oterra™

Studies show phytonutrients support urinary tract *health*

Whitepaper

Prevention is key to supporting urinary tract *health*

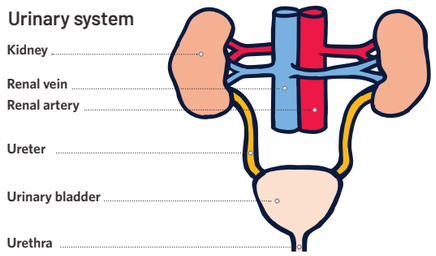
Urinary tract infections (UTIs) are the most common bacterial infection in adults. Women are disproportionately affected, with approximately one in two women experiencing a UTI at some time. For about 20-30%, UTIs become a recurring problem.[1]

A UTI can occur anywhere in the urinary system. Symptoms may vary depending on the site of infection, which typically occur more frequently in the bladder and urethra. When infection is in the kidneys, it can be more severe and may lead to sepsis or kidney failure.

In approximately 80% of UTIs, Escherichia coli (E. coli) strains are the most common uropathogens.[2] Other bacteria that cause UTIs are:[2]

- Klebsiella species
- Proteus mirabilis
- Enterococcus species
- Staphylococcus saprophyticus

As the vast majority of UTIs are caused by bacteria, antibiotic therapy is commonly recommended. Antibiotics are also prescribed as prophylaxis to prevent UTI recurrence.



Antimicrobial resistance is driving the need for *alternative* treatments

Consequently, antimicrobial resistance is on the rise. The World Health Organization (WHO) reports that in many parts of the world, one of the most widely used antibiotic treatments for UTIs is now ineffectual in more than half of patients.[3,4] There is also growing concern about treatment side effects and lack of long-term benefits.[5]

As a result, any urinary infection in otherwise healthy patients can reoccur and have serious long-term consequences.

Scientific evidence suggests that nonantimicrobial prophylactic strategies may help reduce the rate of infection and lessen the personal burden on the patient.[6]

These challenges are driving interest in finding effective non-antibiotic alternatives for prevention and treatment, such as plant-based compounds.

The role of plant-based *active* compounds in urinary tract

Studies indicate that a number of medicinal plants may have a beneficial effect on urinary tract health. Many are established remedies with active compounds that have proven antimicrobial properties.

Some of the most commonly used plants with antimicrobial activity include:[7]

- Asparagus – *Asparagus officinalis*
- Chamomile – *Matricaria recutita*
- Cranberry – *Vaccinium marcrocarpon*
- Dandelion – *Taraxacum officinalis*
- Garlic – *Allium sativum*
- Horseradish – *Cochlearia armoracia*
- Juniper – *Juniperus communis*

A number of studies show that the active compounds in these plants have the potential to promote cell wall disruption and induce the production of reactive oxygen species. They also have the potential to:[8]

- Inhibit biofilm formation
- Inhibit microbial DNA replication
- Inhibit energy synthesis
- Inhibit bacterial toxins to the host

In short, these compounds may prevent antibacterial resistance and have a synergestic interaction with antibiotics, which may ultimately kill pathogenic organisms.[8]

Cranberry – a *powerful*, proven antimicrobial

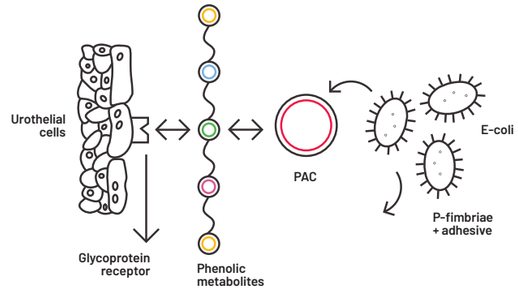
Cranberries are traditionally associated with urinary tract health.[9,10] More recently, the American Urological Association (AUA) highlighted cranberry as an effective means of prevention for UTIs.[11] And the results of several clinical studies indicate that cranberry may decrease recurrent UTIs in healthy women.[12-15]

Rich in phenolic compounds, cranberry contains anthocyanins, flavonols and proanthocyanidins.

In vitro and ex vivo research suggests that A-type proanthocyanidins (PACs) and other polyphenols in cranberry may:[12,16,17]

- Interfere with the adhesion of bacteria (including multi-resistant E-coli) to epithelial cells in the urinary tract
- Reduce the development of uropathogens
- Suppress inflammation
- Be suitable for prophylaxis in certain populations

Bacterial anti-adhesion mechanism of polyphenolic compounds (PACs and other phenolics) in cranberry
(Vaccinium macrocarpon)



To ensure the potency of cranberry products, PAC levels must be properly quantified and standardized. The 4-dimethylaminocinnamaldehyde method is currently recommended.[18] However, there are other methods available that distinguish between A and B-type PACs.

Processing methods can impact PAC composition[19], and may result in products that contain little or no PACs. In addition, the complexities of the PAC structures and A-type linkages mean that the measurement of PAC content is often inaccurate and may not be reproducible.[18]

Study results – dosage and efficacy
The results of a randomized controlled trial evaluating the dosage effect of cranberry powder found that to achieve a bacterial anti-adhesion effect in urine, 36 mg of cranberry PACs is effective, but in some cases 72 mg may offer better protection. As anti-adhesion activity decreases over time, it is recommended that cranberry products are consumed in the morning and evening.[19]

Studies also indicate that cranberry juice may help prevent UTIs during pregnancy.[20] A randomized controlled trial comparing the efficacy of cranberry juice with a placebo on 188 women under 16 weeks pregnant showed a 57% reduction in bacteriuria and 41% reduction in all UTIs.[20]

Another randomized controlled study on 760 pregnant woman compared the effect of cranberry juice and water. The study reported positive results – 70.5% of the participants who drank cranberry juice showed a significant reduction in UTIs compared to 32.16% of women who drank water.[22]

The global UTI *treatment* market is expected to reach USD 12.41 billion by 2025[2]

Cranberry has proven *benefits* for urinary tract health though study results differ

Safe and easy to use, cranberry products have a major advantage when used for the prevention of UTIs and for its bacterial anti-adhesion effect. There are however conflicting conclusions about efficacy. This is primarily due to variability in clinical studies, such as the use of different cranberry products and doses, as well as a lack of guidance for subject selection.[10,24]

Further studies are needed to support the efficacy of cranberry products, as well as the correct dosage and formulation for optimal clincal effect. This will make it easier for healthcare practitioners and consumers to make appropriate and informed choices for supporting urinary tract health.

Rich in proanthocyanidins and other phenolic compounds, our NutriPhy® Cranberry has urinary tract health benefits.

References:

1. Medina M and E Castillo-Pino, 2019. An introduction to the epidemiology and burden of urinary tract infections. Ther. Adv. Urol., 11, 3-7 2. Linhares I et al. 2013. Frequency and antimicrobial resistance patterns of bacteria implicated in community urinary tract infections: a ten-year surveillance study (2000–2009). BMC Infectious Diseases, 13(19), 1-14. 3. WHO, 15 February 2018. Antimicrobial resistance. Fact sheets (https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance) 4. https://www.health.harvard.edu/womens-health/the-growing-problem-of-drug-resistant-utis. Accessed February, 2020 5. Fleming-Dutra K et al. 2016. Prevalence of inappropriate antibiotic prescriptions among US ambulatory care visits, 2010-2011. Journal of the American Medical Association, 315(17), 1864-1873. 6. Bag A et al. 2008. Medicinal Plants and Urinary Tract Infections: An update. Pharmacognosy Reviews [Phcog Rev.], 2(4), 277-284. 7. Cowan M, 1999. Plant products as antimicrobial agents. Clin. Microbiol. Rev., 12(4), 564-582 8. Mickymaray S, 2019. Efficacy and Mechanism of Traditional Medicinal Plants and Bioactive Compounds against Clinically Important Pathogens. Antibiotics (Basel), 8(4), 251-257 9. Liska D et al., 2016. Cranberries and Urinary Tract Infections: How Can the Same Evidence Lead to Conflicting Advice? American Society for Nutrition. Adv Nutr., 7, 498-506 10. Jepson R et al. 2012. Cranberries for preventing urinary tract infections. Cochrane Database of Systematic Reviews. Published online October 17, 2012 11. Anger J et al. "Recurrent Uncomplicated Urinary Tract Infections in Women: AUA/CUA/SUFU Guideline." Published on American Urological Association website at https://www.auanet.org/guidelines/recurrent-uti. (2019). Accessed May 30, 2019 12. Vasileiou I et al., 2013. Current clinical status on the preventive effects of cranberry consumption against urinary tract infections. Nutr. Res., 33, 595-607 13. Caljouw M et al., 2014. Effectiveness of cranberry capsules to prevent urinary tract infections in vulnerable older persons: a double-blind randomized placebo controlled trial in long-term care facilities. J. Am. Geriatr. Soc., 62, 103-10 14. Stapleton A et al., 2012. Recurrent urinary tract infection and urinary Escherichia coli in women ingesting cranberry juice daily: a randomized controlled trial. Mayo Clin. Proc., 87, 143-50 15. Takahashi S et al., 2013. A randomized clinical trial to evaluate the preventive effect of cranberry juice (UR65) for patients with recurrent urinary tract infection. J. Infect. Chemother., 19, 112-7 16. Blumberg J et al., 2013. Cranberries and their bioactive constituents in human health. Adv. Nutr., 4, 618-32 17. Gonzalez D et al, 2015. Anti-Adhesive Activity of Cranberry Phenolic Compounds and Their Microbial-Derived Metabolites against Uropathogenic Escherichia coli in Bladder Epithelial Cell Cultures. Int J Mol Sci. 2015 Jun; 16(6): 12119-12130 18. Prior R et al., 2010. Multi-laboratory validation of a standard method for quantifying proanthocyanidins in cranberry powders. Journal of the Science of Food & Agriculture, 90(9), 1473-1478 19. Howell A et al., 2010. Dosage effect on uropathogenic Escherichia coli anti-adhesion activity in urine following consumption of cranberry powder standardized for proanthocyanidin content: a multicentric randomized double blind study. BMC Infectious Diseases, 10(94), 1-14 20. Ghouri F et al., 2018. A systematic review of non-antibiotic measures for the prevention of urinary tract infections in pregnancy. BMC Pregnancy Childbirth., 18(99), 1-10 21. Wing DA, Rumney PJ, Preslicka CW, Chung JH. Daily cranberry juice for the prevention of asymptomatic bacteriuria in pregnancy: a randomized, controlled pilot study. J Urol. 2008;180(4):1367-72 22. Essadi F, Elmehashi MO. Efficacy of cranberry juice for the prevention of urinary tract infections in pregnancy [abstract]. Poster Session. J Matern Fetal Neonatal Med. 2010;23(sup1):378 23. Fior Markets https://www.globenewswire.com/news-release/2019/09/12/1914668/0/en/global-urinary-tract-infection-treatment-market-is-expected-to-reach-usd-12-41-billion-by-2025-fior-markets.html 24. Renard J et al., 2015. Recurrent Lower Urinary Tract Infections Have a Detrimental Effect on Patient Quality of Life: a Prospective, Observational Study, Infect Dis Ther. 2015 Mar; 4(1): 125–135

020018G-EN