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FILE: ■ Dark Chocolate (*Theobroma cacao*)
■ C-Reactive Protein
■ Inflammation

HC 100181-363

Date: October 31, 2008

RE: Effects of Dark Chocolate Consumption on Anti-inflammatory Marker in Healthy Italians

di Giuseppe R, Di Castelnuovo A, Centritto F, et al. Regular consumption of dark chocolate is associated with low serum concentrations of C-reactive protein in a healthy Italian population. *J Nutr.* 2008;138:1939–1945.

Cocoa (*Theobroma cacao*), a constituent of chocolate, contains high concentrations of flavonoids, which have been shown to have antioxidant properties. In vitro studies have shown that cocoa flavanols promote endothelium-dependent vessel relaxation and modulate the response of cytokines and eicosanoids, which are involved in the inflammatory response. Clinical studies have shown that dark chocolate consumption increases serum high-density-lipoprotein (HDL; so-called "good cholesterol"), but does not affect serum total or low-density-lipoprotein cholesterol (LDL; so-called "bad cholesterol"). An observational study showed that habitual cocoa intake was associated with a reduction in blood pressure, cardiovascular disease (CVD) risk, and all-cause mortality. The authors hypothesized that the consumption of dark chocolate would decrease concentrations of C-reactive protein (CRP)—a marker of inflammation considered an independent indicator of CVD. Thus, the objective of this study was to evaluate the relation between dark chocolate consumption and serum CRP concentrations in healthy Italian adults from the Moli-sani project—an ongoing cohort study of health in Europe.

A total study population of 10,994 men and women aged ≥ 35 years were randomly recruited between March 2005 and July 2007. Those with CVD, consuming a special diet, or undergoing pharmacologic treatment for diabetes, hypertension, or dyslipidemia were excluded. Of the remaining subjects, 2 subpopulations were extracted: 1317 subjects who never ate chocolate (control group; 51% men) and 824 subjects who regularly ate dark chocolate (test group; 55% men). Dietary intakes were evaluated by using the food-frequency questionnaire of the European Prospective Investigation into Cancer and Nutrition. Body mass index and blood pressure were measured, and fasting blood samples

were collected from all subjects for the measurement of serum lipid, glucose, and high-sensitivity CRP concentrations. Relations between chocolate consumption and CRP concentrations were evaluated by univariate and multivariate-adjusted analyses of variance.

The median intake of dark chocolate in the test group was 5.7 g/d. Compared with the control group, the test group was younger; had a lower body mass index and systolic blood pressure; consumed more nuts, seeds, dairy products, fish, coffee, and tea; and consumed less meat, alcohol, and refined cereals. Chocolate consumption was positively associated with total energy intake. Serum CRP concentrations >3 mg/L (indicating higher levels of inflammation) were higher in the control group (19%) than in the test group (14%). Age-adjusted serum CRP concentrations were significantly lower ($P < 0.0005$) in the test group (1.06–1.20 mg/L) than in the control group (1.24–1.36 mg/L). [Editor's note: While this statement is correct, the mis-association of the higher figures with the group having lower values and vice versa is not correct, as is shown by the reverse figures in Table 4.] After multivariate adjustment (age, sex, social status, and physical activity), dark chocolate consumption was still inversely associated with serum CRP concentrations. A J-shaped dose-response curve was observed between dark chocolate consumption and serum CRP concentrations; that is, after an initial decrease in serum CRP with increasing consumption of dark chocolate, the curve reached a plateau at a higher intake (6.7 g/d, corresponding to 20 g of chocolate every 3 days) and reversed above this consumption level. Glucose and lipid concentrations were not significantly different between the test and control groups.

Dark chocolate consumption was associated with lower systolic blood pressure, healthier dietary habits, lower serum CRP concentrations, lower physical activity, higher energy intakes, and lower body mass index. The cross-sectional nature of the study, however, did not enable determination of causality, and it is possible that the participants inaccurately reported their chocolate intakes. The findings suggest that "regular consumption of small doses of dark chocolate may reduce inflammation" and thereby potentially lower the risk of an adverse cardiovascular event. The authors recommend that additional studies be conducted to elucidate the mechanisms responsible for the observed inverse association between dark chocolate consumption and lower serum CRP concentrations.

—Brenda Milot, ELS

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