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File: ■ Cinnamon (*Cinnamomum* spp.)
■ Diabetes Mellitus
■ Glycemic Control

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RE: Systematic Review of Cinnamon for Glycemic Control in Diabetes

Leach MJ, Kumar S. Cinnamon for diabetes mellitus. *Cochrane Database Syst Rev*. 2012;9:CD007170. doi: 10.1002/14651858.CD007170.pub2.

Diabetes mellitus is a chronic metabolic disease associated with increased risk of cardiovascular disease, retinopathy, nephropathy, neuropathy, and other disorders. Control of glycemia can be a key modulator that reduces the risk of these disorders. A number of animal studies have been performed to assess the effects of cinnamon (*Cinnamomum aromaticum* syn. *C. cassia*) on glycemic control. In addition, it has been used for this purpose in Chinese and Ayurvedic medicine. The putative active ingredient is cinnamaldehyde; however, its mechanism of action regarding lowering glycemia is not clear but may involve increasing serum insulin levels, hepatic glycogen storage, improving insulin-receptor signaling, an insulinomimetic effect, or a reduction in intestinal alpha-glucosidase activity. This meta-analysis, conducted by the Cochrane Collaboration, sought to evaluate the effects of cinnamon on glycemic control in humans.

To retrieve randomized, controlled trials focusing on glycemic control in humans, the authors searched through AARP AgeLine, AMED, AMI, BioMed Central gateway, CAM on PubMed, CINAHL, Dissertations Abstracts International, EMBASE, Health Source: Nursing/Academic edition, International Pharmaceutical Abstracts, MEDLINE, Natural Medicines Comprehensive Database, The Cochrane Library, and the TRIP database. Clinical trial registers and the reference lists of included trials were also searched up to January 2012. Studies had to have used a monopreparation of cinnamon in any dose or form, compared to placebo, a medication, or no treatment. Studies in which cinnamon was co-administered with insulin, oral hypoglycemic agents, or both were included. Patients with either type 1 or type 2 diabetes were included, as determined by standard criteria valid at the time of study.

The search uncovered 395 studies, of which 10 prospective, parallel-group design, randomized, controlled trials were included, totaling 577 participants (range of n=14-109). Two studies were multicentered. Six studies were double-blinded, 2 single-blinded, and the remainder were unclear with respect to blinding. The duration of the studies ranged from 4.3-16 weeks (mean of 10.8 weeks). No studies had a run-in period, and 2

studies had a 20-day follow-up. The mean age of the patients was 52-63 years, with 1 trial in adolescents averaging 15 years of age. Most of the patients had a body mass index (BMI) that classified them as obese. Eight trials recorded the duration of the disease, which averaged 6-7 years. Patients had type 2 diabetes in all but 1 study. Five trials did not report details of withdrawals. Two trials did not report findings on all primary and secondary outcome measures.

The primary outcome measures were fasting blood glucose levels (FBGL), postprandial glucose (PPG), and adverse events. Secondary outcome measures included glycosylated hemoglobin A1c (HbA1c), serum insulin, insulin sensitivity (homeostasis model assessment of insulin resistance [HOMA-IR]), health-related quality of life (HRQoL), morbidity (all-cause morbidity, as well as diabetes and cardiovascular-related morbidity). Any study duration was acceptable for all of these parameters except HbA1c, for which changes cannot be detected in less than 3 months; therefore, only data for HbA1c gathered over 3 months or more were included.

The species of cinnamon used in a majority of the studies (7) was cassia (Chinese cinnamon; *Cinnamomum aromaticum* syn. *C. cassia*). One study used *C. burmanni*, and 2 did not define the type of cinnamon used. The daily dose of cinnamon was variable and included doses of 0.5, 1, 1.5, 2, 3, and 6 g. All but 1 study used a matching placebo.

The risk of bias in the studies was assessed to be high or not clear in all but 2 trials, which were determined to have moderate risk. A number of the studies did not record details of the concomitant use of diabetes medications, which may introduce an additional risk of bias.

Eight trials reported data on FBGL (n=338). There was no statistically significant difference in FBGL between cinnamon and placebo (mean difference [MD]: -0.83 mmol/L; 95% confidence interval [CI]: -1.67 to 0.02; P=0.06). The level of heterogeneity was high (I^2=82%), which could not be explained by sub-group and sensitivity analysis; however, funnel plot analysis determined 2 studies were extreme outliers in terms of their effects. When these 2 studies were removed from the analysis, the level of heterogeneity dropped to 0%, but there was still no statistically significant difference in FBGL between the cinnamon and placebo groups (MD: -0.08 mmol/L; 95% CI: -0.34 to 0.18; P=0.55).

One trial reported data on PPG (n=40). There was no statistically significant difference in PPG between the cinnamon and placebo groups (MD: -0.39 mmol/L; 95% CI: -0.83 to 0.05; P=0.08).

Four trials reported data on adverse events (n=264), including 3 events in participants receiving cinnamon (n=133), and 4 events in participants receiving controls (n=131). Adverse events in the treatment groups included rash, hives, and a hypoglycemic seizure; and, in the control group, included stomach ache, nausea, and mild gastric pain. There was no statistically significant difference in the rate of adverse events between the cinnamon and placebo groups (odds ratio [OR]: 0.83; 95% CI: 0.22 to 3.07; P=0.77).

Six trials reported data on HbA1c (n=405). There was no statistically significant difference in HbA1c between the cinnamon and control groups (MD: -0.06%; 95% CI: -0.29 to 0.18; P=0.63). Subgroup analyses for dosage and diabetes type did not change the result.

Two trials reported data on serum insulin (n=81). There was no statistically significant difference in serum insulin between the cinnamon and placebo groups (MD: -6.77 pmol/L; 95% CI: -37.0 to 23.46; P=0.66). Subgroup analyses for dosage and diabetes type did not change the result.

Two trials reported data on insulin sensitivity (n=82). There was no statistically significant difference in insulin sensitivity between the cinnamon and placebo groups as measured by the ratio of carbohydrates to insulin (CHO/unit insulin; MD: 0; 95% CI: -1.56 to 1.56; P=1.00) or by HOMA-IR (MD: 0.22; 95% CI: -0.70 to 1.14; P=0.64).

None of the trials assessed HRQoL, morbidity, or costs as endpoints.

In this meta-analysis, no effects of cinnamon on the primary or secondary endpoints were found. In general, cinnamon was well tolerated. The authors conclude that, "The best available evidence does not support the use of orally administered cinnamon for diabetes mellitus," but continue that, "There is adequate justification for conducting further studies in this area." Suggested avenues for continued study include testing in young children with diabetes and assessing the effects of different species, extraction methods, and types of preparations. The authors suggest that, given the results of their subgroup analyses, it is unlikely that differences in cinnamon dosage, frequency of administration, or treatment duration would generate different results. More rigorous trials would also help to illuminate the potential benefits of cinnamon.

—Risa Schulman, PhD

The American Botanical Council has chosen not to reprint the original article.