruit juice also significantly reduced plasma glucose levels and the area under the curve at 1.5 hours after drinking. In a third trial, drinking homogenized suspension of vegetable pulp resulted in a significant reduction of FBS and postprandial blood sugar (PPS) levels in 86 patients (18%).

Conversely, 2 randomized, placebo-controlled trials showed different results. One study indicated no significant changes to FBS, PPS, or fructosamine. The second study showed no significant reduction of FBS or HbA1c levels.

Additional clinical trials assessed the hypoglycemic activity of bitter melon in combination or in comparison with oral hypoglycemic drugs. One of the studies indicated that FBS and PPS levels were reduced with a half-dose of oral hypoglycemic drugs supplemented with a dose of 400 mg of bitter melon for 7 days. Moreover, another study found a significant reduction of fructosamine levels in patients taking a hypoglycemic drug and 2000 mg of bitter melon.

Overall, the quality of the bitter melon trials ranged from 0 to 4 on the Jadad scale and there is good scientific evidence (Level B2) that bitter melon is effective at reducing blood glucose levels in diabetics, with the exception of 2 clinical trials.

Cinnamon (*Cinnamomum* spp.)

The bark of the cinnamon tree has been used in cooking and in traditional Chinese medicine and Ayurveda for centuries. There are 5 recent patents and patent applications that disclose information on the composition of cinnamon used for metabolic disease and diabetes. There

were 4 clinical trials that assessed the hypoglycemic effects of cinnamon in diabetics. In 1 study, FBS levels were reduced in all treatment groups by 18-29%, while no significant changes were detected in the placebo groups. Another study combining hypoglycemic drugs with a cinnamon supplement (3 g) indicated that FBS and PPS levels were significantly reduced compared to the placebo group, and a decrease in FBS correlated significantly with baseline concentrations; however, no significant differences were detected in HbA1c levels. In a larger trial of patients with type 2 diabetes, study results indicated that cinnamon significantly lowered HbA1c levels. In a randomized, placebo-controlled trial with type 2 diabetics, HbA1c and FBS levels were reduced significantly compared to placebo.

In contrast, a study conducted on postmenopausal patients with type 2 diabetes indicated there were no significant changes in FBS or HbA1c levels or insulin sensitivity. Furthermore, a prospective, double-blind, placebo-controlled trial revealed no significant differences in HbA1c levels, total insulin intake, or the number of hypoglycemic episodes between groups. Likewise, a randomized, double-blind, placebo-controlled trial in type 2 diabetics revealed no significant differences in FBS, HbA1c, or insulin levels between the treatment and placebo groups. There were also three small clinical trials that investigated the hypoglycemic effect of cinnamon in healthy volunteers.

Four cinnamon trials had a score of 2 or 3 on the Jadad scale, indicating a positive effect on lowering blood glucose. Therefore, there is very strong evidence (Level A) to support that cinnamon is effective at lowering blood glucose in patients with type 2 diabetes. However, these effects were not detected in type 1 diabetics or in postmenopausal patients with type 2 diabetes.

In summary, this review evaluated the efficacy of 5 herbal supplements that have been reported to be effective for controlling hyperglycemia. Most trials that evaluated the effects of amla were composite supplements that contained other herbs which made it difficult to evaluate an effective dose for amla as an individual supplement. The results of multiple clinical trials indicated that fenugreek, alone or in combination with other hypoglycemic drugs, had significant hypoglycemic effects in patients with diabetes, although these effects were diminished in healthy, obese, or overweight individuals. Based on several clinical trials, supplementation with green tea was found to have minimal effects on hyperglycemia in diabetics. On the other hand, most of the clinical trials indicated that bitter melon produced hypoglycemic effects in patients with diabetes. Moreover, the combination of antidiabetic drugs with bitter melon proved to be effective. There is also very strong evidence that cinnamon has hypoglycemic activity in patients with type 2 diabetes, but these effects were lessened in postmenopausal type 2 diabetics; also, the negative result in one of the trials in patients with type 2 diabetes may have been related to the difference in ethnic background.

—*Laura M. Bystrom, PhD*

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