

## Cocoa, diabetes, and hypertension: should we eat more chocolate?<sup>1,2</sup>

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Biochemical and physiologic associations among hypertension, diabetes, and cardiovascular disease have grown steadily, supported by basic, clinical, and epidemiologic research. The possibilities for treating these pathologies include pharmacologic approaches, lifestyle adjustment, and diet modification. The identification of foods that have cardiovascular health benefits has become a major public health objective. There is now a large body of epidemiologic evidence that supports the concept that diets rich in fruit and vegetables attenuate or delay the onset of certain chronic diseases, including cardiovascular and related diseases (1). However, the physiologic and molecular mechanisms by which fruit and vegetables act to reduce the risk of vascular disease remain elusive. The existence of data showing that the health benefits of fruit and vegetables are causally linked to their flavonoid content is a starting point from which to address such mechanistic uncertainties. With respect to cardiovascular health, one class of flavonoids, the flavanols, is receiving increasing attention (2). Cacao, tea, grapes, and grapefruit are examples of edible plants that are rich in flavanols. Translational research that relates the consumption of these foods to cardiovascular health is of particular interest.

In this issue of the Journal, Grassi et al (3) report that the consumption of dark chocolate improves glucose metabolism and decreases blood pressure. They studied 15 healthy young adults with typical Italian diets that were supplemented daily with 100 g dark chocolate or 90 g white chocolate, each of which provided 480 kcal. The polyphenol contents of the dark and white chocolate were assumed to be 500 and 0 mg, respectively. The subjects were divided into 2 groups, each of which ingested one of the types of chocolate for 15 d, ingested no chocolate for a subsequent 7 d, and then ingested the other chocolate for an additional 15 d. The authors found that the dark chocolate supplement was associated with improved insulin resistance and sensitivity and decreased systolic blood pressure, whereas white chocolate had no effect. No data were shown on the changes in blood pressure during each study, although such data might have been useful to differentiate the potential short- and long-term effects of dark chocolate consumption. Also, it would have been useful to show insulin sensitivity and blood pressure values for each individual to assess a potential association between these 2 events. Nevertheless, the findings of this study are of particular interest in terms of identifying potentially healthy foods.


Cocoa is rich in flavanols, which are one class of polyphenols that are present in plants as nonconjugated molecules, including

(-)-epicatechin and (+)-catechin, and as oligomers of these molecules, also named procyanidins. The concentration of flavanols in any chocolate depends on both the flavanol content of the cacao plant and the procedures used for transforming the cacao into chocolate. Then, the accurate assessment of the flavanol content is pertinent to interpreting its biological effects. Although Grassi et al indicated that 100 g of the chocolate they used contains 500 mg polyphenols, they did not report how they determined this quantity. Furthermore, the reference cited justifying the use of this special kind of chocolate did not explain how the claimed polyphenol content was determined (4). Nevertheless, chocolate containing 500 mg polyphenol could contain a relatively high concentration of flavanols (100–200 mg). Therefore, the interpretation that flavanols and procyanidins contained in the dark chocolate used in this study may be associated with the observed health effects is tempting but remains speculative.

As Grassi et al indicated, the regulation of nitric oxide (NO) production by the flavanols present in dark chocolate could explain its effects on both insulin sensitivity and blood pressure. This interpretation is supported by other data that have shown effects of flavanol on NO production (5). However, it is uncertain how flavanols interact with the biological system to increase NO bioavailability. Insulin-mediated cell signaling could be one mechanism, because insulin can modulate several signaling molecules involved in NO-synthase regulation (6). A second mechanism could be an oxidant-mediated cell signaling, because flavanols can modulate oxidative stress and the cell redox state, which in turn defines NO availability and NO-synthase activity (7). A third mechanism could involve the renin-angiotensin system (8) through the inhibition of the angiotensin-converting enzyme (9). This inhibitory effect favors NO production by preventing the induction of NADPH-oxidase activity and the resulting production of superoxide anion, which trigger NO oxidation to peroxynitrite (10), and by preserving bradykinin at adequate concentrations to maintain NO-synthase activity and NO production (11). These potential mechanisms of NO regulation, insulin- and oxidant-mediated signaling, and angiotensin-converting enzyme function may be physiologically related (12).

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Other studies with other flavanol-containing foods, such as tea and wine, have shown similar effects on vascular and blood pressure regulation (2). The identification of healthy foods and the understanding of how food components influence normal physiology will help to improve the health of the population. This could be especially relevant with regard to untreated pathologic states. Indeed,  $\approx 30\text{--}40\%$  of hypertensive persons in the United States and  $\approx 60\text{--}75\%$  of those in Canada and Europe go untreated. In the United States,  $\approx 5$  million persons have undiagnosed diabetes. Further studies in larger groups and in diabetic and hypertensive individuals are needed to confirm the healthy effects of chocolate, cocoa, and flavanols. 

The author had no conflict of interest related to this article.

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