# Cranberry juice and urinary tract infections

**ROGER WYNDHAM** MB BS, FRACP

**A recent Cochrane review has concluded that there is evidence to recommend daily cranberry juice for the prevention of symptomatic UTIs in women.**

Women are often affected by urinary tracts infections (UTIs), up to 11% of women experiencing an episode in a year, and 50% reporting an episode in their lifetime. Recurrences are also common; various studies have shown that 25 to 40% of women will have had a further episode by the end of one year, and 3% or more will continue to have recurrences. These frustrate and distress patients, and may also contribute to the development of antibiotic resistance. The cost to the community is large, around US$1.6 billion annually in the USA.[1]

Personal hygiene appears to have little influence on the risk of recurrence; maintenance of a high fluid intake and post-coital voiding appear logical practices, but neither has been shown to be effective in clinical trials. Cranberry juice has long been advocated for the prevention and treatment of UTIs, but until recently there have been few clinical trials testing its efficacy.

## What is cranberry?

The cranberry, *Vaccinium macrocarpon*, is a native North American bog plant belonging to the Ericaceae family, and is related to the lignonberry and, less closely, to the blueberry and bilberry and the heathers, heaths, rhododendrons and azaleas.[2] The indigenous Americans have used cranberry medicinally for years, and therapeutic applications documented in the 17th century include the relief of fever, gut disturbance, liver disorders and scurvy.

Dr Wyndham is a Renal Physician, Concord and Nepean Hospitals, Sydney, NSW.

Cranberry juice can be consumed either as a juice or in a tablet form; many people find the juice pleasant to take and it has no known side effects. This makes it a logical candidate for further consideration.

## Mode of action in UTI prevention

It was shown in the 1880s that cranberry ingestion increased the urinary excretion of hippuric acid, due to the conversion of the benzoic acid in the berries. This was thought to be the explanation for its use in treating urinary infection, as hippuric acid was known to be bacteriostatic. More recent work, however, has shown that the appearance of hippurate is slight and transient and not sufficient to affect bacterial growth. In 1984, Sobota first reported inhibition of bacterial (*Escherichia coli*) adherence by cranberry juice and proposed a scientific basis for its use in the treatment of UTI.[3]

*E. coli* possess on their surface fine hair-like structures that adhere to receptors on epithelial cell surfaces. These fimbriae are of two types, type 1 fimbriae (which are mannose-sensitive) and P-fimbriae (which are mannose-resistant). Fructose in cranberries appears to inhibit adhesion by type 1 fimbriae, while proanthocyanidin (PAC) pigments extracted from the berries have been shown to inhibit the activity of P-fimbriae.[4,5] The onset of action is within two hours of ingesting cranberry products and the effect may last up to 10 hours; it is independent of bacterial antibiotic resistance. Cranberry juice reduces adhesion forces of P-fimbriated *E. coli* by altering the conformation of polymers on the cell surface;[6] the effect is unaltered by changes in pH.

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## What is the evidence?

A Cochrane review in 2004 on the use of cranberries for the prevention of UTI concluded that there was evidence to recommend cranberry juice for the prevention of symptomatic UTIs in women, but there was little evidence for its use in treatment of UTI, in the management of asymptomatic bacteriuria, or in the prevention of UTIs in children.[7] Although the reviewers found many trials of cranberry products, only two well conducted randomised controlled trials (RCTs) were worthy of inclusion in a meta-analysis.[8,9] Others suffered from poor study design, particularly with regard to randomisation and blinding of treatment. Some trials not included in the Cochrane analysis because of methodological deficiencies detailed large numbers of dropouts or withdrawals, indicating that cranberry juice may not be an acceptable long term treatment. The trials also indicated the lack of any consistency as to the preparation type and the dose and duration of therapy to yield effective treatment.

Since the Cochrane review, one further well controlled RCT has been published.[10] The outcome details of the three studies are presented in the Table. The first two studies targeted women with a history of symptomatic UTIs and the third included institutionalised women at high risk of UTIs. The outcome in each was the prevention of further symptomatic UTIs.

The Kontiokari study included 150 women, mean age 30.3 years, with a history of *E. coli* UTI in the previous 12 months.[8]

**Table. Evidence for the use of cranberry juice in preventing UTIs**

| Study authors | Preparation | Dose | No. patients completing/enrolled | Outcome (≥ 1 UTI) | Relative risk | p-value |
|---|---|---|---|---|---|---|
| **Kontiokari, et al (2001)[8]** | Cranberry–lingonberry juice | 50 mL (7.5 g cranberry) | 46/50 | 8 (16%) | 0.43 | 0.023 |
| | Lactobacillus GG drink | 100 mL | 46/50 | 19 (39%) | | |
| | No intervention | | 45/50 | 18 (36%) | | |
| **Stothers (2002)[9]** | Cranberry juice* | 250 mL tds | 48/50 | 20% | 0.62 | <0.05† |
| | Cranberry tablets | bd | 50/50 | 18% | 0.56 | |
| | Placebo juice/tablets | | 50/50 | 32% | | |
| **McMurdo, et al (2005)[10]** | Cranberry juice | 150 mL bd | 134/187 | 7 (5%) | 0.51 | 0.12 |
| | Placebo beverage | 150 mL bd | 127/189 | 14 (11%) | | |

*Cranberry concentrate 1:30 was given either in 250 mL juice or as tablets; †p-value for overall reduction in number of UTIs for cranberry preparations.

Subjects were randomised to one of three study arms: cranberry–lingonberry juice (50 mL containing 7.5 g cranberry concentrate and 1.7 g lingonberry concentrate daily for six months); a lactobacillus GG preparation (100 mL, five days a week for one year); or no intervention. The cranberry group had fewer UTIs at six months. Although *E. coli* was the causative bacterium in 80% of episodes, the proportion of episodes caused by *E. coli* did not differ between the study groups.

Stothers recruited 150 sexually active women aged 21 to 72 years with a history of recurrent UTI.[9] They were randomised to receive for 12 months one of cranberry juice plus placebo tablets, placebo juice plus cranberry tablets (1:30 parts concentrated juice) or placebo juice plus placebo tablets; tablets were taken twice daily, juice 250 mL three times daily. Both cranberry juice and cranberry tablets produced a significant (>50%) reduction in the number of symptomatic UTIs experienced, and only one in five women in the active treatment groups had a significant UTI, compared with one in three in the placebo group.

The McMurdo study included patients aged 60 years and over who were inpatients of a geriatrics assessment unit or rehabilitation units for elderly people in Tayside, Scotland.[10] Of 376 participants randomised, 14 of 189 patients receiving 150 mL of placebo beverage twice daily developed a symptomatic UTI, compared with seven of 187 patients receiving 150 mL of cranberry juice twice daily. Thirteen of 14 infections in the placebo group were due to *E. coli*, compared with four of seven in the treatment group. Side effects were few, with no significant difference between treatment and placebo groups.

## Conclusions

From the available evidence, it appears that the daily intake of cranberry juice or cranberry extracts may help prevent UTIs in women. In these studies the type of cranberry preparation is different, as is the dose and the dosing frequency. It is clear that further well designed studies are required to define the role of cranberries in the management of UTI more precisely.

It is difficult to make recommendations, but 150 mL of cranberry juice or one tablet (1:30 parts concentrated juice) twice a day would seem a reasonable regimen. MT

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**DECLARATION OF INTEREST: None.**