The Berry Best

Guidebook

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Love Cranberries, and Cranberries Will Love You Back

Without exception, registered dietitians (RDNs) recommend eating more fruits and vegetables. It's easy to recommend cranberries for their powerful bioactive compounds with many proven benefits for the body. High-quality scientific research on the berry's total body benefits reveals:

- Cranberries are rich in bioactive compounds including polyphenols such as anthocyanins, flavonoids, and proanthocyanidins (PACs).[1,2]
- The benefits for cranberry and UTI are well-established, but go beyond UTIs to include benefits on stomach, gut, and cardiovascular health.
- Research continues to grow showing promising benefits of cranberries for their impact and influence on many areas of health.

The benefits of daily cranberry consumption on prevention of urinary tract infections (UTIs) have been well-established in numerous meta-analyses of clinical trials. However, research is indicating that cranberries can have positive effects on a number of other important health targets, including improvements in the gut microbiome and reducing risk factors for stomach ulcers and heart disease.

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Cranberry Equivalencies

Cranberries as Part of a Healthy Diet

Cranberries and cranberry juice are an important part of a healthy diet.[4] An extensive literature review of healthy foods includes cranberries as part of a short list of foods that benefit the gut microbiome and overall health.[5]

An examination of chokeberry, elderberry, pomegranate, and cranberry juices with no added sugar or preservatives revealed that cranberry juice is a rich source of bioactive polyphenols and has the lowest sugar content of all the juices.[6]

A study of more than 186,000 people showed a significantly reduced risk of all-cause, cancer-specific, and cardiovascular disease-specific mortality among those who added dried fruit, like dried cranberries, to their breakfast cereal such as porridge, bran cereal, or muesli.[7]

Cranberry Equivalencies

Most cranberries are harvested between September and October in the U.S., yet they can be enjoyed year-round. All forms of cranberry (juice, fresh, sauce, or dried berries) are healthy. These are the amounts needed to give your body the same level of goodness.[8] But why stop there? More cranberries = more goodness!

- *8 to 10 oz. serving of 27% cranberry juice cocktail*
- *2 oz. serving 100% cranberry juice*
- *1/4 cup fresh or frozen cranberries – 0.9 g fiber*[9]
- *1/4 cup cranberry sauce – 0.76 g fiber*[10]
- *1/3 cup sweetened dried cranberries – 2.79 g fiber*[11]

Cranberries have very little natural sugar, and sweeteners can help people enjoy cranberry products. There are “light” product versions for those that like a sweet taste but are avoiding sugar and pure cranberry juice for a tangy no sugar option. Try adding 100% pure cranberry juice to seltzer or other beverages, and unsweetened cranberry products can be added into other foods such as smoothies, salads, or hot or cold cereal.

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Cranberries are special as they are one of the only foods rich in A-type PACs.

These bioactive compounds give cranberries the ability to inhibit bacterial adhesion in the body leading to many health benefits.[1]

Cranberries are simply the berry best. The high PAC content of cranberries ranks them at the top of the list of berries to choose for their health benefits.[2]

When compared to other anthocyanin-containing berries, cranberry anthocyanins are the most highly available to the body.[3]

Stomach Suppression of *H. pylori*

Up to half of the world's population is infected with the *H. pylori* bacterium.

It is the most important cause of peptic ulcer which can lead to stomach cancer. If you don't get rid of an *H. pylori* infection, this increases the chances of getting stomach cancer six-fold.[12,13]

H. pylori is highly contagious, transmitted through the mouth into the stomach by close contact with infected people or by consuming infected food or water. Over time, *H. pylori* has evolved to produce a high pH layer that protects it from stomach acid allowing it to dissolve the mucus layer and adhere to the stomach lining. This can lead to a cascade of inflammatory changes. Treatment from a healthcare professional (HCP) is essential to cure an *H. pylori* infection.[12,13]

The proanthocyanidins (PACs) found in cranberries help suppress *H. pylori.*[14,15,16] While more research is needed, the research found that drinking cranberry juice containing 44 mg PACs twice daily, found in about 1/2 of cup 100% pure, unsweetened cranberry juice at morning and night for eight weeks resulted in a 20% reduction of the *H. pylori* infection rate when compared to drinking less juice or a placebo. Regularly drinking this amount of pure cranberry juice has the potential to be a complementary strategy for management of *H. pylori* infection in adults which can be consumed directly or mixed with other foods or beverages.[14,15,16]

Proanthocyanins (PACs) found in cranberries can help suppress an *H. pylori* infection in the stomach.

Gut Microbiome

Fruits and vegetables play an important role in maintaining a healthy gut microbiome which can protect the body against germs and help overall health and immunity.[17,18,19]

The beneficial bioactive compounds and fiber in cranberries help keep the microbiota in your gut healthy which aids in breaking down and utilizing health-promoting compounds in foods.[19,20]

Fiber and polyphenols in cranberries help gut microbiota

Cranberries, cranberry sauce, and dried cranberries contain fiber which can help produce metabolites to support gut microbiota.[19,20] Cranberry polyphenols are potential prebiotics which are thought to help improve the composition of the gut microbiota.[21]

Cranberry PACs reversed negative effects of a high-fat, high-sugar diet in mice that caused weight gain, increased intestinal permeability, allowing adherent-invasive Escherichia coli (*E. coli*) to colonize gut mucosa and induce inflammation.[22]

Cranberries are important for gut microbiota diversity and production of healthy metabolites

An evaluation of food data collected from more than 3800 people through the National Health and Nutrition Examination Survey (NHANES 2005-2010) was used to develop a dietary index for healthy gut microbiota. The research identified cranberries as part of a small list of foods found to benefit gut microbiota diversity and production of short-chain fatty acids (SCFAs).[5,18]

SCFAs are a metabolite produced by the fermentation of dietary fiber by the gut microbiome. A growing body of research supports their role in anti-inflammation and immune regulation.[27]

Dried cranberries increase healthy bacteria and decrease unhealthy bacteria. Eating dried cranberries has been linked to an increase in *Bacteroidetes*, bacteria associated with positive health effects. Eating them is also shown to decrease *Firmicutes*, bacteria associated with negative health effects including energy absorption linked to obesity.[23,24]

Emerging research suggests that cranberry extract has the potential to benefit the gut microbiome by increasing beneficial *Bifidobacterium adolescentis*, reducing adhesion of negative *Proteobacteria*, a shift in bacterial population from acetate to proprionate, and an increase in healthy butyrate production.[25]

Cranberries Benefit the Gut & Urinary Tract Lining

A healthy gut microbiome can support the integrity of the gut barrier,[18,19] and emerging research suggests that cranberry polyphenols may play a part in supporting the integrity and functionality of the gut barrier and possibly the lining of the urinary tract.[26]

A healthy gut barrier can help keep harmful substances from leaking into the body and causing inflammatory changes. This can lead to chronic inflammation which has been linked to cardiovascular disease, cancer, diabetes, Alzheimer's disease, and chronic kidney disease.[5,18]

> **Cranberries contain a type of tannin polyphenol called proanthocyanidin which helps prevent pathogenic bacterial adhesion in multiple areas in the body (urinary tract, stomach, and oral cavity). Bacteria sticking to surfaces in the body is the first step in the infection process, so preventing this adhesion step with daily cranberry intake can keep the infection from proceeding further. Preventing infections lowers the ultimate need for antibiotic treatments, potentially slowing the pace of antibiotic resistance development, a current worldwide crisis.**
>
> Amy Howell, PhD, Associate Research Scientist (retired) Rutgers University

Urinary Tract Health

Forty percent of women and 20% of men in the U.S. will have a UTI at least once, and about 10% of women will have a UTI yearly.[28,29]

Cranberry products offer an easy, accessible, and affordable way to prevent and reduce the incidence of UTIs. Decades of research supports the benefit of proanthocyanidins (PACs) in cranberries to provide urinary tract benefits by interfering with the ability of uropathogenic *E. coli (UPEC)* bacteria to adhere to the wall of the urinary tract, the first step in the infection process. ***Emerging research supports the use of a cranberry juice-derived supplement product containing 36 mg PACs against two of the most important bacterial types causing UTIs, P-type and Type 1 E. coli.***[30]

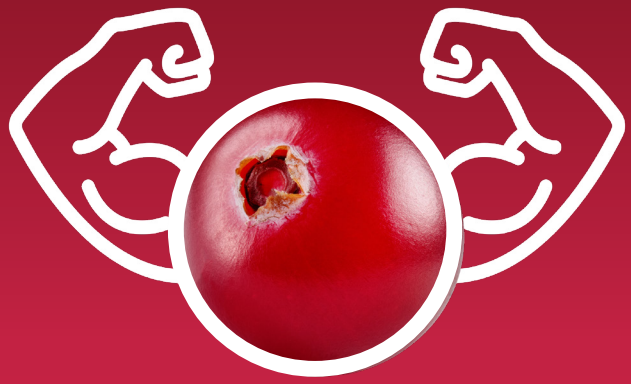
Prevention of Urinary Tract Infections

In the most comprehensive scientific review to date, The Cochrane Database of Systematic Reviews examined the effectiveness of cranberry juice and supplements on UTI prevention. The findings support the use of cranberry juice, tablets, or capsules to help prevent UTIs in women with recurrent UTIs (rUTIs), in children, and in those at-risk of UTIs after an intervention. The review findings have been reinforced with an update which included analysis of 26 more studies for a total of 50 studies with 8857 participants.[31]

In a WikiGuidelines Group Consensus Statement, the researchers examined evidence to create a clinical guideline for the diagnosis and management of UTIs. This study set out to answer the question: *Is there a role for cranberry juice or supplements in prevention of UTIs*? The results of this study confirm the Cochrane review findings with benefits for cranberry for women with recurrent UTIs, children, and individuals susceptible to UTIs after an intervention, citing insufficient evidence in older adults, pregnant women, and those with bladder emptying problems.[32]

A critical analysis of eight studies found that the use of cranberry products may be beneficial to prevent UTIs in the elderly in residential care facilities.[33]

A cohort study examined the incidence of post-operative UTIs in women after pelvic surgery. The results showed that the women taking part in a clinical bundle of care including urine culture two weeks before surgery with oral antibiotic if positive, discharge home with monitoring of voiding, urine culture if warranted, and 150 mg PAC daily oral cranberry supplement led to significantly decreased UTI rates and length of hospital stay. These results show promise for the benefit of cranberry PAC as part of a clinical bundle of care after certain intervention procedures.[115]



Cranberry Fights Biofilm: A Layer of Bacteria that Grows and Sticks to a Surface

Certain bad bacteria can form colonies or biofilms on surfaces such as the bladder which can harbor the bacteria protecting them from antibiotics and serve as a reservoir for future bacterial infections.

Biofilm formation can happen during the early stages of the development of an infection in the body. Cranberry polyphenols help prevent biofilm formation, which benefits health in many ways by keeping bad bacteria at bay.[19,34,35]

Urinary Tract Health

Prevention of Urinary Tract Infections

Research suggests that using cranberry juice in the management of UTIs led to a 49% lower rate of antibiotic use than placebo liquid and a 59% lower rate when compared to no treatment[36]

A double-blind placebo-controlled trial of women with rUTIs showed that whole cranberry powder supplements reduced the risk of culture-confirmed UTIs when compared to a placebo.[37]

A meta-analysis of ten randomized controlled trials revealed a strong correlation between the daily intake of at least 36 mg PACs in cranberry products and prevention of UTIs. The results suggest a need for guidelines for appropriate duration of use of cranberry products.[38]

Uropathogenic *E. coli* (UPEC) can adapt and shift to elongate into a filamentous shape to help improve their survival. Evidence shows that SulA is a prime antivirulence target, especially in the treatment of UTIs. Research suggests that cranberries may prevent SulA-mediated filamentation of UPEC. The research identified several subfractions of cranberries which may retain anti-filamentation properties.[39]

Using cranberry juice to manage UTIs led to a lower rate of antibiotic use.

Urinary Tract Health

Research suggests that cranberry may block UPEC bacteria through the blood-urinary barrier helping reduce the risk for UTIs.[26]

Research suggests that ***cranberry may block uropathogenic E. coli bacteria from binding to the surface cells of the urinary tract*** potentially protecting the cell barrier from damage.[40]

HCP Involvement in UTI Awareness and Complementary Strategies for Management

There is a need for greater involvement from HCPs to discuss UTI management with clients.[41,42] Shared decision making between HCPs and clients can help open the lines of communication and improve client knowledge of cranberry as a complementary strategy for UTI prevention.[41,43]

Hydration Offers Protection from UTIs

- Drinking cranberry juice increases fluid intake, and as a hydrating beverage, this may reduce risk for UTIs.[44-47] Hydration helps increase urinary frequency and urine flow which helps flush bacteria from the urinary tract, helping to prevent UTIs.[48]
- In a randomized controlled trial of 140 women with rUTIs, increasing water intake by an additional 51 ounces or about 6 1/2 cups per day, resulted in 1.5 fewer UTIs and 1.7 fewer antibiotic prescriptions per woman per year.[49,50]

Cranberries are a great UTI defender. Research suggests they may help improve the ability of cells in the urinary tract to prevent harmful bacteria to pass through the blood-urinary barrier.

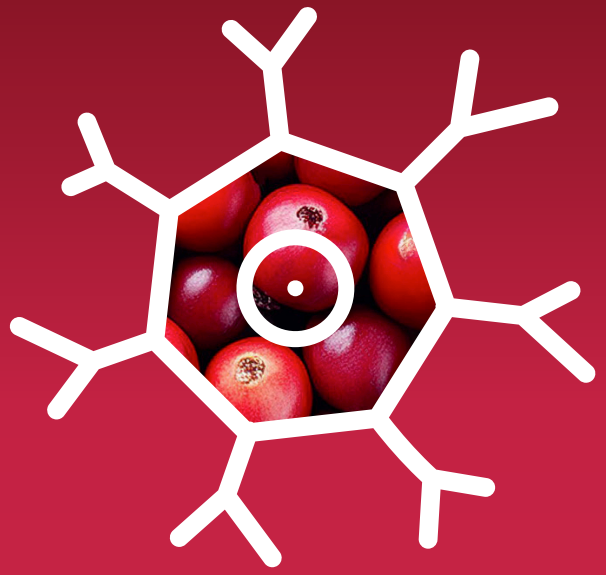
Support of Nerve Cells & Cognition

An increase in fruit and vegetable intake may offer some protection against dementia and Parkinson's disease.[51,52]

Anthocyanins, the flavonoids found in cranberries which give them their rich red color, have potent health benefits. Once consumed, they are absorbed into the bloodstream quickly and have been shown to cross the blood-brain barrier.[53]

Anthocyanins have antioxidative and anti-inflammatory effects which may help them offer support to nerve cells in the brain. Research has uncovered the effects of anthocyanins in signaling pathways implicated in the development of Alzheimer's disease, the most common form of dementia, and Parkinson's disease.[53,54]

- Animal models support the effects of anthocyanins on potentially delaying the development of Alzheimer's disease. Research has shown the ability of cranberry anthocyanins to ward off memory and learning deficits in rats with induced sporadic dementia of Alzheimer's type.[55] Anthocyanin-rich cranberry extracts help hinder harmful peptide formation in vitro, helping to preserve cognitive function in disease-model mice.[56]
- Cranberry juice showed promise in providing potential protection from Parkinson's disease in a study on rats.[54]
- In a randomized, placebo-controlled study of healthy adults, consuming freeze-dried cranberries - equivalent to 1 cup of fresh cranberries per day - for 12 weeks led to a significant decrease in low-density lipoprotein (LDL) cholesterol levels, known to contribute to atherosclerosis, supporting the potential benefit of cranberries to improve vascular health.
    - Cognitive performance was measured through cognitive tests and comprehensive MRI assessments.
    - The improvements in vascular health are thought to improve the amount of blood delivered to nerves, the spinal cord, and the brain.
    - ***These findings support the notion that cranberry supplementation may improve memory performance.***[57]



The anthocyanins in cranberries can be absorbed into the bloodstream quickly and have been shown to cross the blood-brain barrier.

Oral Health

What you eat and drink can have a big impact on oral health, and fruits and vegetables are shown to protect against tooth decay/cavities, and gum disease.[58]

The unique compounds found in cranberries, especially the PACs, may help support oral health.[58, 118]

Cranberry polyphenols inhibit the effects of *Streptococcus mutans*[60] in the oral cavity affecting both the properties and development of biofilm.[59] Bad bacteria can form biofilms to attach to mouth surfaces and promote an infection[35] or cause an imbalance of bacteria in the mouth.

The isolated polyphenols in cranberries and cranberry juice have been shown to help manage the development of dental plaque, tooth decay/cavities, and gum disease.[59,61,62] Development of products containing these isolated bioactive polyphenols have potential for improving oral cavity health.

An examination of oral biofilm found in donor saliva suggests that cranberry shows promise for antimicrobial and anti-adhesion action against a range of bad bacteria.[63]

The unique compounds found in cranberries, especially the PACs, may help support oral health.

Cardiometabolic Health

Cardiometabolic diseases are the cause of more than 4.8 million deaths of people ages 25 to 64 years in the U.S.[64]

What you choose to eat is important to help prevent cardiometabolic diseases. The Centers for Disease Control and Prevention recommends eating more fruits, vegetables and fiber, and limiting saturated fat, sodium, sugar, and alcohol.[65]

Cardiometabolic disease includes conditions that affect the heart, blood vessels, and metabolism such as heart disease, stroke, obesity, and diabetes.[64]

Lower Overall Mortality Risk

Increased intake of flavonoid-rich berries is linked to overall lower mortality risk. An examination of more than 37,000 participants in the National Health and Nutrition Examination Survey (NHANES) from 1994 to 2014 found that those who consumed cranberries had reduced risk of all-cause mortality and a significantly lower risk of dying from cardiometabolic disease.[66]

Cranberries Protect Against Inflammation & Oxidative Stress

Inflammation and oxidative stress in the body are associated with cardiometabolic conditions. Evidence suggests that polyphenols and vitamin C in cranberries protect against oxidative stress, increase antioxidant capacity, improve immune response, and help the body manage inflammation.[5,18,27,52,119,120]

Whole cranberries, dried cranberries, and cranberry sauce also have fiber that helps the gut produce SCFAs, metabolites which help manage inflammation.[5,9,10,11,18]

Evidence suggests that polyphenols and vitamin C in cranberries protect against oxidative stress, increase antioxidant capacity, improve immune response, and help the body manage inflammation.

Cardiovascular Health

Between 2017 and 2020, 48.6% of adults in the U.S. had some form of cardiovascular disease.[67]

The American Heart Association recommends fruits and vegetables to help prevent cardiovascular disease.[68] The polyphenols in cranberries are helpful to improve cardiovascular health.

Improves Blood Pressure

Although more research is needed, consuming cranberry juice might help improve blood pressure.[69] A randomized, placebo-controlled trial of 40 participants found that drinking two cups of 27% cranberry juice cocktail or one cup 100% pure cranberry juice, consumed at one time or divided between morning and evening, for eight weeks led to lower diastolic blood pressure by 1.79 ± 0.9 mm/Hg from baseline (measured on a continuous basis for 24 hours).[70]

Research Suggests Benefit of Polyphenol-Rich Beverage for Lipid Metabolism

Consuming a polyphenol-rich beverage containing chokeberry, cranberry, and pomegranate juice for eight weeks suggests reductions in energy intake, improvements in lipid metabolism, which is the process of manufacturing, breaking down, and storing fat in cells for energy,[116] modulation of phosphodiesterase in platelets, which helps regulate heart and blood vessel contraction,[117] and maintenance of DNA integrity.[71]

Polyphenols in cranberries are helpful to improve cardiovascular health.

Cardiovascular Health

Raises High-Density Lipoprotein Levels (HDL)

An analysis of over 260 participants with metabolic syndrome in eight different cranberry intervention studies found that cranberries can increase high-density lipoprotein (HDL – or good cholesterol) levels by 2.01 mg/dl higher than the placebo group.[3] ***An increase of just 1 mg/dl in HDL can reduce the risk of cardiovascular disease by 2 to 3%.***[72,73]

Improves Vascular Health

A study of 45 healthy men consuming the equivalent of 1 cup of cranberries daily for a month resulted in significant improvements in flow-mediated dilation (FMD), the ability of an artery to dilate, or expand, when blood flow increases. The results showed significant improvements in FMD just two hours after first consuming cranberries, showing both immediate and ongoing benefits.[74]

Cranberries may improve the ability of arteries to expand when blood flow increases, which can help blood flow more easily.

Diabetes & Blood Sugar Management

In the United States, 11.6% of the population has diabetes.[75]

A higher intake of fruits and vegetables, especially berries, is linked to a lower risk of type 2 diabetes,[76] the most common type of diabetes. The polyphenols in cranberries may help reduce the risk of diabetes.

Reduces fasting blood sugar and hemoglobin A1C

A review of 22 randomized clinical trials found that cranberry consumption significantly reduced the levels of fasting blood sugar and hemoglobin A1C (HbA1C) in people with diabetes.[77] Of the 22 studies examined, seven used cranberry capsules and 15 used cranberry juice or smoothies.

Improves cardiometabolic biomarkers

A double-blind trial examined two groups of participants including 56 men and women who consumed one cup of low-calorie cranberry juice (LCCJ) or a placebo twice daily for eight weeks. The LCCJ group showed improvements in insulin resistance, blood sugar, triglyceride and C-reactive protein levels, and diastolic blood pressure.[78] LCCJ is similar to products available labeled "light" cranberry juice.

Helps lower triglyceride levels and certain markers of oxidative stress

A double-blind trial of two groups of participants including 35 men and women with high fasting blood sugar or poor glucose tolerance consumed about two cups of LCCJ or a placebo every day for eight weeks. The findings showed that LCCJ consumption can help lower triglyceride levels and certain oxidative stress markers.[79]

Cranberries have the potential to help reduce fasting blood sugar and hemoglobin A1C.

Exercise Performance & Muscle Function

A small study of trained endurance athletes suggests that supplementation with cranberry extract for 28 days improved physiological markers of performance which may help delay onset of muscle fatigue.[80]

A small study of adults who regularly exercise suggests that cranberry extract helps increase how well muscles can use oxygen to produce energy, which could lead to improvements in muscle function in active adults.[81]

Cranberry may impact immune changes from post-exercise stress

A 4-week randomized placebo-controlled double-blind crossover study of non-elite cyclists showed a slight post-exercise elevation of select oxylipins and proteins linked to innate immunity without negative effects on blood cortisol levels or muscle damage biomarkers from consuming 8 ounces of an unsweetened cranberry beverage when compared to a placebo.[82]

Cranberry may help increase how well muscles can use oxygen to produce energy.

Anti-Aging & Cellular Health

Emerging research suggests that cranberry's bioactive compounds help a cell process called mitophagy,[83] the removal and recycling of damaged mitochondria and regulation of the development of new mitochondria.[84]

The bioactive compounds found in cranberries are thought to help mitophagy, which is the removal and recycling of damaged mitochondria in the body's cells.

Rheumatoid Arthritis Support

Research suggests that consumption of 16 ounces of low-calorie cranberry juice daily for 90 days may reduce severity of rheumatoid arthritis in women. The benefit may be due to the bioactive compounds found in cranberries including the polyphenol resveratrol and the flavonoid quercetin.[1,4,85]

Endocrine Health

Emerging research from an animal model suggests a benefit for cranberry in attenuating premature ovarian failure, a common cause of infertility in women under 40 years old.[86]

Research suggests the bioactive compounds found in cranberries may reduce severity of rheumatoid arthritis in women.

Management of Liver Disease

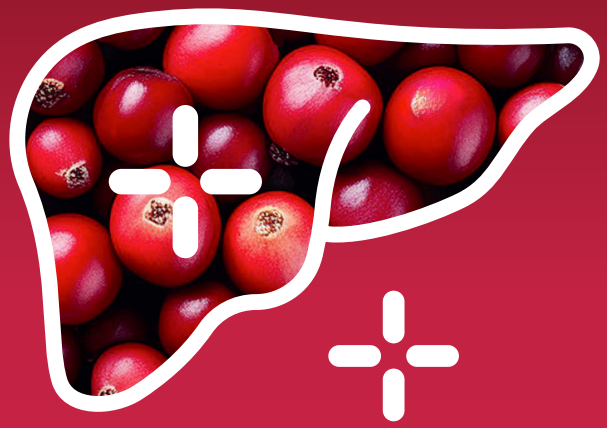
Animal studies have shown promising results for the potential benefits of cranberry for the prevention and management of non-alcoholic fatty liver disease (NAFLD).[87,88]

The findings suggest that the anti-oxidative and anti-inflammatory actions of cranberry PACs may help to prevent obesity, improve insulin resistance, lower high blood cholesterol levels, and reduce buildup of fat in the liver.[88]

In an animal model, cranberry extract helped suppress changes to the liver due to induced liver injury. ***Cranberry was shown to help protect against inflammation, oxidative stress, and fibrosis, a buildup of scar tissue that can damage the functioning of the liver.***[89]

Research suggests that the bioactive compound procyanidin A2 found in cranberries may help reduce oleic acid-induced fat storage and oxidative stress in liver cancer cells.[90]

Research suggests that cranberry supplements paired with a weight loss diet may benefit total antioxidant capacity in blood levels of people with NAFLD which shows promise for possible anti-oxidative effects.[91]



Cranberry may help reduce buildup of fat in the liver, protect against inflammation, oxidative stress, and fibrosis.

Digestive Support

Constipation

Constipation is a common complaint among all age groups, *accounting for about 2.5 million visits to a healthcare professional yearly.*[92]

Using health data from more than 17,000 people as part of the 2005 to 2010 cycles of the National Health and Nutrition Examination Survey (NHANES), *cranberries were found to be on the list of foods associated with higher diversity of gut microbiota (DI-GM) linked to lower rates of constipation.*[93]

Inflammatory Bowel Disease

An animal model suggests that *cranberry extract may help manage symptoms of inflammatory bowel disease through potential beneficial effects on colonic ferroptosis, a type of cell death in colon cells.*[94]

The benefit may be related to the ability of cranberry extract to prevent colonic inflammation through reducing the overproduction of pro-inflammatory cytokines.[95]

Cranberries support digestion and can help manage constipation.

Anticancer

REPRODUCTIVE CANCER

In the U.S., about 40% of cancer cases could be prevented with changes to diet and other health habits.

The American Institute for Cancer Research recommends a diet rich in whole grains, vegetables, fruits, and beans as healthy choices to lower cancer risk.[96] The polyphenols, including PACs, and vitamin C found in cranberries are the main sources of cranberry's potential anticancer properties.

Reproductive Cancers

A review of experimental models shows promise for the therapeutic effects of bioactive compounds found in cranberries on reproductive cancer cells such as prostate, ovarian, and cervical cancers.[97]

Cranberries are high in ursolic acid, a phytochemical found in the skin of cranberries which has antioxidant, anti-inflammatory, and anticancer properties.[1,98] This review examined in vitro and animal studies. The review of in vitro studies suggests that ursolic acid is beneficial against prostate cancer cells due to promotion of apoptosis - cell death which helps to maintain a healthy balance of cells in the body - and inhibition of cell cycle progression. The review of animal studies suggests reduced prostate tumor volume and increased survival rates in mice.[98]

In vitro research suggests that certain cranberry flavonols and cranberry PACs have cytotoxic effects against ovarian cancer cells. This research shows promise for newly characterized cranberry flavonoids quercitin aglycone and PAC DP-9 on in vitro cytotoxicity and anti-proliferation – a decrease in number of cancer cells.[99]

In vitro research suggests that certain cranberry flavonols and cranberry PACs have cytotoxic effects against ovarian cancer cells.

Anticancer

BLADDER CANCER
BARRETT'S ESOPHAGUS & ESOPHAGEAL CANCER

Bladder Cancer

An examination of the potential role of cranberries in bladder cancer (BC) proposes that the bioactive compounds found in cranberries may inhibit growth of BC cells. The effects of cranberry on BC are thought to be due to flavonoids.

Cranberry is proposed to affect BC in these additional ways:

- Be selectively toxic to BC cells
- Decrease tumor size, growth, and division of BC cells
- Inhibit VEGF (vascular endothelial growth factor) which stimulates the growth of blood vessels linked to tumor growth
- Prevent UTIs, which can be a side effect of certain BC treatments[100]

Barrett's Esophagus & Esophageal Cancer

Inflammation from gastroesophageal reflux disease (GERD) can shift healthy bacteria on the esophagus to unhealthy, pathogenic bacteria. These unwanted changes in the esophageal microbiome can cause Barrett's esophagus, which can lead to esophageal cancer. Animal studies have shown the potential prebiotic effect of cranberry PACs to support a healthier esophageal microbiome.[101]

Transporters expressed in the intestine play a role in circulation of bile acids. An animal model showed promising evidence of cranberry PACs helping to ease bile reflux-induced transporter dysregulation which may contribute to the prevention of esophageal cancer.[102]

Emerging evidence shows promise for the potential prebiotic ability of cranberry PACs to support a healthier esophageal microbiome.

Anticancer

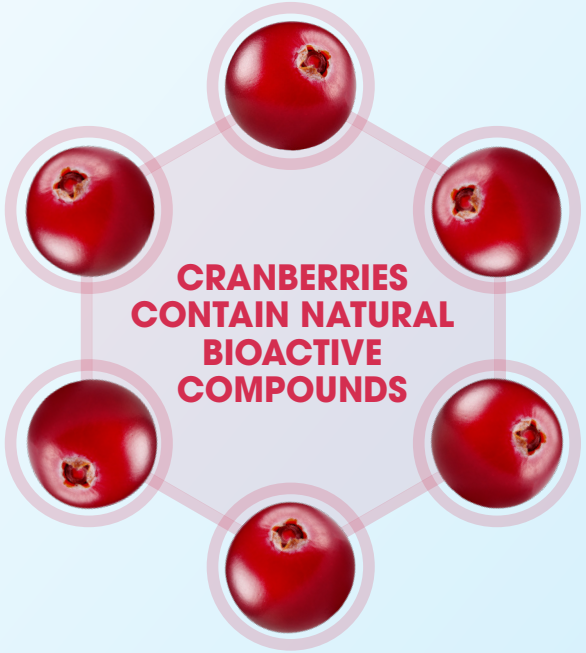
LUNG CANCER & ORAL CANCER

Lung Cancer

Emerging research suggests a benefit for cranberry extract having inhibitory effects on the growth of lung adenocarcinoma cells by potential modulation of cell activity.[103]

Oral Cancer

Emerging research suggests that the bioactive compounds found in cranberries have antitumor and cell growth inhibition properties that may help reduce the risk of oral cancer.[104]

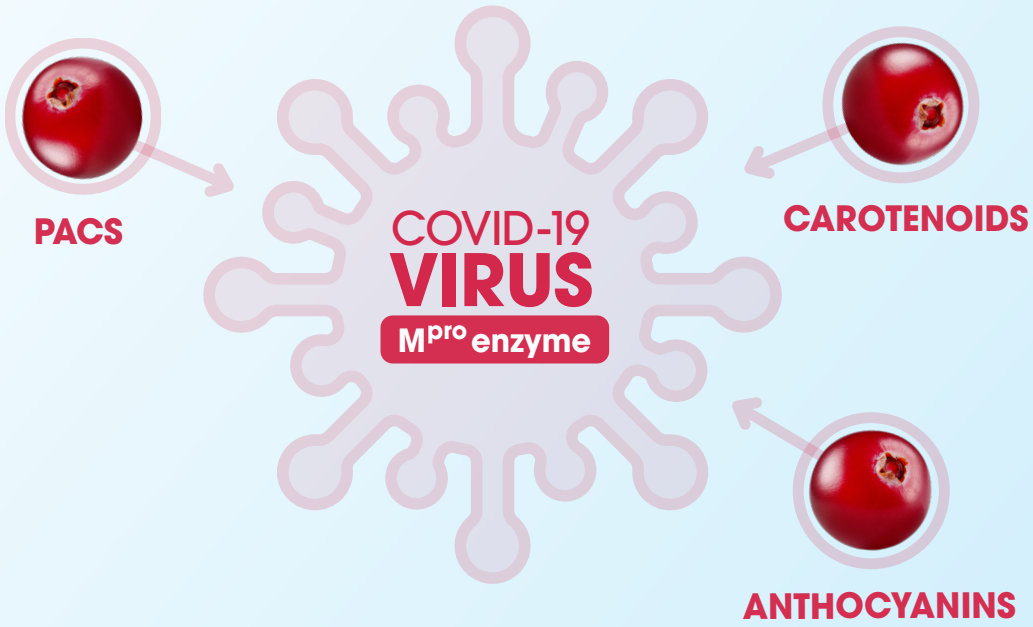


Early research suggests that the bioactive compounds found in cranberries have antitumor and cell growth inhibition properties.

Immunity & Virus Management

- Emerging research shows that certain cranberry bioactive compounds including anthocyanins, carotenoids, and PACs have powerful effects against a main villain of the COVID-19 virus, the M^{pro} enzyme.[105] M^{pro} is a protein whose structure has remained similar in most variants of the COVID-19 virus, making it a great target for development of protective strategies.
- Research suggests that cranberry polyphenols improve gut bacteria which helps with immunity benefits.[106] Dried cranberries have been shown to decrease negative *Firmicutes* bacteria and increase healthful *Bacteroidetes* bacteria.[23,24] Cranberries also help increase production of SCFAs, which have a role in supporting immunity.[5,18]

Cranberry bioactive compounds have powerful effects against the M^{pro} enzyme.



Research suggests that cranberry polyphenols improve gut bacteria which helps benefit immunity.

Cranberry Dietary Supplements for Maintenance of Urinary Tract Health

When it comes to utilizing cranberry for health benefits, there are a number of options available.

- Cranberry products come in many forms including juice, sauce, dried whole fruit and powder extracts, with all of these product forms having the potential to deliver health benefits.
- Many consumers are using cranberry dietary supplements, particularly to help prevent UTIs. They have some key advantages - portability, long shelf-life, ease of dose determination, and no added sugar. But there are different factors that can influence the efficacy and stability of the bioactive components in these products, depending on formulation and processing.
- Cranberry polyphenols, especially the proanthocyanins (PACs) have been associated with many of the health benefits attributed to cranberry consumption, including UTI prevention. PACs are high in the dried juice extracts and can help keep UTI-causing E. coli from sticking to the bladder. After juice is removed, PACs in the skins and pulp are bound to the fibers and are not as helpful for UTI prevention but may have some benefit for gut health. There are also supplements that can be blends of inexpensive pulp with a small amount of juice, which is more expensive but delivers most of the bioactivity.[107]

Many consumers are using cranberry dietary supplements, particularly to help prevent UTIs.

Cranberry Dietary Supplements for Maintenance of Urinary Tract Health

A key issue is standardization of supplements, especially accurate determination of bioactive compounds, such as PAC.

Research has demonstrated that consuming products containing 36 mg of cranberry PAC per day can help prevent recurrent UTIs.

Check your cranberry supplement label for the following:

- It is important to read the labels on products that say "cranberry" to be sure you are getting a high-PAC, juice-based extract for targeted UTI prevention benefit, instead of a whole berry product that is not enriched in PACs.
- Look for the 36 mg PAC/serving measured by DMAC-A2, which is the method accepted by the industry and often printed on the label.[108] Other methods can overestimate the actual PAC content of products and consumers may not get the expected health benefits.
- Most supplements have added ingredients called excipients, which can serve as fillers, stabilizers, or purported bioactivity enhancers. Watch out for cellulose-based excipients or oil gel caps because these additives can bind up PACs and reduce their bioavailability. There is little to no evidence that certain additives improve bioactivity by "shielding" the active compounds in the GI tract.
- It is important to purchase supplements made by reputable companies, as adulteration can be an issue. PACs can be extracted cheaply from other sources like grape seeds, peanut skins, and hibiscus, but they will not have the same benefits for UTI prevention.
- Once the products are processed into supplements, consumers can extend the shelf-life by keeping supplement bottles tightly closed in a dark place, as high humidity and light can degrade polyphenols.

Consuming products containing 36 mg of cranberry PAC per day can help prevent recurrent UTIs.

Cranberry Dietary Supplements for Maintenance of Urinary Tract Health

The UTI prevention potential of supplements can be measured using the bacterial anti-adhesion assay, which determines how effectively the PACs prevent uropathogenic *E. coli* bacteria from sticking to cells in the bladder.

- Bacteria cause infections when they attach to the bladder wall, so inhibiting this step can help prevent UTIs. Linking the 36 mg PAC content to this anti-adhesion activity by reporting it on supplement labels is a good way to improve consumer confidence in supplements targeted for UTI prevention. Positive clinical trial data on a particular supplement is also a good way to build confidence.
- There are factors that can affect the level of polyphenols in products and their overall stability. If harsh processing techniques are used, such as very high pressures or temperatures, more polyphenols can be extracted from the fruit, but their structures can be damaged and result in lower bioactivity and health benefits over time.[109]
- If a supplement is priced very low, you may only be getting fiber and a touch of cranberry juice, so you get what you pay for with cranberry supplements.

When looking for an effective cranberry supplement, especially to prevent UTIs, determine if the cranberry supplement meets the following criteria:

1. Is it a cranberry juice-derived formulation?
2. Is it standardized for 36 mg PAC using the DMAC/A2 method?
3. Has the product been tested for bacterial anti-adhesion bioactivity?

Bacteria cause infections when they attach to the bladder wall, so inhibiting this step can help prevent UTIs.

No Interaction with Blood Thinner Warfarin (Coumadin®) and Certain Antibiotics

Research on cranberry juice and Warfarin (Coumadin®) and certain antibiotics reveals:

- Complete avoidance of cranberry juice in people using Warfarin (Coumadin®) is not warranted. However, having large amounts daily, such as 1-2 liters of cranberry juice containing 27% cranberry, or taking more than the recommended amount of cranberry juice-based dietary supplements daily for more than 3-4 weeks may temporarily change the effects of Warfarin (Coumadin®).[110]
- Clinical research demonstrates that cranberry intake can prevent urinary tract infections, but when an infection occurs, antibiotics are prescribed to treat the infections. When certain antibiotics are prescribed, in some cases food-drug interactions can occur which can change the potency of the antibiotics. A systematic review found no significant interaction between cranberry juice and the bioavailability of amoxicillin and cefaclor.[111]
- The current U.S. Food and Drug Administration medication guide for Warfarin (Coumadin®) states: *Some foods and beverages can interact with Warfarin (Coumadin®) and affect your treatment and dose. Eat a normal, balanced diet. Talk to your healthcare provider before you make any diet changes. Do not eat large amounts of leafy, green vegetables. Leafy, green vegetables contain vitamin K. Certain vegetable oils also contain large amounts of vitamin K. Too much vitamin K can lower the effect of Warfarin (Coumadin®). Always tell all of your healthcare providers that you take Warfarin (Coumadin®).*[112] *A consistent diet is one way to help keep Warfarin (Coumadin®) working at its best. It's important to discuss any major changes to the foods you typically eat with your HCP.*[112]

Cranberry PACs may enhance the effectiveness of certain antibiotics.

Beta-lactam antibiotics are commonly used to treat bacterial infections including ***Staphylococcus*** and Enterobacteriaceae-associated infections.

Resistance to this antibiotic is becoming more common, which presents an issue for global health.[113] Research suggests that PACs from cranberry extracts may increase the effectiveness of beta-lactam antibiotics possibly through interference with resistance mechanisms.[114]

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