

The Longwood Herbal Task Force  
(<http://www.mcp.edu/herbal/default.htm>) and  
The Center for Holistic Pediatric Education and Research  
(<http://www.childrenshospital.org/holistic/>)

## Cranberry (*Vaccinium macrocarpon*)

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**Principal Proposed Use:** UTI prophylaxis

**Other Proposed Uses:** UTI treatment, urolithiasis, *Candida* infections

### *Overview*

The major clinical use for cranberry is to prevent recurrent urinary tract infections. Initially its benefits were attributed to acidification of the urine and then to its hippuric acid content, but more recent studies indicate that proanthocyanidins and other high molecular weight compounds found in cranberries interfere with the adhesion of uropathogenic bacteria to bladder mucosa. Epidemiologic data, case series and randomized controlled trials support the use of cranberry as a prophylactic agent for recurrent cystitis. There are no data supporting its use to treat acute cystitis, pyelonephritis, renal stones, *Candida* infections or any other medical condition. Cranberries should NOT be the sole treatment for UTI. Cranberries are presumed to be safe for use with other medications and during pregnancy, lactation and childhood.

### *Historical and Popular Uses*

A North American native, cranberry was historically used not only as a food, but also as medicine. It was introduced to European settlers by the Penobscot Tribe of Maine who used cranberries to treat kidney stones and other urinary problems<sup>1</sup>. Cranberries were also used to “clear the blood”, and as treatment for stomach ailments, liver problems, gall bladder disease, vomiting, appetite loss and scurvy<sup>2</sup>. Eastern Europeans adopted cranberry as a cancer remedy and antipyretic.

The part used both as food and medicine is the ripe fruit, which is extremely sour. Most cranberry preparations are highly sweetened with sugar, corn syrup, saccharin or fructose to

enhance palatability; cranberry cocktail juices are generally diluted 70% or more with water. Many commercial growers rely heavily on herbicides and pesticides, and residues of these products may find their way into the final cranberry preparation<sup>3,4</sup>. Exposure of residents who live close to cranberry bogs to these chemicals has raised concerns about carcinogenicity associated with these chemical exposures<sup>5</sup>.

Cranberry was a popular treatment for urinary tract infections (UTIs) prior to the introduction of antibiotics, and continues to be used widely as self-treatment for this purpose<sup>6,7,8</sup>. Randomized, controlled clinical trials as well as animal and *in vitro* data support its use specifically as a preventive agent for women prone to recurrent bladder infections.

Cranberry is also used as a home remedy for renal stones. Some herbalists recommend it to treat *Candida* infections. In 1997, cranberry was one of the top ten selling herbal remedies in the US<sup>9</sup>.

## **Botany**

*Medicinal species: Vaccinium macrocarpon* a.k.a. *V. oxycoccus* a.k.a. *Oxycoccus macrocarpus*<sup>10</sup>

*Common names:* American cranberry, bear berry, black cranberry, cranberry, low cranberry, trailing swamp cranberry

*Botanical Family:* Ericaceae, which also includes blueberry (*V. angustifolium*) and bilberry (*V. myrtillus*)

*Plant description:* Cranberry is a small evergreen shrub grown in bogs in damp forests and open ponds. It requires wet, boggy, acidic soil. It is rarely grown in home gardens. The pink flowers are followed by small reddish-black berries in June or July.

*Where it's grown:* Cranberry is mainly grown in the US from as far north as Alaska to as far south as Tennessee. Most commercial production is in Massachusetts and Washington<sup>11</sup>.

## *Biochemistry*

### **Cranberry: Potentially Active Chemical Constituents**

- Carbohydrates: glucose, fructose
- Organic acids: ascorbic acid, benzoic acid, citric acid, quinic acid, malic acid<sup>12</sup>
- Other compounds: proanthocyanidins, Vitamin C, triterpenoids, catechins, lectins

Cranberries are about 88% water.

During the 1800's German physicians noted an increase in urinary levels of *hippuric acid* in patients consuming large quantities of cranberries. Hippuric acid is bacteriostatic to many bacteria in an acidic environment; however, this is no longer believed to be cranberry's primary mechanism of action<sup>13,14,15</sup>.

*Fructose* appears to interfere with type 1 fimbrial adherence of some bacteria. Because most strains that rely on type 1 adherence are non-pathogenic, this is no longer felt to be an important effect<sup>16</sup>.

Among the previously unidentified components in cranberry juice are *proanthocyanidins*, which are also found in blueberries. Proanthocyanidins specifically interfere with type P fimbrial adherence of uropathogenic *E. coli*<sup>17</sup>; this is now thought to be the major mechanism by which cranberry juice reduces the risk of UTI<sup>16,18,19,20</sup>.

## *Experimental Studies*

### **Cranberry: Potential Clinical Benefits**

1. Cardiovascular: none
2. Pulmonary: none
3. Renal and electrolyte balance: Treatment and prevention of renal stones; reduction of odor associated with incontinence; urine acidifier. See also Antimicrobial.
4. Gastrointestinal/hepatic: none
5. Neuropsychiatric: none
6. Endocrine: none
7. Hematologic: none
8. Rheumatologic: none
9. Reproductive: none
10. Immune modulation: none
11. Antimicrobial: UTI prophylaxis; treatment of yeast infections; prevention of dental caries
12. Antineoplastic: none
13. Antioxidant: none
14. Skin and mucus membranes: none
15. Other/miscellaneous: none

1. **Cardiovascular:** none
2. **Pulmonary:** none
3. **Renal and electrolyte balance:** Treatment and prevention of renal stones; reduction of odor associated with incontinence; urine acidifier.
  - a. Treatment and prevention of renal stones. Historically, cranberry juice has been used to prevent and treat renal stones. Some modern herbalists also recommend it for this purpose<sup>21</sup>. One study showed a dose-dependent increase in urinary calcium excretion in normal men given cranberry juice<sup>22</sup>. However, increasing urinary calcium excretion may, in fact, increase the risk of renal stones. There are no animal or human studies evaluating the safety or effectiveness of treating renal stones with cranberry products.
  - b. Reduction of odor associated with incontinence

- i. *In vitro data:* none
  - ii. *Animal data:* none
  - iii. *Human data:* In case series of incontinent adults and studies of children who require intermittent catheterization, there have been significant subjective reductions in urinary odors in those given daily cranberry juice<sup>23,24,25,26</sup>. This effect appears to be secondary to its effect in reducing subclinical cystitis rather than on the tone of the urethral sphincter (See antimicrobial effects).
- c. Urine acidifier
- i. *In vitro data:* none
  - ii. *Animal data:* none
  - iii. *Human data:* In an early case series, adults who consumed large amounts of cranberries were noted to have acidic urine<sup>27,28</sup>. In normal subjects in one study, drinking cranberry juice with meals significantly reduced urinary pH for a few hours after the meal<sup>31</sup>. Urinary acidification effects appear to be transient<sup>22</sup>. A patient would need to drink approximately a quart or more (1500 ml) of cranberry juice daily to have a significant long-term impact on urinary acidity<sup>29,30</sup>.

Skin irritation frequently complicates urostomy sites, which often have an alkaline pH. To lower skin pH, ostomy nurses have recommended increasing intake of fluids, vitamin C and cranberries<sup>25</sup>. Based on cranberry's presumed ability to acidify urine, a pre- and post-test design was employed in 13 urostomy patients who were given 160 – 320 ml of cranberry juice daily for six months. Four of six patients who initially had significant peristomal skin problems noted significant improvement while taking cranberry juice, although the pH of the urine was unchanged; none of the other patients developed peristomal skin problems during their treatment with cranberry<sup>32</sup>. Since the urinary pH did not change, the benefits may have been coincidental or due to one of cranberry's other physiologic effects (See antimicrobial section below).

- 4. **Gastrointestinal/hepatic:** none
- 5. **Neuropsychiatric:** none
- 6. **Endocrine:** none

7. **Hematologic:** none
8. **Rheumatologic:** none
9. **Reproductive:** none
10. **Immune modulation:** none
11. **Antimicrobial:** UTI prophylaxis, treatment of yeast infections; prevention of dental caries

- a. UTI prophylaxis

- i. *In vitro data:* Recent studies have focused on cranberry's effects on bacterial adhesion to urinary epithelium rather than on urinary acidification or hippuric acid<sup>33</sup>. Women with recurrent urinary tract infections appear to be especially susceptible to adhesion by uropathogenic bacteria<sup>34</sup>. Uropathogenic strains rely on Type P fimbrial adhesion to allow colonization and infection<sup>6</sup>. The proanthocyanidins in cranberry and blueberry prevent Type P fimbrial adhesion of uropathogenic strains of *E. coli*<sup>16, 18, 19, 20, 35, 36</sup>.

Of 77 clinical isolates of *E. coli* tested in one study, cranberry juice significantly inhibited urinary epithelial adherence in over 60%<sup>37</sup>. In a series of 22 patients who drank 15 ounces of commercial cranberry juice cocktail, the urine of 15 showed significant anti-adherence activity one to three hours later<sup>37</sup>.

- ii. *Animal data:* Cranberry cocktail given to mice for 14 days resulted in an 80% inhibition of *E. coli* adhesion to uroepithelial cells<sup>37</sup>. Cranberry juice also interfered with adherence by other gram negative uropathogens<sup>19</sup>.
- iii. *Human data:* Historical use and case series support the use of cranberry juice in preventing urinary tract infections<sup>14, 15, 38, 39, 40, 41</sup>. For example, among 28 nursing home patients with a history of recurrent UTI who were given 4 - 6 ounces of cranberry juice daily for seven weeks, 19 had no further urinary tract infections during the seven week follow-up period<sup>42</sup>.

Data from case-control and cross-over trials also support the use of cranberry in preventing UTIs. In a case-control study comparing young women suffering from their first UTI with similar women who had not had urinary tract infections, drinking cranberry juice was associated with a 50% reduction in risk<sup>43</sup>. Among 10 young women with recurrent UTIs enrolled in a cross-over trial of prophylactic treatment

with cranberry (400 mg capsules BID), during the three months of treatment there were only six UTI's, compared with 15 UTI's during the three months on placebo ( $P < 0.05$ )<sup>44</sup>. In a randomized controlled cross-over trial of inpatients in a Dutch hospital, during the four weeks patients received cranberry juice (15 ml twice daily), there were significantly fewer cases of bacteriuria<sup>45</sup>.

In a double-blind controlled trial among 153 elderly women randomized to take 300 ml daily of a commercially available cranberry juice cocktail (26% cranberry juice) vs. similar appearing juice lacking cranberry, those taking cranberry juice had a significantly lower risk of bacteriuria over six months of follow-up<sup>46</sup>. This study was criticized because of a question as to whether the placebo group was really at a higher baseline risk of developing UTI's. There was a higher subjectively reported rate of bladder infections in the placebo group than in the cranberry group before the study began. However, even controlling for this apparent difference (there was actually no difference in the rate of microbiologically documented infections), the cranberry group still did significantly better than the placebo group.

These comparison studies evaluated cranberry's benefits as a preventive therapy, not as a primary treatment for patients with existing infections. There are no studies comparing the effectiveness of cranberry to antibacterial medications as a sole treatment for UTI's in adults or in children, nor in its effectiveness as an adjunct to standard therapy.

- b. Treatment of yeast infections. Some herbalists recommend cranberry as an adjunctive treatment for *Candida* infections<sup>47</sup>.
  - i. *In vitro data*: Cranberry juice exerted fungistatic effects against eight dermatophytic fungi and several other fungi, but no effects against *Candida albicans*<sup>48,49</sup>.
  - ii. *Animal data*: none
  - iii. *Human data*: There are no controlled trials evaluating the effectiveness of cranberry in preventing or treating dermal or systemic fungal infections either alone or as an adjunctive treatment.

- c. Prevention of dental caries. Dentists are interested in reducing bacterially-induced tooth decay, and are thus interested in substances like cranberry that may interfere with bacterial adherence to the teeth and gums.
  - i. *In vitro data:* The stability of dental plaque depends to some extent on bacterial interspecies adhesion or co-aggregation. In one study, 58% of co-aggregating bacterial pairs had a reversal of their co-aggregation by a high molecular weight constituent of cranberries<sup>50</sup>.
  - ii. *Animal data:* none
  - iii. *Human data:* There are no controlled trials evaluating the effectiveness of cranberry as a prophylactic treatment for caries. Due to the high sugar content of many cranberry juice cocktail preparations, caution should be used in recommending large amounts of these products to caries-prone persons.

12. **Antineoplastic:** none

13. **Antioxidant:** none

14. **Skin and mucus membranes:** none

15. **Other/miscellaneous:** none

## ***Toxicity and Contraindications***

*All herbal products carry the potential for contamination with other herbal products, pesticides, herbicides, heavy metals, and pharmaceuticals.*

*Furthermore, allergic reactions can occur to any natural product in sensitive persons*

*Allergic reactions have not been reported? Have been reported?*

*Potentially toxic compounds in cranberry: None*

*Acute toxicity: Drinking large amounts may cause diarrhea and stomach upset.*

*Chronic toxicity: None reported*

*Limitations during other illnesses or in patients with specific organ dysfunction: Due to the high sugar content of most commercial cranberry cocktail preparations (except those sweetened with artificial sweeteners), caution should be used in recommending large amounts of cranberry juice to patients prone to hyperglycemia, obesity or dental caries.*

*Interactions with other herbs or pharmaceuticals: In one study, elderly adults taking omeprazole who were given cranberry juice had an increased absorption of vitamin B12 compared with those taking omeprazole with water<sup>51</sup>. There is no known contraindication to combining cranberry juice with antimicrobial medications except in cases in which urinary acidification might be problematic.*

*Safety during pregnancy, lactation and/or childhood: Presumed safe based on food use; however, safety of newer concentrated cranberry products or large amounts of cranberry juice is unclear.*

## ***Typical dosages***

*Provision of dosage information does NOT constitute a recommendation or endorsement, but rather indicates the range of doses commonly used in herbal practice.*

*Doses are given for single herb use and must be adjusted when using herbs in combinations. Doses may also vary according to the type and severity of the condition treated and individual patient conditions.*

*Adult doses for UTI prophylaxis:* There is disagreement on the optimal form and dose of cranberry to prevent UTI<sup>6,11,52,53</sup>. Some reputable physicians and herbalists recommend:

*Cranberry cocktail:* 90 - 150 ml or 3 - 16 fluid ounces twice daily<sup>54,55</sup>.

*Unsweetened cranberry juice:* 15 - 30 ml daily<sup>47</sup>.

*Encapsulated cranberry juice powder:* One to six 300 – 400 milligram hard gelatin capsules twice daily<sup>56,6,52,53</sup>. Soft gelatin capsules contain substantial amounts of vegetable oil and much less of the organic acids and other compounds found in fresh juice and hard capsule preparations<sup>55</sup>.

*Fresh or frozen cranberries:* 1.5 ounces twice daily<sup>6,52</sup>.

*Pediatric dosages:* Unknown

*Availability of standardized preparations:* No

*Dosages used in herbal combinations:* Variable

## ***See also:***

Cranberry Clinician Information Summary:

<http://www.mcp.edu/herbal/cranberry/cranberry.cis.pdf>

Cranberry Patient Fact Sheet:

<http://www.mcp.edu/herbal/cranberry/cranberry.ph.pdf>

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