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Review Article

Cranberries For Preventing Urinary Tract Infection: A Systematic Review

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ABSTRACT

The unique polyphenols found in cranberries (*Vaccinium macrocarpon*) include flavonoids and phenolic acids, which have been shown to have protective properties against urinary tract infections (UTIs), the second most prevalent infection type in the world. Due to high recurrence rates and antibiotic resistance, UTIs can cause serious morbidity, particularly in healthy females. The search for prophylactic and therapeutic alternatives to antibiotics for the prevention and treatment of UTIs is ongoing. In contrast to cranberries, which are frequently suggested in conventional medicine for the prevention of UTIs, probiotics have become a novel substitute for antibiotics in the fight against these infections and are the focus of recent studies in this field. In addition to the most prevalent bacteria that cause simple UTIs, uropathogenic *Escherichia coli* (UPEC), other etiological It is necessary to clearly define the data supporting viable non- drug therapies because more than 50% of women experience at least one urinary tract infection (UTI) episode in their lifetime and antimicrobial resistance is becoming more common. To manage UTIs, this study compares the effects of cranberry juice, cranberry pills, and more liquids.

INTRODUCTION

One of the most prevalent bacterial infections is urinary tract infection (UTI). Throughout their lives, more than 50% of females [1], [2], and 20% of males [3] experience at least one episode; in youngsters, this is the most prevalent bacterial infection [4]. The bacteria that cause UTIs are becoming more resistant to antibiotics, even though antimicrobials have historically had a high

rapid cure rate [5]. According to certain evaluations, medication-resistant bacteria were found in more than 90% of UTIs, with the majority of them being resistant to two or more medicines [6, 7]. Now is the moment to take action and find evidence- based non-drug therapies for the prevention and treatment of UTIs, as microbial resistance is beginning to reduce the effectiveness of antibiotics in this regard [8].

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It has been suggested that increasing the amount of liquids a patient consumes or offering them cranberry juice or tablets may be beneficial. There is a wide range of research to support this, though, and studies showing the health benefits of cranberries [10], [11] seem to occur just as frequently as those that do not [12], [13]. The lack of research to independently ascertain whether any therapeutic effects seen in cranberries are caused by the corresponding rise in fluid [14] or particular components within the cranberry itself further complicates matters. Clinicians who want to use literature to inform recommendations on UTI treatment options have difficulties because of these situations and factors. The European Association of Urology guidelines, for example, take into account the most recent research on the effectiveness of cranberry products in preventing urinary tract infections.



Figure 1: Cranberries

Sign And Symptoms Of Uti:

Here are the common signs and symptoms of Urinary Tract Infections (UTIs):

Typical Symptoms:

1. Burning sensation while urinating (dysuria)
2. Frequent urination (frequency)
3. Urgent need to urinate (urgency)
4. Cloudy or strong-smelling urine
5. Blood in urine (hematuria)
6. Pain in lower abdomen (suprapubic pain)
7. Fever and chills
8. Discomfort or pain in the pelvic area

Additional Symptoms:

1. Urinary incontinence
2. Nocturia (waking up to urinate at night)
3. Straining to urinate
4. Feeling of incomplete bladder emptying
5. Urinary tract spasms
6. Flank pain (pain in sides or back)
7. Nausea and vomiting

Severe Symptoms (Seek Medical Attention Immediately):

1. Severe back or side pain
2. High fever (over 103°F)
3. Vomiting or nausea
4. Blood in urine with clots
5. Difficulty starting or stopping urination
6. Complete inability to urinate
7. Severe abdominal pain

METHODS:

2.1. Search Strategy:

From the beginning to February 3, 2020, we searched Medline, Embase, The Cochrane Library, Amed, Web of Science, and Cinahl. Additionally, we looked for pertinent studies on Google Scholar, the WHO International Clinical Trials Registry Platform (ICTRIP), and Clinical Trials.gov. Cranberry, vaccinium, and urinary tract infection were among the search phrases used, although they weren't the only ones (see Table S1 for the detailed search strategy). Neither time nor language limitations were applied. To discover pertinent studies, we spoke with local specialists and cranberry product makers Ocean Spray and Trophikos, LLC. We then manually examined the bibliographies of a few chosen papers to locate further relevant studies. Cranberry product manufacturers were not involved in any other aspects of this systematic review. Two reviewers (OAG) separately evaluated each citation for eligibility.

2.2. Eligibility Criteria and Study Selection:

For patients 18 years of age and older, we included randomized controlled trials (RCTs) that compared the efficacy of cranberry extract with any other medication for acute, uncomplicated UTIs. Cohort studies, case-control studies, and quasi-randomized studies evaluating the effectiveness of cranberries in treating acute urinary tract infections were also eligible. Cranberry extract had to be taken orally as juice, fruit, pills, tablets, or capsules to be included. Data that allowed the influence of cranberries on the outcome or outcomes of interest to be identified were needed in studies where a cranberry product was coupled with another intervention or exposure. At least one of our primary or secondary outcomes has to be reported by the included studies. The evaluation of participants' symptoms, clinical condition, and well-being (such as symptom load or time to symptom resolution) were the main outcomes.

2.1. Risk of Bias:

Using the Cochrane risk of bias tool, we evaluated the included studies' risk of bias. The risk of bias in the listed papers was evaluated independently by two reviewers (OAG and EAS), with differences being settled by discussion. The Oxford Levels of Evidence 2 criteria were used to categorize the hierarchy of evidence of the included studies.

2.1. Data Extraction:

Data on the study setting, participants, length, intervention and comparator, and outcomes were gathered from the included studies. RevMan was used to graphically depict the risk of bias across the research, and a summary table was utilized to display the findings of the included studies. Two reviewers (OAG and EAS) independently extracted the data, and disputes were settled by discussion. We presented the results narratively since we lacked the data necessary to undertake data synthesis.

1.1. Clinical study:

Clinical research on UTI prevention. In 1966, the first clinical study assessing cranberry's impact on the urinary tract was released. The effects of cranberry juice were reported by Papas et al. 30 in 60 bacteriuric patients who were given 480 milliliters of juice every day for three weeks. Following treatment, 53% of the participants experienced a positive response, and 20% saw a more modest benefit; nonetheless, the majority of the subjects experienced a recurrence of bacteriuria 6 weeks after treatment was discontinued. Clinical research on UTI prevention. In 1966, the first clinical study assessing cranberry's impact on the urinary tract was released. The effects of cranberry juice were reported by Papas et al. 30 in 60 bacteriuric patients who were given 480 milliliters of juice every day for three weeks. Approximately a dozen clinical trials assessing different cranberry products have been conducted since the Papas et al. study. The impact of cranberries in avoiding urinary tract symptoms has been examined in all of these follow-up trials. UTI was the main parameter examined in some of them, while bacteriuria was the main endpoint in others. Approximately a dozen clinical trials assessing different cranberry products have been conducted since the Papas et al. study. The impact of cranberries in avoiding urinary tract symptoms has been examined in all of these follow-up trials. UTI was the main parameter examined in some of them, while bacteriuria was the main endpoint in others. Patients with a variety of medical illnesses, elderly or pediatric patients, and sexually active adult women have all been evaluated in these trials. The pertinent prospective clinical trials involving cranberry products. Randomized studies that looked at adult women were published by Kontiokari et al., Stothers, and Walker et al. . 150 women were split into three groups in the open, randomized, controlled trial by

Kontiokari et al.. One group drank 50 mL of cranberry-lingonberry juice concentrate, which contained 7.5 g of cranberry concentrate and 1.7 g of lingonberry concentrate (lingonberries are another fruit in the *Vaccinium* genus); another group drank 100 mL of a lactobacillus drink. Randomized studies that looked at adult women were published by Kontiokari et al. Stothers, and Walker et al. No intervention was given to a third group. 16% of the cranberry group, 39% of the lactobacillus group, and 36% of the control group had one UTI recurrence following six months of treatment. For the cranberry group, this means a 20% decrease in absolute risk. Curiously, the percentage of women who experienced recurrence at 12 months was significantly lower in the cranberry group, indicating a residual effect supporting the theory that cranberries select for less adherent bacterial strains, even though the cranberry group stopped their treatment after 6 months (because the manufacturer stopped producing the juice. No intervention was given to a third group.

Drug Interaction:

Cranberries' main component, flavonoids, has been shown to affect the cytochrome P450 (CYP) enzyme, which breaks down drugs. Additionally, flavonoids inhibit aromatase, an enzyme essential to the manufacture of estrogen. Additionally, cranberry juice significantly lowers nifedipine oxidase (CYP3A4) activity, which results in a 39% decrease in oral clearance and an increase in the serum concentration/time curve (64). Cranberries' main component, flavonoids, has been shown to affect the cytochrome P450 (CYP) enzyme, which breaks down drugs. Additionally, flavonoids inhibit aromatase, an enzyme essential to the

manufacture of estrogen. Additionally, cranberry juice significantly lowers nifedipine oxidase (CYP3A4) activity, which results in a 39% decrease in oral clearance and an increase in the serum concentration/time curve.

MECHANISM:

Acidification Of Urine:

Cranberries were first used for their therapeutic qualities by Native Americans. Cranberries were utilized to treat a wide range of illnesses, such as fever, liver issues, stomach problems, and blood diseases. German doctors noticed in the 1880s that eating cranberries increased the amount of hippuric acid excreted in the urine. An article by Blatherwick from 1914 demonstrated that cranberries are high in benzoic acid, which is subsequently eliminated in urine as hippuric acid. Following this, there was a lengthy period when it was believed that the bacteriostatic mechanism of cranberry juice's benefits was based on the excretion of hippuric acid in the urine.

Antiadherent Properties In Mechanistic Studies:

The etiology of UTI begins with uropathogens adhering to uroepithelial cells. The idea that "reported benefits derived from the use of cranberry juice may be related to its ability to inhibit bacterial adherence" was first put forth by Sobota in 1984 (p. 1013). Sobota discovered that in more than 60% of the 77 clinical isolates of *E. coli* isolated from UTI patients, cranberry juice cocktails decreased adherence by more than 75%. After consuming 15 ounces (443.6 millilitres) of cranberry juice cocktail, 15 out of 22 subjects had notable antiadherence activity in their urine 1-3 hours later.

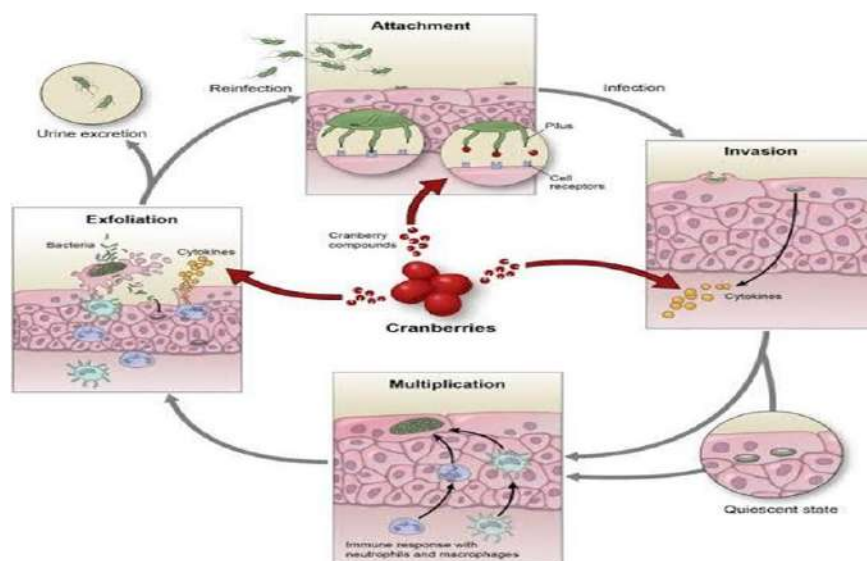


Figure 2: Effect of Cranberry Polyphenols

Advantages:

- 1. Prevent UTIs:** Cranberries may lower the risk of infection by preventing bacteria from sticking to the walls of the bladder and urinary system.
- 2. Decrease recurrence:** In people with a history of recurring infections, cranberry may help avoid repeated UTIs.
- 3. Relieve symptoms:** Cranberry may help lessen UTI symptoms including burning when urinating, frequent urine, and pain in the abdomen.
- 4. antibacterial effects:** Proanthocyanidins found in cranberries may have antibacterial qualities that prevent the growth of germs that cause urinary tract infections.
- 5. Anti-inflammatory effects:** Cranberries may help lower oxidative stress and inflammation in the urinary tract, which can lead to the development of UTIs.
- 6. Urinary tract health:** By preserving a healthy balance, cranberries may help to improve urinary tract health in general.

Disadvantages:

- 1. Prevent UTIs:** Cranberries may lower the risk of infection by preventing bacteria from

sticking to the walls of the bladder and urinary system.

- 2. Decrease recurrence:** In people with a history of recurring infections, cranberry may help avoid repeated UTIs.
- 3. Relieve symptoms:** Cranberry may help lessen UTI symptoms including burning when urinating, frequent urine, and pain in the
- 4. antibacterial effects:** Proanthocyanidins found in cranberries may have antibacterial qualities that prevent the growth of germs that cause urinary tract infections.

Limitation:

- 1. Limited scientific evidence:** Although some studies point to the potential health advantages of cranberries, more research is required as the evidence is not yet complete.
- 2. Variable efficacy:** Depending on the person, the severity of the UTI, and the cranberry product utilized, cranberry's effectiveness may vary.
- 3. Not a substitute for medical treatment:** Antibiotics or other prescribed therapies for UTIs, particularly for severe or recurring infections, should not be replaced by cranberries.

Interactions with medications: Blood thinners and other drugs may interact with cranberries and lose some of their effectiveness.

Application:

1. Dietary supplement: To avoid UTIs, cranberries are taken orally as capsules, tablets, or powders.
2. Juice: Cranberry juice, frequently combined with other juices, is used to treat or prevent UTIs.
3. Extracts: To provide a concentrated dosage of proanthocyanidins, cranberry extracts are added to foods, drinks, and supplements.
4. Tea: Dried cranberry fruit or powder is infused into hot water to make cranberry tea.
5. Food: Foods that include cranberries, like sauces, jellies, and dried cranberries, may help prevent UTIs.
6. Products for urinary tract health: Cranberry is frequently mixed with other components in products made especially to promote the health of the urinary system.

CONCLUSION:

Clinical research findings indicate that cranberry juice may help prevent UTIs in certain individuals. For sexually active adult women who have experienced a UTI in the past, the strongest evidence is currently available. Despite not having been tested precisely, cranberries seem to be useful in this demographic for preventing recurring UTIs. Cranberry eating lowers the incidence of bacteriuria in older adults, even though antibiotics are frequently not used to treat this condition. Cranberries, on the other hand, were not found to be helpful in any of the randomized clinical trials that assessed individuals who were at high risk of UTI, such as those who had neurogenic bladder disease. Clinical research findings indicate that cranberry juice may help prevent UTIs in certain individuals. Trial results consistently demonstrate a ~50% reduction in disease morbidity in the population that benefits most from the preventative impact of cranberry intake (sexually

active women with recurrent UTI). Taking into account the associated burden of long-term daily intake of the substance, this is a relatively minor advantage from a clinical perspective. The inconvenience of having to carry a daily supply of juice if twice or three times a day dosing is required for work, business, or vacation travel, as well as the amount of juice needed to ensure continuous availability, are equally important.

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