P.O. Box 144345 Austin, TX 78714-4345 ▪ 512.926.4900 ▪ Fax: 512.926.2345 ▪ www.herbalgram.org

HerbClip™

File: ■ Ginseng (*Panax* spp., Araliaceae)
■ Glycemic Control
■ Systematic Review/Meta-analysis

HC 111772-594

Date: June 15, 2018

RE: Ginseng Aggregate Data Analyses Show Evidence of Modest yet Significant Benefit for Improving Fasting Blood Glucose

Shishtar E, Sievenpiper JL, Djedovic V, et al. The effect of ginseng (the genus *Panax*) on glycemic control: a systematic review and meta-analysis of randomized controlled clinical trials. *PLoS One*. September 29, 2014;9(9):e107391. doi: 10.1371/journal.pone.0107391.

Diabetes is a global epidemic, and ginseng (*Panax* spp., Araliaceae) is a popular complementary and alternative medicine that has shown promise in type 2 diabetes. However, systematic reviews of ginseng's effects on blood glucose parameters have not been conclusive. The purpose of this systematic review and meta-analysis was to evaluate the effect of ginseng on glycemic control in people with and without diabetes.

The authors' search of the MEDLINE, EMBASE, CINAHL, and CENTRAL databases from inception through July 3, 2013, used the following terms and variations thereof, in ways to maximize useful results from each database: panax, ginseng, ninjin, renshen, shinseng, jen adj shen, schinseng, ginsenoside(s), glucose tolerance test, OGTT, hemoglobin A, glycosylated, HBA1C, fructosamine, insulin, glucose, hyperglycemia, hyperglycaemia, glycaemia, hyperinsulin, dysglycemia, diabetes mellitus, "diabetes millitus [*sic*]," HOMA, glycemia, gly, albumin, diabetes, metabolic syndrome, homeostasis model assessment, hyperglycemic, hyperglycaemic, type1/ or type 1 diabetes, type2/ or type 2 diabetes, gestational/ or gestational diabetes, and prediabetic state/ or prediabetes. (Please see Table S1 for the complete search strategy.)

Eligible studies were at least 30 days long and evaluated the effect of oral ginseng (all species of the genus *Panax*) supplementation on at least one of the four following glycemic control metrics in people with and without diabetes: fasting blood glucose (FBG), fasting plasma insulin (FPI), glycated hemoglobin (HbA1c), and homeostasis model assessment of insulin resistance (HOMA-IR). Excluded trials tested multi-herbal preparations, did not have a suitable control, or did not provide satisfactory data on endpoints.

Fifteen reports encompassing 16 trials and 770 participants with a median age of 51 years were included in the analysis (FBG: 16 trials, n = 770; FPI: 10 trials, n = 349; HbA1c: nine trials, n = 264; HOMA-IR: seven trials, n = 305). Half of the trials were conducted in Asia and half (25% each) in North America or Europe. Table 1 summarized the following trial data: subject characteristics; age; body mass index; setting; glucose (mmol/L); insulin (pmol/L);

HbA1c (by percent); HOMA-IR; design; comparator; follow-up time; methodological quality score (MQS); funding sources; manufacturer; and ginseng form, preparation, dose, and species.

Eleven trials (68.8%) used parallel designs and five (31.3%) used crossover designs. Asian ginseng (*P. ginseng*) was studied in 75% of trials, American ginseng (*P. quinquefolius*) in 18.8%, and the remainder was unspecified. The intervention in all trials was powdered ginseng in capsules. Preparations included Korean red ginseng (*P. ginseng*), American ginseng, or *P. ginseng* whole root/rootlets or extracts; two trials did not include this information. Thirteen trials (81.2%) used a placebo as the comparator, two (12.5%) used a control group that did not receive ginseng, and one (6.25%) used fermented soy (*Glycine max*, Fabaceae) bean. The average follow-up was eight weeks. The median MQS was 8 and most trials (n = 11) were high quality (MQS ≥ 8).

Compared to control, ginseng significantly reduced FBG (mean difference [MD] = −0.31 mmol/L, P = 0.03). Subgroup analyses revealed that the presence of diabetes impacted ginseng's FBG-lowering effect (between-group MD = −0.96, P = 0.001). Studies of those with diabetes had an MD of −0.84 mmol/l (95% confidence interval [CI], −1.22 to −0.46), while studies of those without had an MD of 0.11 mmol/l (95% CI, −0.19 to 0.42). A linear association between baseline FBG and treatment differences in FBG was seen in the continuous meta-regression analyses (P = 0.001).

There was no statistically significant difference between ginseng and control for FPI, HbA1c, or HOMA-IR, but subgroup analysis revealed a significant reduction in HbA1c in parallel trials compared to crossover trials (MD = 0.22%, P = 0.01). Significant study heterogeneity was found in the analyses of FBG (P < 0.001), HbA1c (P = 0.002), and HOMA-IR (P < 0.001). Funnel plot analyses revealed there may have been publication bias in favor of "small and/or imprecise studies with FBG and HbA1c reducing effects … ." but neither Egger's nor Begg's test confirmed this.

The authors state their study is limited by relatively short trial duration, subject heterogeneity (those with and without diabetes), and different ginseng preparations. The decrease in FBG was greater in those with diabetes, suggesting ginseng supplementation may be more beneficial in people with higher FBG. Inadequate washout and participant glycemic control, as well as relatively short trial duration, may explain why HbA1c improvement was seen only in parallel trials. The included trials had insufficient data on safety, ginseng dose equivalents, and ginsenoside profiles to include these in the meta-analysis.

The authors conclude that ginseng significantly and modestly decreased FBG in people with and without diabetes. More data are needed from larger and longer randomized controlled trials focusing on ginseng's effect on HbA1c and FBG.

The study was part of author Shishtar's master's thesis; Shishtar was supported by a fellowship from the Embassy of the State of Kuwait. Please see the exhaustive paragraph "Competing Interests" for information on the authors' affiliations.

—Heather Anderson, MD

Referenced article can be accessed at
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0107391.