

Beyond Cranberry...

For those looking toward non-pharmacologic alternatives to treat uncomplicated urinary tract infections (UTI's) several options exist. Some are "old cures" now validated by rigorous research. Various over-the-counter formulae await motivated consumers who have grown tired of treating their animals with antibiotics and fearful that with each course they are fostering more resistant strains of bacteria. Typically, mixtures may contain botanical diuretics, urinary antiseptics, anti-adhesion plants, or anti-inflammatory agents. Fortunately, most of the products enticing consumers appear relatively innocuous, at least based on information gleaned from human trials. Additional options, such as probiotics and acupuncture, may not typically be considered "first-line" alternatives for UTI's, but could be helpful integrative adjuncts, nonetheless.

Diuretic herbs

Herbal diuretics span a continuum in terms of strength.¹ Weak diuretics include plants such as cleavers, horsetail, and pipsissewa. Dandelion and stinging nettle fall in the moderate category, while parsley, celery, birch, lovage, and goldenrod rank as strong diuretics. Parsley's diuretic effect, recognized since ancient times, appears to be mediated through an inhibitory action on the sodium-potassium pump.² Each of these plants also has a spectrum of other benefits. For example, parsley and its relative, celery, possess calcium channel-blocking activity in vitro, which helps explain their spasmolytic activity. Goldenrod, birch, parsley, and stinging nettle counter inflammation; birch offers antimicrobial benefits; and dandelion acts as a "bitter digestive tonic". Combination products designed for animals with urinary tract disorders frequently contain one or more herbs with diuretic properties.

Urinary antiseptics

The same chemicals that plants produce for self-defense against microbial attacks can likewise serve in a preventive or antibacterial manner for animals with urinary tract infections. Many plant compounds appear in the urine after renal excretion. Herbs noted for their antibacterial effects include uva ursi (or "bearberry") and juniper. Uva ursi leaves contain a glycoside known as arbutoside, which forms glucose and hydroquinone in the gut. Following absorption, hydroquinone reaches the liver and becomes glucuronidated. After renal excretion, the glucuronide portion falls away, provided that the urinary pH rises above 7, thereby allowing hydroquinone to act directly against urinary pathogens. Chronic administration of uva ursi may invite problems, since long-term exposure to synthetic hydroquinones is carcinogenic.³

¹ Yarnell E. Botanical medicines for the urinary tract. *World J Urol.* 2002;20:285-293.

² Kreydiyyeh SI and Usta J. Diuretic effect and mechanism of action of parsley. *J Ethnopharmacology.* 2002;79:353-357.

³ Yarnell E. Botanical medicines for the urinary tract. *World J Urol.* 2002;20:285-293.

Juniper leaves contain terpenoids with antimicrobial actions; some terpenoids also cause diuresis as well. Folkloric writings claim that juniper can be nephrotoxic. However, two separate reviews surmise that early reports of renal damage may have arisen either from contaminants or misidentification of plants thought to be juniper.⁴

Anti-adhesion herbs

Two well-known botanical compounds interfere with adhesion of *E. coli* to bladder epithelium: cranberry (the old stand-by for UTI's) and berberine (found in plants such as Oregon grape and goldenseal). Proanthocyanidins in cranberry inhibit microbial binding to bladder epithelium. They further inhibit the ability of *E. coli* to bind to intestinal mucosa, and prevent *H. pylori* from adhering to gastric mucosa. Blueberries contain proanthocyanidins as well, which confer similar anti-adhesion properties.⁵ Specific glycoprotein receptors known as "fimbriae" or "lectins" on the surface of bacterial cells bind to sugars residing on the mucosal cell surfaces of the host.⁶ High molecular weight components in juices such as cranberry are thought to reduce bacterial adherence capacity by competing for binding sites. Increasing numbers of dry foods for cats and dogs are listing cranberries and blueberries as ingredients, likely for this purpose.

Although cranberry has been deemed overall to be safe and is widely used, the effects of cranberry juice on "urinary stone forming propensity" appear to be mixed.⁷ According to a 2005 article in the *Journal of Urology* by Gettman et al, cranberry juice may heighten the risk of calcium oxalate and uric acid stone formation but reduce the risk of brushite stones. On the other hand, a 2003 article in the *British Journal of Urology International* concluded, "Cranberry juice has antilithogenic properties and, as such, deserves consideration as a conservative therapeutic protocol in managing calcium oxalate urolithiasis".⁸

Chinese Herbal risks

While most herbs for urinary tract infections raise relatively minor concerns, one urinary herb in particular may contain the renotoxic chemical, aristolochic acid (AA). AA causes lesions in the kidney now known as "Chinese herb nephropathy", which resembles renal interstitial fibrosis.⁹ The Chinese herbal

⁴ Yarnell E. Botanical medicines for the urinary tract. *World J Urol.* 2002;20:285-293.

⁵ Yarnell E. Botanical medicines for the urinary tract. *World J Urol.* 2002;20:285-293.

⁶ Vattem DA, Ghaedian R, and Shetty K. Enhancing health benefits of berries through phenolic antioxidant enrichment: focus on cranberry. *Asia Pac J Clin Nutr.* 2005;14(2):120-130.

⁷ Gettman MT, Ogan K, Brinkley LJ, Adams-Huet B, et al. Effect of cranberry juice consumption on urinary stone risk factors. *J Urol.* 2005;174:590-594.

⁸ McHarg T, Rodgers A, and Charlton K. Influence of cranberry juice on the urinary risk factors for calcium oxalate kidney stone formation. *BJU International.* 2003;92:765-768.

⁹ Zhu S, Liu J, Chen L, et al. Chemopreventive effect of five drugs on renal interstitial fibrosis induced by an aristolochic acid-containing Chinese herb in rats. *Am J Nephrol.* 2005;25(1):23-29.

combination commonly suggested for animals with “simple acute cystitis”, known as Ba Zheng San (or “Eight Rectifiers Powder”),¹⁰ lists its main ingredient as mutong. “Mutong” may refer to several different plants, given that traditional Chinese medical herbal prescribing practices allow substitutions.¹¹ Some of these plants that qualify as mutong contain aristolochic acid.¹² Animals afflicted with chronic renal failure are more affected by this constituent, which is not only nephrotoxic, but also carcinogenic.¹³

Probiotics

Many urinary tract pathogens arise from the intestinal microflora.¹⁴ Prophylactic measures designed to reduce the recurrence of UTI's now include administration of probiotics and/or “probiotics”, which provide nourishment for these beneficial bacteria. Some investigators are now promoting lactulose as an agent that can alter pathogenicity of the fecal flora.¹⁵ Promoting a more healthy intestinal ecology by controlling the load of pathogenic bacteria in the gut offers one more relatively non-toxic means of preventing infection in the urinary tract.

Acupuncture

Finally, as another preventive procedure, acupuncture may prevent recurrent UTI's by restoring healthful micturition. Two studies indicate that acupuncture applied to points in the caudal truncal region and pelvic limbs reduced residual urine volume. UTI's in women prone to developing cystitis recurred only half as often in those patients receiving acupuncture, compared to those left untreated.¹⁶¹⁷ The authors conjecture that acupuncture improved urodynamics via a pelvic reflex arc involving structures such as the pudendal and sacral nerves. This finding is further supported by other acupuncture research affecting the pelvic

¹⁰ Wynn S and Marsden S. *Manual of Natural Veterinary Medicine – Science and Tradition*. St. Louis: Mosby, 2003. P. 598.

¹¹ Wu KM, Farrelly JG, Upton R, and Chen J. Complexities of the herbal nomenclature system in traditional Chinese medicine (TCM): Lessons learned from the misuse of *Aristolochia*-related species and the importance of the pharmaceutical name during botanical drug product development. *Phytomedicine*. 2006; Epub ahead of print.

¹² Zhu YP. Toxicity of the Chinese herb mu tong (*Aristolochia manshuriensis*). What history tells us. *Adverse Drug React Toxicol Rev*. 2002;21(4):171-177.

¹³ Cheng C-L, Chen K-J, Shih P-H, Lu L-Y et al. Chronic renal failure rats are highly sensitive to aristolochic acids, which are nephrotoxic and carcinogenic agents. *Cancer Letters*. 2006;232:236-242.

¹⁴ Tannock GW. The bowel microflora: an important source of urinary tract pathogens. *World J Urol*. 1999;17:339-344.

¹⁵ Battle M, Martin T, and Fulton J. Letters. Lactulose may help prevent urinary tract infections. *BMJ*. 2001;323:936.

¹⁶ Alraek T, Soedal LIF, Fagerheim SU, et al. Acupuncture treatment in the prevention of uncomplicated recurrent lower urinary tract infections in adult women. *American Journal of Public Health*. 2002;92(10):1609-1610.

¹⁷ Aune A, Alraek T, LiHua H, and Baerhim, A. Acupuncture in the prophylaxis of recurrent lower urinary tract infection in adult women. *Scand J Prim Health Care*. 1998;16:37-39.

reflex arc in cases of sensory urgency following transurethral resection of the prostate.¹⁸

¹⁸ Ricci L, Minardi D, Romoli M, et al. Acupuncture reflexotherapy in the treatment of sensory urgency that persists after transurethral resection of the prostate: a preliminary report. *Neurourology and Urodynamics*. 2004;23:58-62.