D-Mannose SAP

*Science-based urinary antiadhesion formula for urinary tract infections**

Annually, urinary tract infections (UTIs) are responsible for more than 11 million physician visits in the United States.* Although normally a commensal inhabitant of the intestinal and gastrointestinal tract of humans, *Escherichia coli* is the most common urinary-tract pathogen, whose overgrowth and overcolonization account for 85% of UTIs.* Cranberries have been used as a medicinal agent for centuries to promote health, but recently the scientific literature has proven that proanthocyanidins, contained in cranberries, as well as a simple sugar, D-mannose, specifically inhibit the adhesion and proliferation of *E. coli* in the urinary tract.* Cranberry extracts and D-mannose each independently inhibit one of two adhesion methods utilized by *E. coli*. Combined together in a synergistic and novel formula, **D-Mannose SAP** addresses both type 1 (FimH) and p-type fimbrial-mediated adhesion by *E. coli* to the urinary tract mucosa.* **D-Mannose SAP** is specifically targeted for the treatment and prevention of *E. coli* UTI.*

SUPPLEMENT FACTS

Serving Size: 1 Rounded Teaspoon (5 g) **Servings:** Approx. 10

	Amount Per Serving	% Daily Value
D-Mannose	4600 mg	**
Cranberry (*Vaccinium macrocarpon*)	400 mg	**

**Daily Value not established

This product is non-GMO.

Contains no: Gluten, wheat, eggs, yeast, citrus, preservatives, artificial flavor or color, or starch.

DIRECTIONS FOR USE

Adults: Take 5 g (approx. 1 teaspoon) once or twice daily or as directed by your healthcare practitioner.

INDICATION

D-Mannose SAP:

- Provides therapeutic dosages of both D-mannose and cranberry extract, both known E. coli-adhesion inhibitors in the genitourinary tract.*
- May be effective for the treatment of acute E. coli urinary tract infections and for the prevention of recurrent urinary tract infections.*

PURITY, CLEANLINESS, AND STABILITY

Third-party testing is performed on the finished product to ensure **D-Mannose SAP** is free of heavy metals, pesticides, volatile organics, and other impurities.

*** These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**

Scientific Advisory Panel (SAP): adding nutraceutical research to achieve optimum health

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URINARY TRACT INFECTIONS AND *E. COLI*

Urinary tract infection (UTI) is defined by the presence of microorganisms in the urinary tract, including the bladder, prostate, urinary collecting system, and the kidneys. Annually, UTIs are responsible for more than 11 million physician visits in the United States. The most common urinary pathogen, whose overgrowth and overcolonization account for 85% of UTIs, is *Escherichia coli* (*E. coli*).[1][2]

UTIs have a high resistance to first-line antibiotic therapies, and treatment with antibiotics is associated with side effects such as nausea, diarrhea, *Candida* infections, and dysbiosis.[3]

UTIs are approximately 30 times more prevalent in the adult female population, but may occur in men and children. It is estimated that 60% of women will experience at least a single UTI during their lifetime, and of these women, 33% will experience frequent and recurrence infections. Women are more susceptible to UTIs, due to a shorter urethra that allows for more ready colonization and ascension to the bladder. Pregnancy, sexual activity, aging, and the use of medical devices (i.e. catheters) increase the risk and severity of UTIs. Symptoms of UTI include increased frequency and urgency of urination, cloudy urine, painful urination, and lower-back pain.[4]

MECHANISM OF ACTION

The bacterial cell wall of *E. coli* includes protein-like fibres called fimbriae, which readily attach to uroepithelial cells. Adhesion is the first and most critical step to colonization by *E. coli* and subsequent development of UTI. Proanthocyanidins and fructose, found in high concentrations in cranberry extract, in addition to D-mannose, competitively inhibit uroepithelial adhesion by *E. coli* fimbriae. *E. coli* fimbriae produce two fimbrial receptor proteins: type 1 fimbriae receptors are considered mannose-sensitive, and p-type fimbriae receptors are considered mannose-resistant.[5][6]

By inhibiting adhesion, cranberry extract and D-mannose are both effective at increasing urinary excretion of *E. coli*. Cranberry extracts have been shown in studies to effectively inhibit p-type *E. coli* fimbriae within 2–10 hours of ingestion. D-Mannose and fructose, a sugar found in cranberry extracts, specifically inhibit type 1 fimbrial receptors (specifically a protein called FimH),[7][8] while proanthocyanidins from cranberry extracts specifically target p-type receptors.[9]

CRANBERRY AND D-MANNOSE RESEARCH

Multiple randomized intervention trials have observed a clinical benefit of cranberry products in preventing UTI.[10][11][12][13] These findings include reported reduction of urinary bacteria and discharges following cranberry-juice intake. Increased intake of cranberry products has also been associated with a decrease risk of UTI.[14]

D-Mannose has been proven to not only block bacterial adhesion on uroepithelial cells, but also antagonize invasion and biofilm formation, effectively inhibiting the colonization of bacteria on the mucosal surfaces of the genitourinary tract.[15][16]

SAFETY OF D-MANNOSE SAP

Intake of cranberries and D-mannose is considered safe. High intakes of cranberry extracts or juices may have laxative effect. Cranberries contain moderately high levels of oxalates, and Terris et al. reported that patients at risk of nephrolithiasis should avoid dietary supplementation of cranberries.[17] In 2004, the Committee for Safety of Medicines warned healthcare professionals about the possibility of interaction between warfarin and cranberry juice,[18] though little clinical evidence or literature exist to corroborate this. Caution is advised for the use of cranberry-containing products with concurrent warfarin use.

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Science-based urinary antiadhesion formula for urinary tract infections

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INDICATION-SPECIFIC DOSAGE SUMMARY BASED ON HUMAN CLINICAL RESEARCH#

#Please note these suggestions are guidelines based on the clinical studies. Evidence for efficacy and safety has been qualitatively (study quality in terms of study design, sample size, appropriate methods of analysis, use of appropriate placebo/control, bias etc.) assessed and has been rated using a 5-star ★ rating classification.

Indication	Suggested D-Mannose SAP dosage	Supporting evidence and study outcomes	Study design	Outcomes measures	Safety	Evidence quality rating
WOMEN HEALTH						
UTI [1],[2],[3],[4],[5],[6]	1 teaspoon per day	Significantly less incidence of recurrent UTI compared to the no-prophylaxis group; also, a considerably lower risk of recurrent UTI episodes and lower side effects.	Randomized, prospective, controlled study (*n* = 308; 6 months). 2 g/d of D-mannose powder.	Number of patients in each group without recurrent UTI, risk of recurrent UTI episodes, and side effects during prophylaxis.	No severe adverse effects reported (8% reported diarrhea).	★★★
	1 to 1.5 teaspoons per day	Significant prevention of UTI in D-mannose group compared to other treatment methods; also, a substantial reducing of the number of symptomatic UTIs.	21 randomized, controlled studies (*n* = 3,892, 3 days to 12 months). 2 to 3 g/d of D-mannose + 500 mg of cranberry.	Number of UTI, time to first UTI, % of patients UTI-free, duration of UTI, and symptoms score.	No severe adverse effects reported (diarrhea, headache, sinusitis, constipation, heartburn).	★★★★★
	1 teaspoon per day	Significant decline in the meantime to UTI recurrence compared to antibiotic treatment; also, a substantial decrease in mean evaluation of bladder pain (VASp), urinary urgency score (VASu), and average numbers of 24-hour voiding.	Randomized, crossover, pilot study (*n* = 60; 22 weeks). 3 g/d of D-mannose for 2 weeks, followed by 2 g/d of D-mannose for the next 20 weeks.	Evaluation of the elapsed time to recurrence, VASp, and VASu.	No severe adverse effects reported (irritable bowel syndrome, constipation).	★★★★
	0.5 teaspoon per day	Significantly low UTIs in the treatment group compared to the control group.	Randomized, controlled, single-centre study (*n* = 55; 90 days). 1 g of D-mannose and 36 mg of cranberry dry extract + 1 billion CFU of *Lactobacillus paracasei* LC11.	Rate of UTI recurrence, including pain in the projection of the urinary bladder, frequent urination, a sensation of urethral discomfort, and a positive urine culture.	No severe adverse effects reported.	★★
	1.5 teaspoons per day	Significant improvement from UTI-related symptoms and a substantial improvement in quality of life (QoL).	Randomized, pilot study (*n* = 44; 10 days). 3 g/d of D-mannose.	Urinary Tract Infection Symptoms Assessment (UTISA), including dysuria, frequency, urgency, suprapubic pain, gross hematuria, and QoL.	No severe adverse effects reported.	★★
	1 teaspoon per day	Significant reduction in recurrent UTIs in D-mannose–receiving participants (15%) compared to the no-prophylaxis group (60%).	Randomized, controlled study (*n* = 308; 6 months). 2 g/d of D-mannose powder.	Reduction in microbiologically proven UTI.	No severe adverse effects reported (diarrhea).	★★★
Recurrent UTI [7]	0.5 to 1 teaspoon per day	D-Mannose proved to be as effective as antibiotics in preventing recurrent UTIs.	2 randomized controlled studies, 1 randomized crossover study, and 4 prospective cohort studies (*n* = 592; 10 days to 6 months). 420 mg/d to 2 g/d of D-mannose.	Relative risk (RR) of recurrent UTI, mannose v. antibiotics.	No severe adverse effects reported (diarrhea).	★★★★

Cystitis [8],[9],[10]	0.5 to 1.5 teaspoons per day	D-Mannose is significantly safe and effective in treating nonantimicrobial prophylaxis or recurrent UTIs in women.	6 randomized, controlled studies, 1 randomized crossover study, 5 prospective cohort studies, 1 retrospective analysis (*n* = 344; 3 days to 6 months). 250 mg/d to 3 g/d of D-mannose.	Prevention of recurrent UTIs or urodynamics-associated UTI, QoL, safety, tolerability, and maximally tolerated dose.	No severe adverse effects reported (diarrhea).	★★★★
	0.5 teaspoons per day	Significant positive results for the presence of nitrites and leukocyte esterase; also, a substantial improvement from cystitis, specifically dysuria, frequent voiding, urgency, and suprapubic pain.	Prospective pilot study (*n* = 33; 60 days). 500 mg of D-mannose and 1 g of cranberry extract for the first 30 days; 250 mg of D-mannose and 500 mg of cranberry extract for the next 30 days, + 2.5 billion live cells of *L. plantarum* LP01 and 1 billion viable cells of *L. paracasei* LPC09.	Quantification of nitrites and leukocyte esterase in urine samples, assessment of the most typical symptoms of cystitis.	No severe adverse effects reported.	★★
	1 teaspoon per day	Significant decrease in the UTI incidence rate in patients with cystitis cystica (CC) lesions and in patients without CC.	Retrospective cohort study (*n* = 27; 12 months). 2 g/d of D-mannose.	Incidence rate of UTI.	No severe adverse effects reported.	★★
URINARY HEALTH						
UTI [11],[12],[13]	0.5 to 1.5 teaspoons per day	Significant decline with respect to recurrent UTIs and cystitis.	1 randomized, crossover study, 1 randomized controlled study, 4 prospective uncontrolled studies, 1 retrospective case-control study (*n* = 386; 7 days to 30 weeks). 500 mg/d to 3 g/d of D-mannose and 400 to 1,000 mg/d of cranberry extract.	Symptom score of UTI/cystitis, visual analogic scale (VAS), VASp, VASu, dysuria, frequency, urgency, suprapubic pain, gross hematuria, and QoL.	No severe adverse effects reported.	★★★★
	0.5 to 1 teaspoon per day	The review suggests a D-mannose v. placebo-controlled clinical study can help in understanding the efficacy of its treatment against UTIs.	7 randomized, controlled studies (*n* = 712; 15 days to 12 months). 500 mg/d to 2 g/d of D-mannose.	Total number of symptomatic bacteriuria, recurrent symptomatic bacteriuria, QoL, and cure/complete remission of symptomatic and asymptomatic UTI.	No severe adverse effects reported (diarrhea, nausea, headache, skin rash).	★★
	0.5 teaspoon per day	Significantly higher curing rates were noticed at day 7, even in patients infected by antibiotic-resistant strains.	Randomized, double-blind, placebo-controlled, pilot study (*n* = 93; 21 days). 1 g/d of D-mannose and 400 mg/d of cranberry extract.	Efficacy of D-mannose plus cranberry extract on the reduction in the severity, persistence, and recurrence of UTI.	No severe adverse effects reported.	★★★
GENETIC DISORDER						
Phosphomannomutase 2 deficiency [14]	0.5 to 1 teaspoon per kg body weight per day (5 to 33 teaspoons per day).	Significant improvement in protein glycosylation after receiving D-mannose for a mean time of 1 year.	Retrospective study (*n* = 20; 57 to 100 months). 1 to 2 g/kg_{bw}/d of D-mannose (9 to 66 g/d of D-mannose).	Glycoprotein analyses and mean D-mannose concentration before ingestion.	No severe adverse effects reported (diarrhea and flatulence).	★★★

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