CystiCran™

PAC Standardized Cranberry Extract  
(*Vaccinium macrocarpon*)

Concentrated Source of Cranberry PACs for Urinary Tract Health

Cranberries are widely known as a potent source of antioxidants and for their unique anti-adhesion activity which helps protect the body from harmful bacteria that cause urinary tract infections. This unique anti-adhesion activity is primarily due to a natural compound in the fruit called proanthocyanidins (PACs).

CystiCran™ is a patented cranberry extract manufactured using only North American cranberries (*Vaccinium macrocarpon*) and offers standardized PAC levels for specific formulation requirements. CystiCran delivers the industry’s highest levels of concentrated and bio-active North American cranberry PACs found to help maintain a healthy urinary tract.

* U.S. Patents (5,474,774, 5,525,341, 5,646,178, 5,650,432), U.K. Patent (0752871), Australian Patents (703158, 708657)
Urinary Tract Health

Urinary Tract Infections (UTIs) are among the most common of all bacterial infections. UTIs affect over 11 million women in the United States every year and cost the U.S. healthcare system over $2 billion annually. Anyone of any age can have a UTI. However, young to middle-aged women who are sexually active are most often affected by UTIs.

An infection occurs when microorganisms, usually bacteria from the digestive tract, cling to the opening of the urethra and begin to multiply. Most infections arise from one type of bacteria, *Escherichia coli* (*E. coli*), which normally live in the colon and causes about 80% of UTIs in adults. Symptoms of UTIs, both uncomfortable and debilitating, may include pain or burning with urination, the urge to urinate frequently while passing only small quantities of urine, tenderness or a feeling of heaviness in the lower abdomen, cloudy or foul-smelling urine, pain on one side of the back under the rib cage (flank pain), fever, chills, nausea and vomiting.

Proanthocyanidins

Proanthocyanidins (PACs) are a class of biologically active flavonoids found throughout the plant kingdom, and are one of the most potent antioxidants in nature. Typically concentrated in the bark of trees and in the outer shells of fruits and seeds, proanthocyanidins serve to protect plants against oxidative elements such as oxygen and sunshine.

PACs are the phytochemical responsible for many of the health benefits associated with cranberries. Science has shown that cranberries contain unique A-type PACs, seldom found elsewhere in nature, that provide bacterial anti-adhesive properties and help promote urinary tract, gastrointestinal, and oral health. PACs are the “power of the cranberry.” Not all PACs are the same. Though many plant sources contain PACs, a recent study entitled “A-type Cranberry Proanthocyanidins and Uropathogenic Bacterial Anti-Adhesion Activity” Neto, et. al., and published in Phytochemistry (2005) has shown that North American cranberry A-link PACs are the only PACs that provide bacterial anti-adhesion activity.

Only the cranberry’s unique A-linked PACs exhibit *Ex vivo* bacterial anti-adhesion capabilities. B-link PAC found in many plants including; dark chocolate, apples, blueberries, grapes, etc. do not display bacterial anti-adhesion.

Cranberry PACs are Unique!
Source: Howell, et al., Phytochemistry, 2005
**Ex Vivo Studies**

Two cross-over human pilot clinical studies were conducted at Rutgers University to compare the ex vivo bacterial anti-adhesion activity of human urine after consumption of commercially available Cranberry Juice Cocktail (27% Cranberry) and two doses of CystiCran. The results showed that both 120 mg and 360 mg of CystiCran were just as effective at providing anti-adhesion activity as 300 ml of Cranberry Juice Cocktail.

**120 mg CystiCran vs. 10 oz. glass of CJC**

Discussion: Summing all observed anti-adhesion activity recorded for all participants over every time period yielded 40 out of a possible 120 for CystiCran, and 41/120 for CJC. The differences between the products were not statistically significant. The CystiCran activity is substantial from 6–24 hours and reaches peak activity at 9 hours.

**360 mg CystiCran vs. 10 oz. glass of CJC**

Discussion: Summing all observed anti-adhesion activity recorded for all participants over every time period yielded 48 out of a possible 120 for CystiCran, and 41/120 for CJC. The CystiCran activity is substantial from 6–24 hours and reaches peak activity at 9 hours.

**AFFSA Health Claim**

AFFSA Health Claim 2004 – Generic Cranberry Health Claim (36 mg of PACs)

Cranberry is the only fruit in the world with a government sanctioned health claim. On December 3, 2004 the French Food Authority (AFSSA) approved a health claim for the North American Cranberry (*Vaccinium macrocarpon*). The claim states that a product containing at least 36 mg of North American Cranberry PACs may carry the claim “help reduce the adhesion of certain *E. coli* bacteria to the urinary tract walls.”

**PAC Method of Analysis – Buyer Beware**

The international market for cranberry has grown significantly since the AFFSA claim was published in 2004. Consumer awareness of the benefits of cranberry PACs has also grown substantially. However, as a result of increased demand and AFFSA’s failure to specify the Method of Analysis (MOA) for PAC quantification associated with the 2004 claim there has been some manipulation in the market.

Certain cranberry extract suppliers choose to standardize their products using PAC quantification MOA’s that grossly inflate the PAC quantity. Others offer adulterated products spiked with non-cranberry PACs (these contain very low levels of North American cranberry PACs and have little to no anti-adhesion activity). As a result, supplement manufacturers are deceived and at times do not deliver the appropriate efficacious dosage of cranberry to the consumer.

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1. Rutgers University - Bacterial Anti-adhesion Activity of Human Urine: CystiCran (120 mg) vs. Cranberry Juice Concentrate Consumption
2. Rutgers University - Bacterial Anti-adhesion Activity of Human Urine: CystiCran (360 mg) vs. Cranberry Juice Concentrate Consumption
There are many MOA available for quantifying the content of PACs. Each method has its strengths and weaknesses including; reproducibility, cost, availability of reference standards, turn-around time, etc. When AFFSA failed to specify the MOA for measuring PACs in the 2004 claim it opened the door for suppliers to manipulate the MOA and undermine the spirit of the claim.

The AFFSA claim of 36 mg of PACs is based on the quantity of total PACs in a 300 mL glass of cranberry juice cocktail (27% cranberry juice) as measured using the DMAC method. The dossier submitted to AFSSA contained referenced two key literature sources:

1. “Reduction of Bacteriuria and Pyuria After Ingestion of Cranberry Juice”
Published in 1994 in the Journal of the American Medical Association, the “Avorn study,” is the landmark cranberry juice cocktail clinical trial. This study was the first of its kind to conclude that a 300 mL serving of Cranberry Juice Cocktail helps support urinary tract health.

- “Subjects were randomly assigned to consume 300 mL per day of commercially available standard cranberry beverage...:

- “…These findings suggest that use of a cranberry beverage reduces the frequency of bacteriuria pyuria in older women. Prevalent beliefs about the effects of cranberry juice on the urinary tract may have microbiologic justification…”

2. “Analysis and Standardization of Cranberry Products”
Published in 2002 in the Journal of the American Chemical Society, this study linked the quantification of 36 mg of PACs to the DMAC method.

“…Based on the outcome of this work, the DMAC method most appropriately meets our needs for routinely quantifying cranberry UTH-PACs...The method has a relative standard deviation of 4.6 percent, and when analyzing 12 samples of Ocean Spray Cranberry Juice Cocktail® obtained from four different bottling locations, resulted in an average UTH-PAC content of 30 mg/8 fl. oz.,”...

However since the DMAC method was proprietary and not a published or validated method AFFSA did not include it in the claim wording.

*Equates to 36 mg of PACs / 300 mL of CJC

North American cranberry growers, handlers and processors have sponsored the development, validation and publication of an industry standard PAC quantification method known as BL-DMAC method. The BL-DMAC method is accurate, reliable, reproducible, cost-effective and the reference standard use is commercially available. The BL-DMAC method correlates well with the AFFSA health claim as multi-lab results show that 300 ml glass of cranberry juice cocktail (27% cranberry) contains 36 mg of PACs. This industry standardized method will allow formulators to quickly and cost-effectively compare and contrast cranberry ingredients and reduce PAC method manipulation. A combination of testing using BL-DMAC and a bioassay ensuring anti-adhesion activity are the best solution for ensuring a high quality product.
The North American cranberry, *Vaccinium macrocarpon*, Aiton, is a member of the family Ericaceae that is composed of about 1350 species including Scotch Heather (*Calluna vulgaris*), Rhododendrons (*Rhododendron spp.*) and Blueberries (*Vaccinium augustifolium, V. corymbosum*). Cranberries are a low-growing, vining, woody perennial plant with small, alternate, ovate leaves. The plant produces stolons (horizontal stems) up to 6 feet (2 m) long. Short vertical branches, or uprights, 2 to 8 inches (5 to 20 cm) in height, grow from buds on the stolons and these can be either vegetative or fruiting. Each fruiting upright may contain as many as seven flowers. Pollination is primarily via domestic honey bees. *(Source: Cranberry Institute)*

**Applications**

CystiCran is ideal for nutraceutical and functional food applications such as:

- Softgels
- Capsules
- Softchews
- Sachets
- Liquid Supplements
- Tablets

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**References**