Cranberry products to reduce recurrence of urinary tract infections in older people: a narrative review

Mandy R Bryce¹, Colby JC Bryce²

ABSTRACT
Urinary tract infection (UTI) is common in women and older people. Cranberry is effective in preventing UTI. We searched databases of Ovid, Cochrane, Medline, CINAHL, and Google Scholar using keywords (cranberry, urinary tract infection, antibiotic resistance, elderly, and geriatric) to identify systematic reviews that contained randomised controlled trials (with control and experimental groups) that investigated the effectiveness of cranberry interventions in improving urinary tract health in older adults with or without recurrent UTI. A total of six systematic reviews were included. The number of participants in each review ranged from 1494 to 4473, with >10 000 participants overall. All six reviews included participants aged >65 years. Many participants were female and from age-care and hospital settings. All six reviews found some level of support for the cranberry groups to have greater reduction in UTI recurrence than the placebo groups. Nonetheless, one review found non-significant trends. Trends towards a reduction in UTI were noted among older people who regularly consumed cranberry products. More specifically, twice daily consumption of cranberry capsule (containing at least 36 mg proanthocyanidins) was most protective against bacterial adhesion and virulence in the urinary tract.

Key words: Aged; Anti-bacterial agents; Drug resistance, bacterial; Urinary tract infection; Vaccinium macrocarpon

INTRODUCTION
Urinary tract infections (UTI) account for nearly 25% of all infections, with 50% to 60% of women and older adults having one UTI in their lifetime.¹ Women are ten times more likely than men to have UTI owing to women's shorter urethra. Older women are more likely to have recurring UTI and its associated complications owing to lowered immunity.²,³ Traditional treatment for UTI involves antibiotics, which when incorrectly used or overused can result in bacterial drug resistance and hence increased hospital stays, medical costs, and mortality. UTI is increasingly resistant to first-line antibiotic therapy. The efficacy of ampicillin had decreased from 71% in 1990 to 62% in 1999.⁴,⁵ The World Health Organization states that “without urgent action, we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill”.⁶ Undiagnosed UTI can result in pain, behavioural issues, and chronic renal and urological disease.⁴,⁵ Thus, introduction of alternative natural and preventative therapy is crucial for the safety of future generations.

Cranberry (vaccinium macrocarpon) is a native American bog plant closely related to blueberry and bilberry. It is an antioxidant and has a role in fighting infection in the mouth and stomach, preventing cancer cell growth, and promoting cardiovascular health.³ Cranberries contain quinic acid, malic acid, citric acid, glucose, and fructose. Consumption
of cranberries can reduce bacteria, particularly *Escherichia coli* (which is normally found in the intestine but may get caught in the urinary tract) from adhering to the uroepithelial cells that line the walls of the bladder. Cranberry holds back the growth of the hair-like structures on the bladder wall that *E. coli* adheres to. The active component in cranberries for this process is proanthocyanidins.

In the treatment of UTI, cranberries have been used in various dosages: from up to 300 mL in juice form to up to 10 000 mg in capsule form. Although cranberry products are dietary supplement rather than medication, associations between prophylactic cranberry products and urinary tract health have been reported.

**MATERIALS AND METHODS**

Databases of Ovid, Cochrane, Medline, CINAHL, and Google Scholar were searched using keywords (cranberry, urinary tract infection, antibiotic resistance, elderly, and geriatric) to identify systematic reviews that contained randomised controlled trials (with control and experimental groups) that investigated the effectiveness of cranberry interventions in improving urinary tract health in older adults with or without recurrent UTI. Reference lists of these reviews were also searched. Reviews that did not include older people were excluded, as were reviews that involved <1000 participants and that older than 10 years (published prior to 2012).

**RESULTS**

A total of six systematic reviews were included. The number of participants in each review ranged from 1494 to 4473, with >10 000 participants overall. All six reviews included participants aged >65 years; the mean age of participants in the reviews was up to 81 years. Many participants were female and from age-care and hospital settings. Each of the six reviews included studies that involved different cranberry products (capsule, tablets, and juice).

All six reviews found some level of support for the cranberry groups to have greater reduction in UTI recurrence than the placebo groups (Table). Nonetheless, one review found non-significant trends. Trends towards a reduction in UTI were noted among older people who regularly consumed cranberry products. More specifically, twice daily consumption of cranberry capsule (containing at least 36 mg proanthocyanidins) was most protective against bacterial adhesion and virulence in the urinary tract.

Some reviews reported that regular consumption of as little as 50 mL of cranberry juice could reduce the recurrence of UTI, and that daily dosages of 240 to 300 mL of cranberry juice cocktail could prevent 50% of the recurrences of UTI and reduce bacteriuria, and that cranberry was nearly as effective as low-dose antibiotics for UTI prevention in some women and did not cause antibiotic resistance.

**DISCUSSION**

Natural remedies for UTI can lessen reliance on antibiotics and reduce the risk of antibiotic resistance. Although antibiotic therapy is more efficacious in reducing UTI than cranberry products, it is associated with higher risk of severe adverse events and antibiotic resistance. Whereas cranberry capsule consumption is more effective than placebo in decreasing the rate of recurrent UTI, with fewer undesirable events.

Nonetheless, some studies within the reviews reported no benefit of cranberry product consumption. This may be due to extraneous variables that must be taken into consideration. First, there is a need to identify a more acceptable formulation of cranberry. Second, in some studies within the reviews, the participant withdrawal rate was up to 55%, and the adherence to treatment rate was <80% owing to unrelated infections requiring antibiotic therapy, moving away from the area of research, and gastrointestinal symptoms and drug interactions (mainly caused by warfarin). Third, in some studies within the reviews, the sample size was too small to have power to detect a realistic significant difference between treatment groups. Fourth, low compliance and high withdrawal/dropout were associated with palatability/acceptability of the cranberry products, primarily cranberry juice. Fifth, many studies did not report the amount of the active ingredient the product contained; products may not have sufficient potency or may not be accurately replicated. Not all cranberry products contained enough active proanthocyanidins for clinical efficacy.
Future studies should focus on cranberry capsules and stipulate the amount of the active ingredient the product contained. Lastly, heterogeneity was noted across studies.16 There are limitations to the current review. Approximately 17 of 85 studies within the reviews were also included in other reviews. Nonetheless, this should not result in a significant bias on the conclusion given >10,000 participants were represented across the six reviews. In addition, the current review relied exclusively on published studies and may result in publication bias.17 Furthermore, the overall conclusions of each review were difficult to compare given each review differs in inclusion/exclusion criteria, participant age, health status, setting, type of cranberry product, and dosage used.

**CONCLUSION**

Trends towards a reduction in UTI were noted among older people who regularly consumed cranberry products. More specifically, twice daily consumption of cranberry capsule (containing at least 36 mg proanthocyanidins) for multiple months appears to be most effective and generally well-tolerated. With the emergence of antibiotic resistance, alternative natural remedies for UTI should be considered.

### CONTRIBUTORS

All authors designed the study, acquired the data, analysed the data, drafted the manuscript, and critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

### CONFLICTS OF INTEREST

All authors have disclosed no conflicts of interest.

<table>
<thead>
<tr>
<th>Review</th>
<th>No. of studies and participants included</th>
<th>Intervention</th>
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<tr>
<td>Beerepoot et al,11 2013</td>
<td>17 studies; 2165 women with a mean age of ≤79.9 years</td>
<td>Cranberry-containing products, Urovac, oral immunostimulant OM-89, vaginal oestrogens, acupuncture, oral oestrogens, and lactobacilli prophylaxis</td>
<td>Overall, cranberry juice and tablets decreased urinary tract infection recurrence.</td>
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<tr>
<td>Gill et al,12 2020</td>
<td>10 studies; &gt;2000 women aged &gt;45 years (most &gt;65 years)</td>
<td>Cranberry juice, cranberry capsules, cranberry extract, trimethoprim, estriol cream, intravaginal oestrogen ring, lactobacillus, and placebo</td>
<td>Specifically, cranberry capsules were found to have some favourable data and were as such recommended as a therapeutic option to prevent UTI in women aged &gt;45 years</td>
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<tr>
<td>Hisano et al,13 2012</td>
<td>15 studies; &gt;2000 women and inpatients with and without urinary catheters aged &gt;60 years</td>
<td>Cranberry juice, cranberry capsules, lactobacillus, trimethoprim, methenamine hippurate, water, and placebo</td>
<td>Despite reduced symptomatic UTI, results of each study were non-significant and therefore the evidence to recommend cranberry for UTI prevention in older people or those with urinary catheters was inconclusive.</td>
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<tr>
<td>Jepson et al,14 2012</td>
<td>24 studies; 4473 men and women with and without urinary catheters with a mean age of ≤81 years</td>
<td>Cranberry juice/concentrate, cranberry tablets or capsules, no treatment, water, methenamine hippurate, antibiotics, lactobacillus, placebo</td>
<td>A small trend was found with fewer symptomatic UTIs in people taking cranberry products but did not significantly reduce overall occurrence compared with placebo or no treatment groups in those with or without urine catheter.</td>
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<tr>
<td>Tambunan and Rahardjo,15 2019</td>
<td>9 studies; 1542 women aged ≤79 years</td>
<td>Cranberry juice, cranberry capsules, cranberry powder, placebo</td>
<td>Cranberry, especially cranberry capsule consumption, had a significant effect on reducing the incidence of recurrent UTI, compared with placebo, with minor adverse events. Antibiotic use had greater efficacy but was associated with a higher risk of severe adverse events.</td>
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<tr>
<td>Wang et al,16 2012</td>
<td>10 studies; 1494 participants from nursing homes and hospitals with a mean age of ≤78.6 years</td>
<td>Cranberry juice, cranberry capsules, cranberry-containing products, placebo</td>
<td>Consumption of cranberry-containing products was protective against UTIs in women with recurrent UTIs, female populations, cranberry juice drinkers, and people using cranberry-containing products more than twice daily.</td>
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of proanthocyanidins daily). Future studies should focus on cranberry capsules and stipulate the amount of the active ingredient the product contained. Lastly, heterogeneity was noted across studies.16

There are limitations to the current review. Approximately 17 of 85 studies within the reviews were also included in other reviews. Nonetheless, this should not result in a significant bias on the conclusion given >10,000 participants were represented across the six reviews. In addition, the current review relied exclusively on published studies and may result in publication bias.17 Furthermore, the overall conclusions of each review were difficult to compare given each review differs in inclusion/exclusion criteria, participant age, health status, setting, type of cranberry product, and dosage used.

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All authors have disclosed no conflicts of interest.
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DATA AVAILABILITY

All data generated or analysed during the present study are available from the corresponding author on reasonable request.

REFERENCES