

Anti-adhesive Properties of Cranberry Metabolites in Urine

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Consumption of cranberry juice products aids in the prevention of urinary tract infections (UTIs). While many clinical studies have recognized the health effects of cranberries, the mechanism of action is not well understood. To prevent UTIs, cranberry components have to reach the urinary tract without being degraded during digestion. *In vitro* experiments were designed to determine whether cranberry metabolites in urine affect the adhesion forces of bacteria and how long this activity lasts. Using an atomic force microscope (AFM) the adhesion forces between clinical strains of *E. coli* and a silicon nitride surface were determined. Five clinical strains of *E. coli* were attached to glass slides and incubated for 45 minutes in urine samples from volunteers who consumed 16 oz (480 mL) of cranberry juice cocktail (CJC) or 16 oz. of water (control). Urine samples were collected at 0, 2, 4, 6, and 8 hours after consumption. Bacteria exposed to urine after consumption of CJC had significantly lower adhesion forces than *E. coli* exposed to the urine after consumption of water. Further, the adhesion forces of bacteria exposed to urine with CJC metabolites decreased with time from 1.25 ± 0.75 nN (0 hrs after consumption) to 0.38 ± 0.2 nN (8 hrs after consumption), while there was no statistical significant difference between any of the urine samples from the volunteer consuming water. These results indicate that cranberry compounds are not completely degraded during digestion and remain active against bacterial adhesion for more than 8 hrs.

The Beneficial Effects of Long-Term Cranberry Supplementation on Aging

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Diets rich in botanicals are known to have numerous beneficial effects on human health. Many studies have demonstrated the anti-microbial infection, anti-inflammation and anti-

carcinogenesis actions of numerous botanicals. However, not much is known about the effects of botanical consumption on aging and aging-related changes. Here we will present a multi-species study to address these questions. We initially conducted a screen to evaluate the effects of several botanicals on aging using Mexican fruit flies as the model. We found that a botanical containing cranberry and oregano significantly increased lifespan of flies. To further investigate the anti-aging effects of cranberry in higher organisms, we fed male Fisher-344 rats of 6-month old were a cranberry-containing diet for 16 months, and evaluated the effects of a long-term cranberry supplementation on the age-related changes in endocrine pancreas in terms of insulin secretion and beta-cell mass. We found that cranberry delays the age-related decline of fasting plasma insulin and increases beta-cell mass compared to the control rats. This suggests that cranberry can maintain the capacity of beta-cell mass to compensate for changes in functional demand for insulin with increasing age. Taken together, our multi-species study reveals the anti-aging effects of cranberry supplementation and further supports the health benefits of cranberry consumption in human.

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Anti-Cancer Activities of Cranberry Phytochemicals in Human Tumor Cell Lines

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Growing evidence suggests that the fruit of the North American cranberry (*Vaccinium macrocarpon*) contains a variety of bioactive compounds that limit processes associated with carcinogenesis. Cranberries may potentially provide some protection against the development of certain cancers. Biologically active compounds in cranberry fruit include flavonoids (anthocyanins, flavonols and A-type proanthocyanidins), substituted cinnamic acids, carotenoids, and triterpenoids such as ursolic acid. These constituents are diverse and therefore may exert their biological effects by a variety of pathways.

This presentation will provide an overview of recent findings on the anti-cancer properties of cranberry constituents by various researchers. Collaborative studies between scientists at UMass Dartmouth and the University of Prince Edward Island on the content, composition and anti-carcinogenic effects of bioactive phytochemicals from cranberry fruit will be highlighted. Our *in vitro* studies show that compounds in the fruit including ursolic acid, proanthocyanidins and quercetin derivatives limit the proliferation of human breast (MCF-7), colon (HCT116 and HT-29) and prostate (DU145) tumor cell lines in a dose-dependent manner. Cranberry extracts and compounds also induced apoptosis, reduced tumor colony formation and inhibited activities linked to tumor metastasis, suggesting several possible protective mechanisms.

Cranberry Proanthocyanidins Bind to Pathogenic *Escherichia coli* and Inhibit Epithelial Cell Invasion

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Liquid chromatography and matrix assisted laser desorption/ionization time-of-flight mass spectrometry allows characterization of structural changes in cranberry proanthocyanidins (PACs) that result from juice processing. Our research indicates that juice processing affects PACs structure and distribution in juice and presscake and the extent to which anthocyanins are linked to PACs through acetaldehyde derived covalent bonds. Our research also indicates that degree of polymerization of cranberry PACs and variations in target molecules on bacteria surface (O-antigens, proteins in the outer membrane and adhesions) influence agglutination properties of pathogenic *Escherichia coli* and *E. coli* invasion of mouse prostate epithelial cells and Caco-2 intestinal epithelial cells. Cranberry PACs were isolated from juice and fractionated by degree of polymerization. The ability of the PACs to agglutinate *E. coli* and inhibit epithelial cell invasion increased with in PAC fractions with a higher degree of polymerization. Cranberry PACs isolated from press cake were more effective in agglutination and inhibition of epithelial cell invasion than PACs from cranberry juice and the press cake PAC fraction contained PACs of higher degree of polymerization. The implication is that PAC composition of cranberry fruit, juice and byproducts can be manipulated to inhibit pathogenic bacteria in the gut. Since the gut is a potential reservoir for uropathogenic *E. coli* prevention of gut colonization may help prevent *E. coli* urinary tract infection.
