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> File: ■ Cranberry (*Vaccinium macrocarpon*) ■ Urinary Tract Infections ■ Cardiovascular Health

> > HC 021411-498

Date: June 13, 2014

## RE: Review of Cranberry Effects on Urinary Tract Infections and Cardiovascular Health

Blumberg JB, Camesano TA, Cassidy A, et al. Cranberries and their bioactive constituents in human health. *Adv Nutr*. 2013;4(6):618-632.

Berry consumption has been associated with numerous health benefits. In particular, cranberry (*Vaccinium macrocarpon*) is a rich source of polyphenolics that has exhibited biological effects both in vitro and in vivo. This review focuses on the bioactive components of cranberries and their potential effects on urinary tract infections (UTIs) and cardiovascular health.

## Bioactive Components of Cranberry

Some of the bioactive components of cranberries include flavan-3-ols, anthocyanins, phenolic acids, ursolic acid derivatives, and flavonols. These compounds vary in concentration depending on the cultivar and how the berries have been processed (e.g., into juice or powder). In particular, anthocyanins are lost the most from processing. Cranberry flavan-3-ols consist of monomers (e.g., epicatechin and catechin) and oligomers/polymers known as A-type proanthocyanidins (A-type PACs). The monomer components of A-type PACs (predominantly epicatechin) are connected together by a carbon-carbon bond and a distinctive ether bond (A-type linkage). A-type PACs are a unique class of condensed tannins that are found almost exclusively in cranberries (most plants consist of B-type PACs) and are generally in the range of two to ten degrees of polymerization. These fruits are also unique because they consist of sugar derivatives from all six types of anthocyanins, a class of compounds that contribute to the color of cranberries. Phenolic acids are also present, such as hydroxycinnamic acids and the more prevalent hydroxybenzoic acid. Terpenoids are also found in the form of two rare derivatives of ursolic acid. In addition, flavonols are present mostly as glycosides, especially as quercetin 3-galactoside.

## Cranberries and Urinary Tract Health

Cranberries are well known for their use in the treatment of UTIs. Research has indicated that cranberry products may prevent bacteria (P-fimbriated *E. coli*) from adhering to bladder epithelial cells, and thereby treat or prevent UTIs. Another potential mechanism may involve the effects that cranberries have on the gut microbiota. All of

these effects are mostly attributed to A-type PACs.

Clinical trials with cranberry products have produced inconsistent results. Out of two meta-analysis studies, one study indicated cranberry products had significant effects on UTIs. This inconsistency in study results may be due to the variability in study designs, cranberry products, and study compliance. It has also been noted that the pathogenesis of UTIs may be different for young children, sexually active young adults, and the elderly population. In one randomized double-blind study, cranberry juice consumption significantly reduced urinary bacteria in an elderly population after one month. Several studies with adult women that had recurrent UTIs indicated that cranberry juice and other cranberry products generally reduced the incidence of UTIs, although not always significantly. This variability may be due to the lack of placebos, appropriate placebos, or poor study designs. In three independent randomized trials, it was found that cranberry juice had beneficial effects in children with recurrent UTIs. Moreover, one trial indicated there was a correlation with anti-adherence effects and clinical outcomes.

## Cranberries and Cardiovascular Health

Cranberries may also provide cardiovascular benefits by reducing cardiovascular disease (CVD) risk factors associated with dyslipidemia, diabetes, hypertension, inflammation, oxidative stress, endothelial dysfunction, arterial stiffness, and platelet function. Clinical trials have shown that cranberry products improved lipid profiles for patients with hypercholesterolemia, diabetes mellitus, and hypertriglyceridemia. Other studies showed no effects in healthy subjects or patients with CVD. Although several animal studies have indicated cranberries reduce blood pressure, no clinical studies have shown these effects in patients with diabetes mellitus and CVD. Moreover, cranberry supplementation did not improve glycemic control in patients with type 2 diabetes mellitus.

Several studies also showed that cranberry products improved plasma antioxidant capacity and decreased oxidized low-density lipoprotein cholesterol (LDL-C). There is, however, no proof that these effects prevent oxidative damage to lipids or to DNA. Consumption of cranberry juice also reduced inflammatory markers in middle-aged men, while other studies indicated cranberry bioactive components had no effects. In terms of vascular function, cranberry supplementation or bioactive components showed some improvements, although inconsistently, on endothelial vasodilation and arterial stiffness. Different populations and doses may contribute to these inconsistencies. Studies of other polyphenolic-rich beverages and the cranberry anthocyanin, delphinidin-3-glucoside, suggest that cranberry consumption may reduce platelet aggregation.

The benefits of compounds for which cranberries are a good source have been evaluated in several observational studies. Anthocyanin intake has been shown to lower the risk for coronary heart disease (CHD), particularly in younger populations. Studies suggest that these effects may be attributed to improvements in arterial stiffness and blood pressure. There is less evidence that flavonols, flavan-3-ols, or PACs prevent CHD.

Overall, it appears that consumption of cranberries improves UTIs; although more studies are needed that carefully assess dose responses in specific populations and use cranberry products with fully characterized phytochemical profiles. It is less clear how effective cranberries are on cardiovascular health, but one potential mechanism may involve acute improvements on endothelial function. Regardless, much more research is needed to properly evaluate the benefits that cranberry products have on cardiovascular health. Even so, the authors suggest that guidance regarding increased consumption of cranberry and other berry fruits to help achieve a healthy dietary pattern is warranted based on their large array of phytochemicals and micronutrients.

-Laura M. Bystrom, PhD

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