Effect of Cinnamon on Glucose Control and Lipid Parameters

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OBJECTIVE — To perform a meta-analysis of randomized controlled trials of cinnamon to better characterize its impact on glucose and plasma lipids.

RESEARCH DESIGN AND METHODS — A systematic literature search through July 2007 was conducted to identify randomized placebo-controlled trials of cinnamon that reported data on A1C, fasting blood glucose (FBG), or lipid parameters. The mean change in each study end point from baseline was treated as a continuous variable, and the weighted mean difference was calculated as the difference between the mean value in the treatment and control groups. A random-effects model was used.

RESULTS — Five prospective randomized controlled trials ($n = 282$) were identified. Upon meta-analysis, the use of cinnamon did not significantly alter A1C, FBG, or lipid parameters. Subgroup and sensitivity analyses did not significantly change the results.

CONCLUSIONS — Cinnamon does not appear to improve A1C, FBG, or lipid parameters in patients with type 1 or type 2 diabetes.

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Cinnamon contains biologically active substances that have demonstrated insulin-mimetic properties. In vitro (1,2) and in vivo (3,4) studies have shown that cinnamon enhances glucose uptake by activating insulin receptor kinase activity, autophosphorylation of the insulin receptor, and glycogen synthase activity. Other recent studies have demonstrated the ability of cinnamon to reduce lipid levels in fructose-fed rats, potentially via inhibiting hepatic 3-hydroxy-3-methylglutaryl CoA reductase activity (5,6).

Several clinical trials (7–11) have investigated the impact of cinnamon on glucose and plasma lipid concentrations in patients with diabetes but yielded conflicting results and had modest sample sizes. Therefore, we performed a meta-analysis of randomized controlled trials of cinnamon to better characterize its impact on glucose and plasma lipids.

RESEARCH DESIGN AND METHODS

To be included in this meta-analysis, trials had to be randomized placebo-controlled trials of cinnamon and report data on A1C, fasting blood glucose (FBG), or lipid parameters.

Using the above-mentioned inclusion criteria, we conducted a systematic literature search of MEDLINE, CINAHL, Web of Science, and the Cochrane Library from the earliest possible date through July 2007. We used the following medical subject headings and keywords: "*cinnamon*," "*cinnamomum*," "*cinnamomum cassia*," "*cinnamomum zeylanicum*," and "*cinnamomum aromaticum*" in combination with "diabetes mellitus." Results were limited to clinical trials in humans. A manual search of retrieved articles was also performed. Three investigators independently reviewed potentially relevant articles and abstracted necessary data.

The mean change in each study end point from baseline was treated as a continuous variable, and the weighted mean difference was calculated as the difference between the mean value in the treatment and control groups. Advanced statistical methods were used to impute change scores as suggested by Follman and colleagues (12,13). We conducted subgroup and sensitivity analyses to assess whether diabetes type had an effect on our results. A random-effects model was used to calculate weighted mean difference and 95% CIs. Statistical heterogeneity was addressed using the I^2 statistic. Visual inspection of funnel plots was used to assess for publication bias. The funnel plot is a pictorial representation of each study plotted by its effect size on the horizontal axis and variance on the vertical axis. If the plot represents an inverted symmetrical funnel, it is said that publication bias is unlikely. Statistics were performed using StatsDirect, version 2.5.8 (StatsDirect, Cheshire, England).

RESULTS

The initial search yielded 24 potential literature citations. Of those, 14 citations were human studies, and only 6 were clinical trials. Furthermore, one citation was excluded from the analysis because it was not a trial of cinnamon. Thus, a total of five clinical trials ($n = 282$ subjects, follow-up range 5.7–16.0 weeks) were included in the meta-analysis (7–11). All of the studies used *cinnamomum cassia*, and doses ranged from 1 to 6 g. Four studies provided powder-filled capsules (7–9,11), while one provided aqueous-filled capsules (10). Four of the studies dosed cinnamon during meals (8–11). The study by Khan et al. (9) examined three different doses of cinnamon, and the results were combined in this meta-analysis because no dose-response relationship was found with cinnamon between 1 and 6 g (9). Studies were in type 2 diabetic subjects (8–11) or adolescents with type

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Abbreviations: FBG, fasting blood glucose.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Results of meta-analysis of randomized controlled trials evaluating cinnamon*

	Base-case		Type 1 diabetes only		Type 2 diabetes only	
	Weighted mean difference (95% CI)	*n*	Weighted mean difference (95% CI)	*n*	Weighted mean difference (95% CI)	*n*
A1C	0.07 (−0.11 to 0.26)	4 (204)	0.30 (−0.01 to 0.70)	1 (57)	0.01 (−0.20 to 0.22)	3 (147)
FBG	−17.15 (−47.58 to 13.27)	4 (207)	NA	—	−17.15 (−47.58 to 13.27)	4 (207)
Total cholesterol	−9.63 (−35.94 to 16.67)	4 (207)	NA	—	−9.63 (−35.94 to 16.67)	4 (207)
Triglycerides	−28.44 (−61.81 to 4.94)	4 (207)	NA	—	−28.44 (−61.81 to 4.94)	4 (207)
HDL cholesterol	1.58 (−0.74 to 3.89)	3 (147)	NA	—	1.58 (−0.74 to 3.89)	3 (147)
LDL cholesterol	−4.71 (−18.12 to 8.71)	4 (207)	NA	—	−4.71 (−18.12 to 8.71)	4 (207)

All results are reported in mg/dl as weighted mean difference (95% CI) using a random-effects model. *n* = number of studies (number of subjects).

1 diabetes (7). Studies were conducted in the U.S. (7,8), Europe (10,11), and Pakistan (9). Patient withdrawals were appropriately reported in all studies.

Upon meta-analysis, the use of cinnamon did not significantly alter A1C, FBG, or lipid parameters (Table 1). No statistical heterogeneity was observed for the A1C or HDL analyses ($I^2 = 0\%$). Each of the other analyses displayed a high degree of statistical heterogeneity ($I^2 > 79.6\%$ for all). Visual inspection of funnel plots (not shown) could not rule out publication bias for any analysis.

After conducting subgroup and sensitivity analyses, the exclusion of nonblinded trials (9), or evaluating type 1 (7) and type 2 diabetes (8–11) separately did not significantly change our meta-analysis' results. Little to no statistical heterogeneity was observed for any of these subsequent analyses.

CONCLUSIONS — In this meta-analysis of five randomized placebo-controlled trials, patients with type 1 or type 2 diabetes receiving cinnamon did not demonstrate statistically or clinically significant changes in A1C, FBG, or lipid parameters in comparison with subjects receiving placebo.

The median duration of patient treatment and follow-up in all included trials was 12 weeks. This duration of treatment is appropriate to observe clinically significant changes in FBG and lipids (14–16). However, it is likely too short to see the full effect of treatment on A1C (14). Still, we would have expected a trend or tendency toward beneficial changes in A1C with cinnamon supplementation compared with placebo after this shorter time period, if in fact such a benefit truly existed. Instead, A1C levels increased to a greater extent with cinnamon than with placebo in our meta-analysis, thus reducing our confidence in cinnamon's impact on long-term glycemic control.

There are some additional limitations to this meta-analysis that should be noted. First, we identified only a small number of eligible studies. Thus, our meta-analysis may be underpowered to detect statistically significant differences in many of the end points. Post hoc sample size calculations suggest that if the differences were due to a real effect rather than chance, then 1,166–6,853 patients would be needed. Even if the beneficial changes observed in some of end points were found to be statistically significant, their clinical significance could still be debated. We cannot determine the reason for differences between the Khan study and the others. Ethnicity or cultural dietary differences, dose, lack of verification of double blinding, or chance resulting from small sample size in the Khan study could explain the disparate findings. In four of the five studies, including Khan's, authors did not mention whether the aroma associated with cinnamon and placebo were similar, which could have affected the adequacy of double blinding. Finally, as with any meta-analysis, the potential for publication bias is of concern. Visual inspection of our meta-analysis' funnel plot could not rule out publication bias.

Cinnamon does not appear to improve A1C, FBG, or lipid parameters in patients with type 1 or type 2 diabetes. Cinnamon's ability to prevent diabetes in patients with pre-diabetes and those at high risk is unknown.

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