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.

ACTIVE INGREDIENTS

Each 5 g (approx. 2½ teaspoons) contains:

Cranberry (*Vaccinium macrocarpon*)	400 mg
D-Mannose	4600 mg

Contains no: Gluten, wheat, eggs, yeast, citrus, preservatives, artificial flavour or colour, or starch.

DIRECTIONS FOR USE

Adults: Take 5 g (approx. 2½ teaspoons) once or twice daily or as directed by your healthcare practitioner.

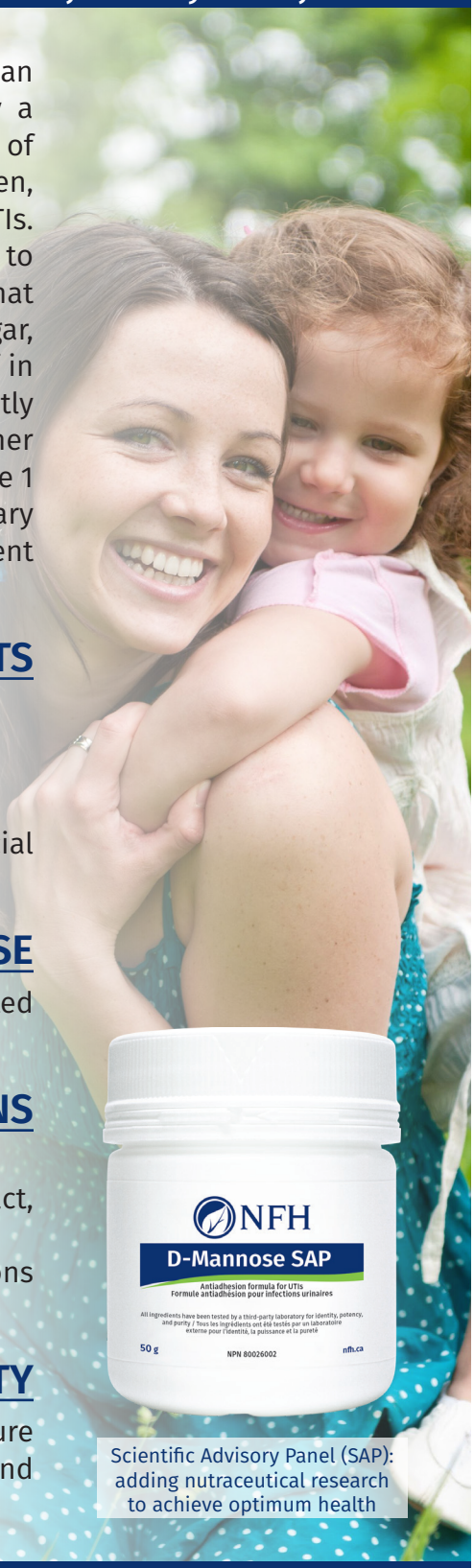
INDICATIONS

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.



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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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