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File: ■ Cocoa (*Theobroma cacao*)
■ Blood Pressure
■ Epicatechin

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RE: Nonlinear Meta-analysis of Cocoa Effects on Blood Pressure Finds It Provides a Dose-dependent Benefit

Ellinger S, Reusch A, Stehle P, Helfrich HP. Epicatechin ingested via cocoa products reduces blood pressure in humans: a nonlinear regression model with a Bayesian approach. *Am J Clin Nutr*. 2012;95(6):1365-1377.

Four separate meta-analyses have been performed on the effects of cocoa (*Theobroma cacao*) on blood pressure (BP), all showing that it provides a benefit. It is thought that these effects are due to the dose of epicatechin; if so, this may explain the differences in results in the studies used in the meta-analyses. This paper reports on the novel use of an alternate meta-analysis using a nonlinear regression model with a Bayesian approach and which includes a Markov chain Monte Carlo method that takes full account of the nonlinearity of the regression model. The authors hoped to thereby understand whether the dose of epicatechin is related to the magnitude of its BP-lowering effect and if this can explain between-study differences in effects.

Medline was searched until July 2011 for randomized, controlled trials (RCTs), which were included if they met the following criteria: (1) control substances were of low-flavanol composition; (2) BP was measured after an overnight fast; (3) mean or median systolic BP (SBP) or diastolic BP (DBP), standard deviations (SDs), standard error of the mean (SEM), 95% credible intervals (CIs), or P-values for changes were given; and (4) data on epicatechin intake were recorded.

Twenty-six RCTs were identified, of which 13 met the inclusion criteria. An additional study was obtained from an author; and 1 study had 3 arms, each of which was considered separately. This yielded a total of 16 studies for consideration (16 on SBP and 15 on DBP).

The regression curve showed that reductions in SBP and DBP were dependent on the dose of epicatechin. The estimated asymptotic value *K* of the treatment effect was -4.6 mmHg (95% CI: -5.4, -3.9 mmHg) for SBP and -2.1 mmHg (95% CI: -2.7, -1.6 mmHg) for DBP (Figure 3). The coefficient *c* reflecting the initial slope of the curve was -2.5

mmHg/mg for SBP (95% CI: -8.4, -0.6 mmHg/mg). For DBP, the mean value for *c* was -4.3 mmHg/mg (95% CI: -9.6, -0.2 mmHg/mg).

From this curve, a mean reduction for a dose of 25 mg of epicatechin for SBP could be estimated to be -4.1 mmHg (95% CI: -4.6, -3.6 mmHg) and for DBP, a mean reduction of -2.0 mmHg (95% CI: -2.4, -1.5 mmHg) could be estimated.

Because the 95% CIs are narrower in the nonlinear regression model than in the regular meta-analyses, the authors conclude that the dose of epicatechin is responsible for the heterogeneity of the studies, and that their model estimates the treatment effects more precisely than the linear regression model. They argue that the likelihood of confounding effects was low and that the merging of data from both ambulatory and 24-hour BP readings should not affect the results since they are very similar in magnitude. Limitations include the inability to understand the effects of low doses of epicatechin (because of lack of data for such doses) and the fact that the data cannot be readily extrapolated to normotensive subjects, since only 25% of the studies examined that population.

The authors conclude that a dose of 25-30 g of high-flavanol cocoa should lower SBP by -4.1 mmHg and DBP by -2.0 mmHg. The cocoa should be consumed in a form that will not lead to unwanted weight gain.

—Risa Schulman, PhD

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