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File: ■ Cocoa (*Theobroma cacao*)
■ Endothelial Function
■ Hyperglycemia
■ Atherosclerosis

HC 091221-458

Date: October 15, 2012

RE: Cocoa Flavanols May Contribute to Vascular Health

Grassi D, Desideri G, Necozione S, et al. Protective effects of flavanol-rich dark chocolate on endothelial function and wave reflection during acute hyperglycemia. *Hypertension.* September 2012;60(3):827-832.

Cocoa (*Theobroma cacao*) and chocolate have been shown to improve endothelial function in healthy, hypertensive, and glucose-intolerant individuals; however, the effects have never been tested in hyperglycemic individuals. Hyperglycemia can cause endothelial dysfunction and impair nitric oxide (NO) production, both of which can lead to atherosclerosis. This randomized, single-blind, controlled, crossover study focused on the effects of a flavanol-rich dark chocolate (DC) on flow-mediated dilation (FMD), wave reflections, blood pressure (BP), endothelin-1 (ET-1), and oxidative stress, before and after an oral glucose tolerance test (OGTT), in healthy subjects.

Subjects included 12 healthy individuals (5 males and 7 females; mean age=28.2 ± 2.7 years) recruited from the staff at the San Salvatore Regional Hospital and University of L'Aquila, Italy. Smokers, those on prescription medications, and intensive athletes were excluded. After a 7-day cocoa-free run-in period, subjects were given 100 g DC bars (Cioccolato Bonajuto; Antica Dolceria Bonajuto; Sicily, Italy) or isocaloric 100 g white chocolate (WC; control) bars (Milka®; Kraft Foods; East Hanover, New Jersey) to consume in the morning for 3 days. After a 7-day washout period, subjects were crossed over to the other treatment. The DC contained 447 mg of epicatechin, 59 mg of catechin, and 14 mg of quercetin, whereas the WC only contained trace amounts of polyphenols. Subjects were instructed to refrain from eating other flavanol-rich foods and to maintain their usual level of exercise. Instructions were given on how to modify diets so that the chocolate calories did not add to usual caloric intake. The subjects were also told not to disclose to the researchers which treatment they were on in order to maintain blinding.

Before and after the OGTT, the following measures were taken: FMD; office systolic BP (SBP) and diastolic BP (DBP); pulse contour analysis for measuring stiffness index (SI), reflection index (RI), and peak-to-peak time (PPT); and serum ET-1 and 8-iso-prostaglandin $F_{2\alpha}$ (8-iso-$PGF_{2\alpha}$).

Baseline clinical characteristics were all within the average range. DC consumption statistically significantly improved FMD compared to WC consumption (8.51 ± 0.69% vs. 7.88 ± 0.68%; P=0.03). After WC consumption, FMD fell statistically significantly in both groups at 60, 120, and 180 minutes post-glucose load, but not in the DC group; DC consumption prevented FMD attenuation (P=0.0007).

DC ingestion decreased baseline SI (P<0.05) and RI values (59.3 ± 12.4% vs. 50.4 ± 8%; P=0.04), and increased PPT (265.5 ± 35.1 ms vs. 295.6 ± 36.2 ms; P=0.05); whereas SI and RI values increased and PPT decreased with WC treatment.

Baseline SBP and DBP were not different between the groups. DBP statistically significantly increased after 30, 60, and 90 minutes following WC treatment; DC treatment attenuated this increase induced by the glucose load for both SBP (P<0.0001) and DBP (P<0.019).

ET-1 statistically significantly increased after WC treatment at 30, 60, 90,120, and 180 minutes following glucose load. DC treatment prevented this increase (P=0.0023). A similar pattern was seen for isoprostane (8-iso-$PGF_{2\alpha}$) with WC consumption at 30 and 60 minutes post-glucose load, which DC consumption attenuated (P=0.0008).

No significant differences were observed regarding glucose and insulin responses during the OGTT, homeostasis model assessment of insulin resistance, quantitative insulin sensitivity check index, or homeostatic model assessment of β-cell function.

This study showed that short-term treatment of healthy subjects with DC can increase endothelium-dependent vasodilation and reduce wave reflections, lipid peroxidation, and ET-1 levels, and protect from acute vascular alterations induced by a glucose load. The authors did not examine mechanisms of action in this study, but note that effects on NO and oxidative stress have been documented. Limitations of the study include its small size, limited duration, and incomplete blinding. In addition, the isocaloric nature of the control did not necessarily reflect real chocolate consumption patterns, though chocolate itself does abide by the recommended proportions of nutrients. Further studies should test the ability of lower doses to cause similar effects.

—Risa Schulman, PhD