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File: ■ Cocoa (*Theobroma cacao*, Malvaceae)
■ Flavanols
■ Absorption, Distribution, Metabolism, and Excretion

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RE: Absorption, Distribution, Metabolism, and Excretion of Cocoa Flavanols Depend on Numerous Factors

Cifuentes-Gomez T, Rodriguez-Mateos A, Gonzalez-Salvador I, Alañon ME, Spencer JPE. Factors affecting the absorption, metabolism, and excretion of cocoa flavanols in humans. *J Agric Food Chem*. September 9, 2015;63(35):7615-7623.

The beneficial effect of flavanols on cardiovascular health has been the subject of extensive research. In this review, the authors examine the current literature on the absorption, distribution, metabolism, and excretion (ADME) of cocoa (*Theobroma cacao*, Malvaceae) flavanols in humans and the extent to which factors such as food matrix and nutrient-nutrient interaction influence flavanol ADME in order to better understand how dietary flavanols affect cardiovascular health.

Flavanols are a specific class of flavonoids found in various foods, with tea (*Camellia sinensis*, Theaceae) and cocoa being among the richest sources**.** The primary flavanols in cocoa beans are (−)-epicatechin (EC), ranging in content from 0.1 to 13.5 mg/g, and oligomeric and polymeric procyanidins, with contents ranging from 18 to 27 mg/g and from 9 to 16 mg/g, respectively. In milk and dark chocolates, the EC content ranges from 0.18 to 1.25 mg/g, oligomeric procyanidin content ranges from 1.1 to 11.2 mg/g, and polymeric procyanidin content ranges from 0.8 to 7.0 mg/g.

Many factors, such as the structure of the food matrix, processing, and the interaction of flavanols with other nutrient and non-nutrient components, can influence the extent to which EC is absorbed or metabolized from cocoa and other flavanol-rich foods in the small intestine, yielding structurally related EC metabolites. The amount consumed and individual genetic polymorphisms in relevant metabolic enzymes can also influence their absorption. Flavanols are typically consumed in complex matrices, as natural or formulated and manufactured products. Most studies investigating the absorption and metabolism of EC after cocoa or chocolate consumption report that it takes between one and two hours for maximum plasma flavanol concentrations.

Reviewing studies comparing the effect of matrix delivery on EC bioavailability, one study compared solid and liquid chocolate consumption in five subjects, which revealed no significant effect of delivery on the appearance of circulating EC metabolites after two hours.[1] In another study, total flavanol and maximum concentration were significantly higher following intake of a cocoa drink compared with that of solid chocolate.[2] Along with two other studies (one reporting a maximum concentration of two hours after intake of a cocoa drink and the other reporting a maximum concentration of 3.2 to 3.8 hours after solid chocolate consumption), the data "suggest faster absorption rates and earlier peak plasma concentrations of EC from liquid food matrices relative to solid chocolate, probably due to a rapid digestive release and rapid stomach-emptying from liquids compared to solids," write the authors.

The effects of carbohydrates, largely the addition of sugar, on flavanol absorption and metabolism have been well studied and, based on the data from available studies, the authors suggest "it seems plausible that carbohydrate-rich meals may act to enhance flavanol absorption without influencing metabolism, although further research is required to confirm such initial observations." The authors identified only one study investigating the effect of lipid (butter; 28.6 g of fat) co-consumption,[3] which found no lipid-flavanol interaction on total flavanol absorption.

Other studies suggest that the interaction of dietary flavanols with proteins does alter the bioavailability and bioefficacy of the flavanols. Milk is the commonly investigated protein, but the fat composition in milk is a confounding factor in determining the specific effects of milk protein on flavanol absorption. In recent studies, investigators suggest that neither whole nor skimmed milk influence flavanol absorption. Other studies evaluating the effects of milk on the flavanol metabolite excretion profile in urine report contradictory results. The authors conclude that milk does not have an overall effect on the absorption of cocoa flavanols, but it might have a small impact on the profile of metabolites produced and their excretion.

Some evidence, although scarce, suggests that monomeric flavanols and procyanidins significantly decrease during fermentation, drying, roasting, and alkalization. Specifically, fermentation ranging from four to ten days reduced EC levels by about 80% when compared to unfermented cocoa beans.[4,5] Drying cocoa beans produces losses in EC levels of around 14%.[6] The effects of roasting cocoa beans vary, with one study showing that EC degradation occurs at roast temperatures above 70°C, and only 18% of EC remaining after roasting at 120°C.[5] Less significant losses at 140-150°C were reported in another study.[6] Analyzing commercially available cocoa powders with various degrees of alkali processing revealed a 40% reduction in total flavanols for those lightly alkalized, a 22% reduction for medium alkalized powders, and an 11% decrease for heavily alkalized cocoa powders.[7] Update June 20, 2018: It has been brought to our attention that this article incorrectly reflects what the original article stated - "Compared to natural cocoas, which averaged 34.6 mg/g ± 6.8 total flavanols, the light alkali-processed cocoas had 39.8% as much total flavanols (13.8 ± 7.3 mg/g), the medium alkali processed cocoa had 22.5% as much total flavanols (7.8 ± 4.0 mg/g), and the heavily alkali processed cocoa had 11.2% as much total flavanols (3.9 ± 1.8 mg/g)." So, the heavily alkali-processed cocoa had the least amount of flavanols with the lightly alkali-processed having 40% total flavanols compared to natural cocoas. (http://www.worldcocoafoundation.org/wp-content/uploads/files_mf/miller2008.pdf)

Available data suggest a good correlation between the intake level of cocoa and plasma EC levels, which increased in an intake-dependent fashion.[8] According to the authors, further studies are needed to fully establish how the absorption, metabolism, and excretion of cocoa flavanols in humans are affected by intake level, food processing techniques, drugs, and genetic polymorphisms, as well as the influence of age, sex, reproductive status, and dietary habits on flavanol intake and health markers. "Such data will help to define a minimum amount of flavanols necessary to achieve population-based health benefits and thus contribute to the creation of flavanol-specific dietary guidelines and recommendations."

—*Shari Henson*

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