

# Significant Reduction in the Recurrence of Urinary Tract Infection (UTI) Symptoms with Cystikare developed by Composition of Cranberry Prophylactic Adjuvant with D-Mannose

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**ABSTRACT** *The market of nutritional supplements for women care is proliferating these days. Urinary tract infections (UTIs) have always been and still continue to be a major health concern to women. UTI stands as the most prevalent bacterial infection suffered by women. Cranberry has been used in preventive and treatment medicines for UTI, since decades now. Most UTIs are acute uncomplicated cystitis caused by Escherichia coli (86%). Women with recurrent UTIs are the group to whom most recommendations regarding cranberry consumption is directed, inclusion of other groups in the efficacy assessment could influence clinical practice quality.*

*To be able to provide effective treatment for urinary health and many other related issues, these plant based compositions should not only have correct balance of antioxidants but also should be upgraded time to time, in accordance to latest clinical findings or developments.*

## UTIs (Urinary Tract Infections)

Due to women's anatomy, UTIs are especially problematic for them, and up to one-third of all women will experience a UTI at some point during their lifetimes. Appropriate treatment of a UTI requires accurate classification that includes infection site, complexity of the infection, and the likelihood of recurrence.

It has been calculated that about one-third of adult women have experienced an episode of symptomatic cystitis at least once. It is also common for these episodes to recur. If predisposing factors are not identified and removed, UTI can lead to more serious consequences, in particular kidney damage and renal failure. The aim of this review was to analyze the factors more commonly correlated with UTI in women, and to see what possible solutions are currently used in general practice and specialized areas, as well as those still under investigation. In a prospective study by Haylen et al 1140 women aged 18–98 years were examined for recurrent UTI in different physiologic and pathologic conditions.<sup>1</sup>

Also, the incidence of UTI in women increases with age. Bacteriuria occurs in about 10%–15% of women aged 65–70 years and in 20%–50% of women aged over 80 years.

**Table 1: Factors linked to an increased risk of Catheter-Associated UTIs (CAUTIs). (in alphabetical order)\***

Advanced age
Anatomic anomalies of the urinary tract
Comorbidities
Concurrent debilitating illness, including ICU admission
Distant coexisting infection
Faecal incontinence
Female sex and pregnancy
Immobility
Immunocompromised status (HIV/AIDS, prolonged steroid use, uncontrolled diabetes)
Institutionalisation or long term care facility residence
Long term catheters
Longer hospital stay
Poor nutritional status
Previous recurrent or difficult to treat UTI
Urological procedures

\*Modified from: American Urology Associations "Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis (2008).

### Uncomplicated versus Complicated UTIs

A complicated UTI is an infection associated with a condition, such as a structural or functional abnormality of the genitourinary tract, or the presence of an underlying disease; this increases the risk of the outcome of a UTI being more serious than expected, as compared to its occurrence in individuals without any identified risk factors (i.e. uncomplicated UTI).

#### Classification based on clinical presentation of urinary tract infection (UTI) and risk factors (RFs)

Type	Category of RF	Example
O	No known/associated RF	Healthy premenopausal women
R	Recurrent UTI RF, but no risk of severe outcome	Sexual behaviour and contraceptive devices Hormonal deficiency postmenopause Secretory type of certain blood groups Controlled diabetes mellitus
E	Extra-urogenital RF, with risk of more severe outcome	Pregnancy Male gender Badly controlled diabetes mellitus Relevant immunosuppression* Connective tissue diseases* Prematurity, newborn
N	Nephropathic disease, with risk of more severe outcome	Relevant renal insufficiency* Polycystic nephropathy
U	Urological RF, with risk of more severe outcome, which can be resolved during therapy	Ureteral obstruction (i.e. stone, stricture) Transient short-term urinary tract catheter Asymptomatic bacteriuria† Controlled neurogenic bladder Urological surgery
C	Permanent urinary catheter and non-resolvable urological RF, with risk of more severe outcome	Long-term urinary tract catheter treatment Non-resolvable urinary obstruction Badly controlled neurogenic bladder

\*Not well defined. †Usually in combination with other RFs (e.g. pregnancy or urological intervention).

Notably, **Uncomplicated UTIs** included all patients who visited the polyclinic with a diagnosis code for UTI but did not correlate this with the actual symptoms. Since patients who were recently discharged from hospitals could have been included as well, nosocomial and community-acquired UTIs were also not accurately differentiated.

Hospitalization is often required in **Complicated UTIs** and therapy should be guided by urine cultures whenever possible to avoid the emergence of resistant strains. Patients can also be treated as outpatients by confident family physicians; treatment for 7–14 days is generally recommended in Complicated UTIs, but the duration should be closely related to the treatment of the underlying abnormality<sup>2</sup>.

### Effectiveness of Cranberry in treating Urinary Tract Infections

At the top of UTI “myth list” is the widely held belief that drinking cranberry juice or taking cranberry supplements can prevent and treat UTIs. “There is an active ingredient in cranberries that can prevent adherence of bacteria to the bladder wall, particularly *E. coli*,” says urologist Courtenay Moore, MD.

The active ingredient in cranberries -- A-type proanthocyanidins (PACs) -- is effective against UTI-causing bacteria, but is found only in cranberry capsules, not in cranberry juice, Boone said.

Cranberries have historically been associated with urinary tract health, particularly among women with recurrent UTIs (rUTIs). Results from several clinical studies have suggested that cranberries may decrease rUTIs in healthy women. In addition, *in vitro* and *ex vivo* research has suggested that cranberry-derived compounds such as A-type proanthocyanidins and other polyphenols may interfere with adhesion of bacteria (including multidrug-resistant *Escherichia coli*) to epithelial cells of the urinary tract, attenuate the development of uropathogen reservoirs (i.e., in the gastrointestinal tract and intracellular pods within the urothelium), and suppress inflammatory cascades. These observations have indicated that cranberries may provide an option for prophylaxis in certain populations<sup>3</sup>.

Cranberries and UTIs have been evaluated in evidence-based systematic reviews and meta-analyses, but instead of providing clarity on the efficacy of the cranberry for prevention of UTIs, these systematic reviews have resulted in conflicting conclusions<sup>3</sup>.

Cranberry appears to work by inhibiting the adhesion of type I and P-fimbriated uro-pathogens (e.g. uropathogenic *E. coli*) to the uroepithelium, thus impairing colonization and subsequent infection. The isolation of the component(s) of cranberry with this activity has been a daunting task, considering the hundreds of compounds found in the fruit and its juice derivatives. Reasonable evidence suggests that the anthocyanidin/proanthocyanidin moieties are potent antiadhesion compounds<sup>4</sup>.

#### **D-Mannose: Promising support for UTIs in women**

It appears that D-Mannose works best if taken preventively or at the very first signs of infection.

The downsides of long-term antibiotic prophylaxis are possible adverse reactions (although rare), costs and increasing bacterial resistance to antibiotics; therefore, alternative prophylactic agents, such as cranberry juice and probiotics have been extensively studied. One such agent is D-mannose, which is normally present in human metabolism and has an important role, especially in the glycosylation of certain proteins. The supposed mechanism of action is inhibition of bacterial adherence to urothelial cells. D-mannose acts as a competitive inhibitor of bacterial adherence. It is important to note that the anti-adhesive effect of mannose depends on the configuration of the molecule. Only D-isomer and  $\alpha$ -anomer ( $\alpha$ -D-mannose) can bind and block the FimH adhesin. Other carbohydrates have little or no anti-adhesive effect<sup>5</sup>.

In fact, there is *in vitro* evidence that mannose can inhibit macrophage activity, which could theoretically retard bacterial clearance from the urinary tract. Additionally, d-mannose may not be effective against certain strains of UPEC or other uropathogenic bacteria that do not express type 1 pili and FimH<sup>6</sup>.

#### **Conclusion**

The process in our understanding of UTI pathogenesis over the past decade has been truly remarkable. The long-term ability of an association of cranberry and D-mannose, an innovative gelling complex, with lactobacillus strains tested to significantly improve the uncomfortable symptoms reported by women with acute cystitis and Urinary Tract Infections.

Also it has been reviewed, it's extremely effective when causative bacteria is *E. coli*. Whenever *E. coli* infect urinary bladder, D-mannose being a simple sugar attaches at fimbriae of *E. coli* and prevents its motion. Cranberry then acidify the urine & reducing bacterial adhesion to UTI. If the combination (cranberry & D-Mannose) does not show significant improvement in 24~ 48 hrs. It is likely that causative organism is not *E. coli*. In such cases a different approach by bacteria analytical examination is required.

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