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File: ■ Cranberry (*Vaccinium macrocarpon)* Juice
■ Flavonoids and Phenolic Acids
■ Bioavailability and Bioactivity

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RE: Flavonoids and Phenolic Acids in Cranberry Juice Are Bioavailable and Increase Antioxidant Activity in Older, Healthy Subjects

McKay DL, Chen CY, Zampariello CA, Blumberg JB. Flavonoids and phenolic acids from cranberry juice are bioavailable and bioactive in healthy older adults. *Food Chem*. February 1, 2015;168:233-240.

Cranberries (*Vaccinium macrocarpon*), which are rich in phenolic phytochemicals, have been associated with antibacterial, antimutagenic, anticarcinogenic, antiangiogenic, and antioxidant activities. Phenolic compounds have antioxidant and anti-inflammatory properties and can modulate enzyme activity and gene expression. However, most of the evidence supporting these activities was determined from in vitro studies and animal models. Furthermore, more research is needed to understand the bioavailability and metabolism of cranberry phenolics in humans. The authors have expanded on their earlier study which examined the pharmacokinetics of cranberry anthocyanins which showed most anthocyanins appeared in plasma within 1 to 2 hours after consumption.[1] In the study reported here, the authors conducted a single-dose pharmacokinetic trial to examine the bioavailability and bioactivity of a broader array of phenolics from cranberry juice.

The study evaluated the acute (24-hour) bioavailability of flavonoids and phenolic acids from a single dose (237 mL) of a double-strength (54% juice), low-calorie, low-sugar cranberry juice cocktail (CJC) (Ocean Spray; Lakeville-Middleboro, Massachusetts). The principal phenolics in the beverage were the anthocyanins peonidin-3-galactoside and -arabinoside, the anthocyanins cyanidin-3-arabinoside and -galactoside, and the flavonols hyperoside and quercetin. Total phenolic content of the single dose of CJC was 188.5 mg.

The study involved 10 healthy, nonsmoking men and postmenopausal women aged 50 to 70 years. The subjects were asked to consume foods low in phenolics for 48 hours before the trial. The day before the trial, the subjects were fed the same meal low in phenols and refrained from food and beverages except for water for the next 12 hours to provide baseline values.

After administration of CJC, blood samples were collected periodically for 10 hours and at 24 hours. Blood samples were assessed for phenolic acids, flavonoids, and total antioxidant capacity: oxygen radical absorbance capacity (ORAC), ferric reducing antioxidant power (FRAP), and total antioxidant performance (TAP). Susceptibility of low-density lipoprotein (LDL) to Cu^{2+}-induced lipid oxidation (LDL oxidation) was also measured.

The authors found the concentration of total phenolics detected in plasma reached a peak of 34.2 µg/mL between 8 and 10 hours after CJC consumption; in urine, the peak was 269.8 µg/mg creatinine, occurring 2 to 4 hours earlier. In plasma, protocatechuic acid, quercetin, and vanillic acid were the most predominant contributors to this total. In urine, protocatechuic acid and 4-OH-phenylacetic acid were the most predominant. Anthocyanins were detected in the urine samples of all subjects at widely varying concentrations. The predominant anthocyanin detected in both plasma and urine was peonidin-3-galactoside.

The authors "provide here the first observation that PAC-A2 [proanthocyanidin-A2] can be quantified in the urine of healthy volunteers following an acute dose of CJC." This finding suggests that PAC-A2 in urine could be a biomarker of cranberry intake and compliance since it does not occur in other plant foods.

Among the 3 assays measuring antioxidant capacity, the mean TAP values increased the most after CJC consumption. Correlations were observed between ORAC and protocatechuic acid (P=0.00), quercetin (P=0.00), epicatechin (P=0.001), 4-OH-3-methoxy-phenylacetic acid (P=0.018), gentisic acid (P=0.045), and 3,4-OH-phenylacetic acid (P=0.03), and between TAP and gentisic acid (P=0.01) and protocatechuic acid (P=0.036). No correlations were observed between FRAP and plasma phenolics. According to the authors, "This is the first study to correlate changes in individual cranberry metabolites, e.g., protocatechuic acid, with an array of measures of antioxidant capacity over time."

Consistent with earlier studies, the authors detected cranberry anthocyanins in plasma and urine and a marked inter-individual variation in anthocyanin pharmacokinetics. "The considerable inter-individual variability in the pharmacokinetics of these phytochemicals appears likely due to individual differences in phase II enzyme polymorphisms as well as composition of gastrointestinal microbiota," the authors write.

"In conclusion, we have demonstrated that phenolic acids and flavonoids, in CJC, are bioavailable and increase antioxidant capacity in healthy older adults. We also found that PAC-A2 is detectable in plasma and quantifiable in urine after an acute dose of cranberry juice," the authors state.

—Shari Henson

Reference

[1]Milbury PE, Vita JA, Blumberg JB. Anthocyanins are bioavailable in humans following an acute dose of cranberry juice. *J Nutr*. June 2010;140(6):1099-1104.

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