

Cranberry for Prevention of Urinary Tract Infections

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Traditionally, cranberry has been used for the treatment and prophylaxis of urinary tract infections. Research suggests that its mechanism of action is preventing bacterial adherence to host cell surface membranes. Systematic reviews have concluded that no reliable evidence supports the use of cranberry in the treatment or prophylaxis of urinary tract infections; however, more recent, randomized controlled trials demonstrate evidence of cranberry's utility in urinary tract infection prophylaxis. Supporting studies in humans are lacking for other clinical uses of cranberry. Cranberry is a safe, well-tolerated herbal supplement that does not have significant drug interactions. (*Am Fam Physician* 2004;70:2175-77. Copyright© 2004 American Academy of Family Physicians.)

American cranberry (*Vaccinium macrocarpon*) is one of only three species of fruit native to North America. The other species are blueberry (*Vaccinium angustifolia*) and bilberry (*Vaccinium myrtillus*). Cranberry typically grows in bogs and is a member of the same family as blueberry and bilberry. Massachusetts and Wisconsin are the main areas of present-day commercial production of cranberry.¹ The ripe fruit was used medicinally by Native Americans for the treatment of bladder and kidney ailments. Pilgrims called the fruit "craneberry" because the stem and flower resembled the head, neck, and beak of a crane.¹ Therapeutic applications of cranberries documented during the 17th century included the relief of blood disorders, stomach ailments, liver problems, vomiting, appetite loss, scurvy, and cancer.² Before the advent of antibiotics, cranberry continued to be a popular treatment for urinary tract infections (UTIs).³

Pharmacology

The mechanism of action of cranberry has prompted much scientific discussion. It was first hypothesized that acidification of the urine contributed to an antibacterial effect. The current proposed mechanism of action focuses primarily on cranberry's ability to prevent bacterial binding to host cell surface

membranes. In vitro studies have observed potent inhibition of bacterial adherence of *Escherichia coli*⁴ and other gram-negative uropathogens.⁵ Cranberry has been found to specifically inhibit hemagglutination of *E. coli* by expression of types 1 and P adhesin⁶ through the component compounds fructose⁷ and proanthocyanidins.⁸

Uses and Efficacy

URINARY TRACT INFECTION

In the United States, one of every five women has been reported to have a lifetime incidence of UTI.⁹ Of these women, 3 percent experience recurrent disease.⁹ Eleven million women receive medication for UTIs annually.¹⁰ A recent Cochrane Database systematic review¹¹ found no randomized trials assessing the effectiveness of cranberry juice in the treatment of UTIs and concluded that there is no evidence to support its use. There is much greater evidence-based information available for the use of cranberry in UTI prophylaxis.

The first relatively large placebo-controlled studies^{12,13} assessing efficacy were conducted in elderly women living in long-term care facilities. The findings of these studies^{12,13} showed that cranberry significantly reduced the frequency of bacteriuria and pyuria, but these were not intention-to-treat analyses. A 1997 study, published as a letter in *The Jour-*

TABLE 1
Key Points About Cranberry

Efficacy	UTI prophylaxis: modest effect UTI treatment: evidence lacking
Adverse effects	May increase urinary oxalate levels
Interactions	No significant herb-drug reactions have been reported.
Dosage	Varies depending on preparation. Cranberry extract tablets: 1 tablet (300 to 400 mg) twice daily; unsweetened juice: 8 oz three times daily
Cost	Tablets: \$10 to \$15 for 30-day supply Unsweetened juice: varies, depending on brand
Bottom line	Safe botanical medicine; effective in UTI prophylaxis

UTI = urinary tract infection.

nal of Family Practice,¹⁴ used a younger cohort of women and was the first study to use cranberry extract tablets rather than juice. Results showed that the cranberry concentrate was more effective than placebo in reducing the occurrence of UTIs.¹⁴ However, only 10 women completed the study.¹⁴ Another pair of studies^{15,16} found cranberry ineffective in decreasing bacteriuria in children with neurogenic bladder requiring intermittent catheterization. A Cochrane Database systematic review,¹⁷ citing small sample sizes and the poor quality of available trials, determined that there was no reliable evidence of effectiveness of cranberry in UTI prophylaxis.

However, since 2001, two good-quality studies have been published. The first trial¹⁸ of 150 women consisted of three arms: (1) cranberry/lingonberry juice; (2) probiotic supplementation with *Lactobacillus GG* drink; and (3) no intervention for 12 months. Findings were a statistically significant 20 percent reduction in absolute risk of infection in women receiving cranberry (number needed to treat: 5) compared with no effect in the probiotic-supplementation and no-intervention groups.¹⁸ Most recently, a randomized, placebo-controlled trial¹⁹ of

150 women over a 12-month period found that cranberry juice and cranberry extract tablets significantly decreased the number of patients having at least one symptomatic UTI per year.

OTHER USES

A single experimental study²⁰ showed that the “high-molecular-weight constituent” of cranberry juice that inhibits the adherence of *E. coli* was effective in reversing and inhibiting the coaggregation of a large portion of dental plaque bacteria. Cranberry also has been recommended as an adjunctive treatment for *Candida* infections. In vitro studies^{21,22} have shown that cranberry juice exerts fungistatic effects against dermatophytic and other fungi but has no effect against *Candida albicans*. There are no controlled trials in humans evaluating the effectiveness of cranberry in treating fungal infections.

Contraindications, Interactions, Adverse Effects

Cranberry has a record of safety, although specific long-term safety data are lacking. No significant herb-drug interactions have been reported. A single study²³ found that cranberry may increase the absorption of vitamin B₁₂ in patients who also are taking proton pump inhibitors and that it may allow the kidneys to metabolize weakly alkaline drugs (such as antidepressants and opioids) more rapidly, thus reducing their effectiveness. A small study²⁴ found a significant rise in urinary oxalate levels, prompting a caution that regular use of cranberry may increase the risk of kidney stone formation in patients with a history of oxalate calculi.

Dosage

Each of the reviewed studies used different doses and formulations of cranberry, including unsweetened cranberry juice, cranberry juice cocktail, and cranberry extract tablets. The recommended dosing for UTI prophylaxis is based on the most recent positive randomized controlled trial¹⁹ that used one tablet of concentrated cranberry extract (300 to 400 mg) twice daily, or 8 oz of pure unsweetened cranberry juice three times daily.

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Final Comment

Cranberry appears to be a safe, herbal choice for UTI prophylaxis and has relatively good tolerability. The most recent studies^{18,19} have found that the use of cranberry for up to 12 months is safe and moderately effective. More evidence is necessary to recommend its use for clinical indications other than UTI prophylaxis. Care should be taken when recommending cranberry for long-term use in patients who are known urinary oxalate stone formers. No significant herb-drug reactions with cranberry have been reported. Reviews the efficacy, safety, and cost of cranberry.

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Strength of Recommendations

Key clinical recommendation	Label	References
A recent Cochrane Database systematic review found no randomized trials assessing the effectiveness of cranberry juice in the treatment of UTIs and concluded that there is no evidence to support its use.	B	11
Most recently, a randomized, placebo-controlled trial of 150 women over a 12-month period found that cranberry juice and cranberry extract tablets significantly decreased the number of patients having at least one symptomatic UTI per year.	A	19

UTI = urinary tract infection.