Cranberry (Vaccinium macrocarpon) is a native evergreen shrub that grows throughout North America. For centuries, cranberry has been used as both food and medicine. In particular, the ripe fruits were primarily used as a traditional medicine for bladder and kidney ailments among Native Americans. An increasing amount of research suggests that cranberry is a unique fruit in that it may provide two different pathways for health: through microbial anti-adhesion activity and other health benefits related to antioxidant activities. In the past decades, many studies have focused their studies on the capacity of the cranberry fruits to support urinary tract health and cardiovascular health. The health promoting activities of cranberry fruits associated with urinary tract and cardiovascular systems are thought to be linked to their very rich content of various bioactive polyphenols with high antioxidative potency. Regarding urinary tract infections (UTIs), mechanisms by which cranberries are beneficial in UTIs may involve the effects of the A-type proanthocyanidins (PACs) in preventing the bacterial adhesion in urinary tract system.

Cranberry with Cranberex™ is an ultra-concentrated, whole fruit extract (200:1) of cranberries from Oregon showcasing high potency standardized active of 15% proanthocyanidins to support urinary tract health and promote cardiovascular health.

Tests by the BL-DMAC method, the only method endorsed by a number of international labs and authorities to quantify the amount of A-Type PACs in cranberries. Cranberry with Cranberex™ is one of the most concentrated cranberry extracts available in the North America and Europe. This potency and standardization connect directly with the dosages established in the key clinical trial that established the link between A-Type PACs and anti-adhesion activity.

Tests that compared PAC levels in Cranberex™ with five leading finished product brands, showed a far greater potency in Cranberex™ (see fig 1).

**Benefits**

- Helps support urinary tract health
- With its outstanding source of antioxidants, helps support cardiovascular health
- Provides a high potency standardized 200:1 whole fruit cranberry extract from Oregon and contains three times more PACs per serving than other leading brands.

**Supplement Facts**

<table>
<thead>
<tr>
<th>Serving Size</th>
<th>1 Veggie Capsule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Servings Per Container</td>
<td>60</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Amount Per Serving</th>
<th>% Daily Value</th>
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</thead>
<tbody>
<tr>
<td>Cranberry Extract (Cranberex™) 240 mg</td>
<td>(Vaccinium macrocarpon, whole fruit) (standardized to 15% PACs, containing 36 mg PACs)</td>
</tr>
</tbody>
</table>

† Daily Value not established.

**Other Ingredients:** Modified cellulose (vegetarian capsule), microcrystalline cellulose, silicon dioxide.

**Suggested Adult Use:** Take 1 capsule twice daily preferably with food, or as recommended by a nutritionally-informed physician.

**Warning:** Consult with your physician if you are taking blood thinners before using this product.

**Non-GMO / Gluten Free / Soy Free / Vegan**

Store in a cool dry place.

Cranberex® is a registered trademark of Ethical Naturals, Inc.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.*
EXTENDED BENEFITS

Helps support urinary tract health*

Urinary tract infection is one of the most commonly acquired bacterial infections and affects millions of women each year around the world. Cranberries have been regarded and researched as a viable and low cost mean to help address the public health management of UTIs and the increasing resistance of certain bacteria against common antibiotics indicated for UTIs. Cranberry science and food experts have claimed and demonstrated that regular consumption of cranberry products may help support urinary tract health. In the past years, cranberry juice and extracts have been clinically tested as a nutritional supplementation in the prevention of low urinary tract infections as well as recurrent urinary tract infections. Consequently, cranberries may benefit certain population groups, including women with history of recurrent UTIs.

For many years, people thought that cranberries were useful in urinary tract infections because of their capability of acidifying the urine making it difficult for bacteria-causing UTIs such as Escherichia Coli (E. coli) to grow in that kind of environment. Based on recent research, we now know that cranberries support the urinary tract system in a unique way: they actually prevent unwanted bacteria like E. coli or Proteus mirabilis from sticking to the surfaces of the lining wall of the urethra and bladder making it easier to flush bacteria out with urination and decreasing the chances of recurrent UTIs. More precisely, the A-Type PACs found in cranberries are the ones involved in the inhibition of the adhesion of E. coli bacteria to walls of the urinary tract. Studies have confirmed that this effect is specific to the A-linked PAC’s found in cranberries, but not to other PAC rich foods with the more common B-type linkages (e.g. chocolate and grapes). Since this bacterial anti-adhesion mechanism does not kill bacteria, there is less chance of selection for resistant bacterial strains. This has been considered as an advantage compared to antibiotics treatment for UTIs and in some cases more effective in reducing the re-occurrence of UTIs.

With its outstanding source of antioxidants, helps support cardiovascular health*

The increased interest of people regarding healthy food products rich in nutraceuticals has led to an increased interest in the research about bioactive compounds in fruits and vegetables. In this respect, berries such as cranberries, have been mainly investigated for their nutritional properties and their bioactive nutrients. It was found that cranberries are a great source of vitamins and bioactive compounds such as phenolic compounds that are scientifically known for their powerful antioxidant activities. Among those phenolic compounds, there are anthocyanins (peonidin), flavonoids (quercetin), tannins (A-type proanthocyanidins), and phenolic acids. Because cranberries contain various antioxidant compounds that may be beneficial for human health, many clinical trials and research have been done and have found that cranberries extracts and juice, may support cardiovascular health reinforcing the notion that consuming fruits and vegetables can have significant benefits on cardiovascular health.

Provides a 200:1 whole fruit cranberry extract from Oregon and contains three times more PACs per serving than other leading brands.

While 90% of the world’s cranberry crops are produced in the United States, 85% of it come from the North East of USA (primarily Wisconsin and Massachusetts). However, a small percentage is grown in the North West of USA, in the cool coastal areas of Oregon. This particular region provides a unique climate that allows to produce cranberry fruits with special qualities. Indeed, the main anthocyanin content in Oregon grown cranberries is significantly higher than in fruits harvested in the North East: Oregon (70 mg/100g) Massachusetts (42 mg/100g), and Wisconsin (37 mg/100g). This high content of therapeutic compound is why the source of cranberries for Cranberex™ is Oregon coastline.

CLINICAL STUDIES

A randomized controlled trial in older women was conducted to compare the effectiveness of cranberry extract with low-dose trimethoprim (TMP-an antibiotic usually indicated in UTIs) in the prevention of recurrent UTIs. The participants were randomly given either 500 mg of cranberry extract or 100 mg of TMP for 6 months. Results showed that the antibiotic TMP had a very limited advantage over cranberry extract in the prevention of recurrent UTIs and had more adverse effects. The authors concluded that their findings will allow older women with recurrent UTIs to discuss with their physicians the inherent attractions of a low cost, natural product with barely any side effects like cranberry extract that does not carry the risk of future antimicrobial resistance.

A randomized placebo-controlled study tested whether whole cranberry fruit powder (containing 0.56% of proanthocyanidins) could prevent recurrent UTI in women. Participants received daily 500 mg of cranberry or placebo for 6 months. Results showed that in the cranberry group, UTIs were significantly fewer and presented a longer time to first UTI than the placebo group. The authors concluded that cranberry fruit powder may reduce the risk of symptomatic UTI in women with a history of recurrent UTIs.

An in-vitro study compared the anti-adhesion activity (AAA) of Cranberex™ with nine other brands of cranberry extract products. Results from this study showed that Cranberex™ met the anti-adhesion criteria at a concentration of only 0.23mg/mL while other key products in the market required a concentration of 7mg - 60mg/mL to achieve the same anti-adhesion result. The study concluded that Cranberex™ had excellent anti-adhesion activity (See Figure 1).

A study was designed to test actual anti-adhesion activity in the urine after consumption of two doses (1 dose in the evening and 1 dose in the morning) of Cranberex™ (at recommended dosage level of 480mg (72mg PAC)) in human participants. The report stated that AAA response increased rapidly in all participants 3 to 6 hours after consumption of Cranberex™. Half of the participants achieved 100% or significant bacterial Anti-Adhesion Activity, while half achieved 50%, resulting in an average of 75% AAA.

An in vitro study tested cranberry phenolic compounds for their capacity to inhibit the of uropathogenic E. coli to epithelial bladder cells. This study demonstrated the anti-adhesive activity of some cranberry-derived phenolic compounds against E. coli and suggested that their presence in the urine could help reduce bacterial colonization and therefore the progression of UTI.

A randomized, double-blind placebo-controlled study was conducted to evaluate the most effective dose per day of cranberry powder standardized for proanthocyanidins (PACs-A-Type linkages; dosages studied were 18 mg PAC, 36 mg, and 72 mg PAC) on uropathogenic E. coli anti-adhesion activity in urine. Two separate bioassays have assessed the ex-vivo urinary bacterial anti-adhesion activity on urine samples collected from 32 volunteers from Japan, Hungary, Spain and France. The results indicated a significant bacterial anti-adhesion activity in urine samples collected from volunteers that consumed cranberry powder compared to placebo. This inhibition was clearly dose-dependent, prolonged (until 24 h with 72 mg of PAC) and increasing with the amount of PAC equivalents consumed in each cranberry powder regimen. The authors concluded that administration of PAC-standardized cranberry powder at dosages containing 72 mg of PAC per day could offer some protection against bacterial adhesion in the urinary tract and the effect may offer a 24-hour protection.

A randomized, double-blind clinical trial clearly affirmed, for the first time, a bacterial anti-adhesion effect in urine, based upon 36mg/day of cranberry PAC (by BL-DMAC method). It also reported that effectiveness was dose-dependent, prolonged up to 24 hours with 72 mg of PAC, and increasing with the amount of PAC (by BL-DMAC method) consumed.

An in-vitro study was conducted to analyze the activity of cranberry concentrate (Vaccinium macrocarpon) on E. coli in uncomplicated UTIs.
The risk of UTIs among women after undergoing gynecologic surgery where a urinary catheterization is necessary is high. A randomized, double-blind, placebo-controlled trial was conducted to evaluate the therapeutic efficacy of cranberry juice capsules in preventing these UTIs post surgeries. Female participants randomly received 2 cranberry juice capsules twice daily for 6 weeks after surgery, or matching placebo. Results showed the occurrence of UTI was significantly lower in the cranberry group compared to the placebo group. This study showed that cranberry could reduce greatly the rate of UTIs during the postoperative period among women that had to undergo benign gynecologic surgery involving urinary catheterization.42

The effects of the consumption of cranberry juice on episodes of clinical UTIs were studied in a randomized, double-blind, placebo-controlled, multicenter clinical trial in women with a history of recent UTI. For 24 weeks, participants received either cranberry beverage (240 mL) or placebo. Results showed that consumption of cranberry juice beverage lowered the number of clinical UTI episodes. The results suggest that cranberry can be a useful strategy for reducing recurrent clinical UTI episodes and antibiotic use associated with the treatment of these events.21,42

A study was conducted to determine the effect of consuming increasing daily doses of low-calorie cranberry juice cocktail (CJC) on the plasma lipid profile of obese men. For that purpose, thirty men consumed increasing doses of CJC during three successive periods of 4 weeks (125 mL/day, 250 mL/day, and 500 mL/day). Before the study and after each phase, changes in physical and metabolic variables were measured. Results showed a significant increase in plasma HDL-cholesterol (known as the “good cholesterol”) concentration after the consumption of 250 mL CJC/day. The authors concluded that polyphenolic compounds from cranberries may be responsible for this effect, supporting the notion that the consumption of flavonoid-rich foods such as cranberries can impact positively cardiovascular health.33 Similar conclusion was found in another study which showed that a 12-week supplementation with low-calorie cranberry juice reduced plasma oxidized LDL, known as the “bad cholesterol” and markers of oxidative stress involved in the development of cardiovascular problems.34

An 8-week randomized, double-blind placebo-controlled trial was conducted in women to evaluate the effect of commercially available low-calorie cranberry juice on cardiovascular health. Participants in the cranberry group received 480 mL daily of cranberry juice while participants from the placebo group received 40 mL daily of placebo drink. Results showed that cranberry juice significantly increased plasma antioxidant capacity and decreased oxidized LDL (markers of oxidative stress in individuals with cardiovascular issues) compared to placebo. From this study, it was concluded that cranberry juice can have beneficial effects on cardiovascular health.35

The objective of a double-blind, placebo-controlled, parallel-arm study was to determine the potential of low-calorie cranberry juice (LCCJ) to lower certain cardiometabolic risk factors to improve cardiovascular health. Fifty-six volunteers completed an eight-week intervention with LCCJ (240 mL twice daily) or a flavor/color-matched placebo beverage. Results showed that fasting serum triglycerides, diastolic blood pressure, and fasting plasma glucose were all lower in the cranberry group compared to the placebo group. The authors concluded that low-calorie cranberry juice could improve several risk factors of cardiovascular diseases in adults and the consumption of high-polyphenol products such as cranberry is a sustainable lifestyle practice that could benefit cardiovascular health.34

“Copies of these tests and studies are available upon request.”

An 8-week randomized, double-blind placebo-controlled trial was conducted to study the effect of cranberry supplement on cardiovascular health among 48 obese and overweight females diagnosed with cardiovascular issues. They were assigned into two groups to receive cranberry supplement or placebo for an eight-week period. Results showed that high-density lipoprotein cholesterol (HDLc) significantly increased at the eighth-week period compared with the placebo samples. The results of the present study revealed that cranberry supplement might be beneficial in improving HDLc and therefore have positive effect on cardiovascular health.36

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SCIENTIFIC REFERENCES


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