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File: ■ Cocoa (*Theobroma cacao*)
■ Chocolate
■ Coronary Heart Disease

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RE: Review of the Effects of Cocoa and Chocolate on Coronary Heart Disease

Khawaja O, Gaziano JM, Djoussé L. Chocolate and coronary heart disease: a systematic review. *Curr Atheroscler Rep*. 2011 Sep 6; [Epub ahead of print]. doi: 10.1007/s11883-011-0203-2.

Cocoa (*Theobroma cacao*) and chocolate have been investigated for their beneficial effects on factors related to coronary heart disease (CHD); however, it is unclear whether the actual risk of CHD is affected. This article reviews the evidence for an effect on clinical and subclinical CHD, CHD risk factors, and biological mechanisms, as well as the limitations of the literature and suggested future directions. The authors reviewed 7 studies that included 2 cross-sectional studies (7187 participants), 2 cohort studies (2385 participants), 1 randomized, single-blind trial (35 participants), 1 prospective study (470 participants), and 1 case-controlled study (77,923 participants).

Chocolate is made from the seeds of the cacao tree and is a combination of cocoa solids, cocoa butter or other fats, and sugar. Milk chocolate also contains milk, while dark chocolate contains added fat and sugar. [Editor's Note: What makes dark chocolate dark is that it contains more cocoa solids than milk chocolate and no milk.] White chocolate consists primarily of cocoa butter, sugar, and milk, and does not contain any cocoa solids or flavonoids. Cocoa contains polyphenols and flavonoids, in particular epicatechin, at a rate of 18-24 µg of epicatechin/100 g in milk chocolate, and 52-125 µg/100 g in dark chocolate. Chocolate also contains saturated fat (60%), monounsaturated fat (35%), and linoleic acid (3%).

The associations between chocolate/cocoa consumption and CHD prevalence, cardiovascular disease (CVD), and all-cause mortality are examined in a number of studies. The cross-sectional National Heart, Lung, and Blood Institute (NHLBI) Family Heart Study in 4,970 subjects showed an inverse relationship with prevalent CHD for those who consumed chocolate ≥5 times per week (odds ratio [OR] of 0.43; 95% confidence interval [CI], 0.28-0.67). A second study reported a 35% reduced risk of CVD with consumption of chocolate ≥1 time per week (multivariable adjusted relative risk [RR] of 0.65 [95% CI, 0.46-0.94]).

In subclinical heart disease, a single-blinded, randomized trial in 39 men showed improved coronary flow velocity reserve in those who ate flavanol-rich dark chocolate (CFVR; 3.38 ± 0.49 before and 4.28 ± 0.85 after dark chocolate intake; P<0.01), but showed no improvement in those who ate white chocolate. A cross-sectional study (NHLBI Family Heart Study) found an association between chocolate consumption and calcified atherosclerotic plaques in coronary arteries in 2,217 participants for chocolate consumption of 1-3 times per month, once per week, and ≥2 times per week (OR of 0.94 [95% CI, 0.66-1.35], 0.78 [95% CI, 0.53-1.13], and 0.68 [95% CI, 0.48-0.97], respectively), compared to no chocolate intake for the reference group.

With respect to CHD mortality, Janszky et al.[1] observed a strong inverse association in post-myocardial infarction patients for those who consumed chocolate less than once per month, up to once per week, and twice or more per week (hazard ratio [HR] of 0.73 [95% CI, 0.41-1.31], 0.56 [95% CI, 0.32-0.99], and 0.34 [95% CI, 0.17-0.70], respectively). A similar association was found in the Iowa Women's Health Study after 13 years of follow-up in postmenopausal women. Buijsse et al.[2] reported an RR of 0.50 (95% CI, 0.32-0.78) for cardiovascular mortality and an RR of 0.53 (95% CI, 0.39-0.72) for all-cause mortality in elderly men when comparing the highest to the lowest tertile of cocoa intake. Another study in postmenopausal women by Mink et al.[3] showed an RR of 0.90 (95% CI, 0.86-0.95) for incident CHD, and 0.88 (95% CI, 0.82-0.96) for total mortality for the highest to the lowest quintile of flavanone consumption. Decreased cardiovascular-related deaths were also noted in an observational study in which subjects consumed cocoa as their main beverage.

The mechanisms involved could include 3 actions: (1) antioxidant activity that would reduce oxidative stress, (2) improvement of endothelial function of blood vessels via increase of nitric oxide (NO), and (3) increased intracellular free calcium concentration and activation of endothelial estrogen receptors. Vasomotor function was improved by 47% in a randomized, controlled, double-blind, crossover study comparing the effect of high- and low-flavanol chocolate given to 16 CHD patients for a month. An increase in the number of endothelial progenitor cells, which are responsible for repair of damaged vasculature, was also seen.

Effects on blood pressure (BP) were studied by Grassi et al.[4] in hypertensive patients with impaired glucose tolerance, showing a 3.83 mmHg decrease in systolic BP and 3.92 mmHg decrease in diastolic BP in those consuming high-flavanol chocolate compared to those consuming white chocolate. A possible mechanism of action was brought to light in a study showing inhibition of angiotensin-converting enzyme (ACE) activity and increased NO in human endothelial cells (P<0.01) after consumption of dark chocolate. Another study showed no effect of 70% cacao dark chocolate (50 g/day) on BP. A meta-analysis concluded that chocolate causes a mean change in systolic BP of -3.2 ± 1.9 mmHg and diastolic BP of -2.0 ± 1.3 mmHg (P=0.003).

Cholesterol-lowering effects have also been explored. One study using dark chocolate reported a decrease in total cholesterol (-6.5%; P<0.0001) and low-density lipoprotein (LDL) cholesterol (-7.5%; P<0.0001), with no effect on serum high-density lipoprotein (HDL) cholesterol, or triglycerides (TG). Another study also showed a decrease in cholesterol along with an increase in HDL cholesterol (1.16 ± 0.08 vs. 1.26 ± 0.08 mmol/L; P=0.05). A meta-analysis by Jia et al.[5] for short-term chocolate consumption concluded that it lowered LDL cholesterol by 5.87 mg/dL and total cholesterol by 5.82 mg/dL, but that this was highly dependent on the amount of cocoa consumed and health

status of the patients (no effects were observed in healthy participants). A second meta-analysis showed that dark chocolate was associated with a reduction in serum LDL (-5.90 mg/dL [95% CI, -10.47 to -1.32]) and total cholesterol (-6.23 mg/dL [95% CI, -11.60 to -0.85]), but not with an increase in HDL cholesterol or TG.

Insulin resistance was decreased after consumption of flavanol-rich dark chocolate (P<0.0001), along with enhanced insulin sensitivity (P<0.05) and improved beta-cell function (P=0.035), compared to no effect for white chocolate. A second study also saw an improvement in insulin resistance (0.31% reduction).

Reduction in platelet aggregation has also been reported in one study following 100 g of dark chocolate consumption. A possible mechanism of action could be reduced adenosine diphosphate (ADP)/collagen-activated platelet-related primary hemostasis due to a reduction in activated glycoprotein IIb/IIIa surface proteins.

According to the authors, the existing literature, while showing effects, has the limitations of short duration of studies; lack of clear notation of type or amount of chocolate used, or separation of dark and milk chocolate, which may have led to an underestimation of effects; lack of clarity of optimal intake level; lack of recording of polyphenol content; and heterogeneity of studies making interpretation difficult.

Future studies should pay attention to these factors, as well as to separating out lifestyle factors. The authors conclude by noting that, "Long term, double-blind, randomized controlled trials with hard clinical endpoints are needed before recommending cocoa or its products as a treatment option in patients with high risk for CHD or for healthy individuals. In the meantime, it would be safer to consume dark chocolate only in moderate amounts."

—Risa Schulman, PhD

References

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