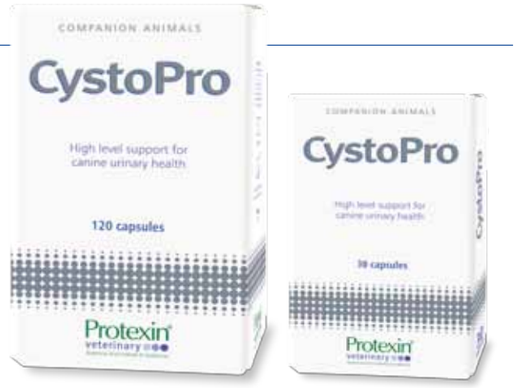
CystoPro

Supporting Canine Urinary Health

Presentation

Each capsule of CystoPro contains:

- 20mg Proanthocyanidins
- 125mg N-acetyl D-glucosamine
- *Enterococcus faecium* (NCIMB 10415) E1707 $1x10^{11}$ CFU/kg
- Mannan-oligosaccharide
- Artificial chicken flavour



CystoPro is available in boxes of 30 and 120 capsules

Directions For Use

Body weight	Number of capsules per day
<20kg	1 capsule
20-40kg	2 capsules
40-60kg	3 capsules

Capsules can be given whole or opened and the contents sprinkled onto food.

Give for as long as considered necessary or as advised by your veterinary surgeon.

References:

1. Ling GV. 1984. Therapeutic strategies involving antimicrobial treatment of the canine urinary tract. *J Am Vet Med Assoc.* **185**: 1162-1164.
2. Lees GE. 1996. Bacterial urinary tract infections. *Vet Clin North Am Small Anim Pract.* **26**: 297-304.
3. Thomsen MK, Svane LC, Poulsen PH. 1986. Canine urinary tract infection. Detection, prevalence and therapeutic consequences of bacteriuria. *Nord Vet Med.* **38**: 394-402.
4. Ling GV, Norris CR, Franti CE, *et al.* 2001. Interrelations of organism prevalence, specimen collection method, and host age, sex, and breed among 8,354 canine urinary tract infections (1969-1995). *J Vet Intern Med.* **15**: 341-347.
5. Forrester SD, Troy GC, Dalton MN, Huffman JW, Holtzman G, 1999. Retrospective evaluation of urinary tract infection in 42 dogs with hyperadrenocorticism or diabetes mellitus or both. *J Vet Intern Med.* **13:** 557–560.
6. Wooley RE, Blue JL. 1976. Bacterial isolations from canine and feline urine. *Mod Vet Pract.* **57**: 535-538.
7. Barsanti JA. 2006. Genitourinary infections. In: Greene CE, ed. *Infectious diseases of the dog and cat.* Edition 3. St Louis: Saunders: 935-961.
8. Bubenik LJ, Hosgood GL, Waldron DR, Snow LA. 2007. Frequency of urinary tract infection in catheterized dogs and comparison of bacterial culture and susceptibility testing results for catheterized and non-catheterized dogs with urinary tract infections. *J Am Vet Med Assoc.* **231**(6): 893-9.
9. Howell AB *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 Disease.* **10**: 94.
10. Reid G *et al.* 2001. Cranberry juice consumption may reduce biofilms on uroepithelial cells: Pilot study in spinal cord injured patients. *Spinal Cord.* **39**: 26-30.
11. Howell AB, Griffin DW, Whalen MO. 2011. Standardized cranberry tablet inhibits uropathogenic bacterial adhesion in canine urine. Poster presented at *Berry Health Benefits Symposium.*

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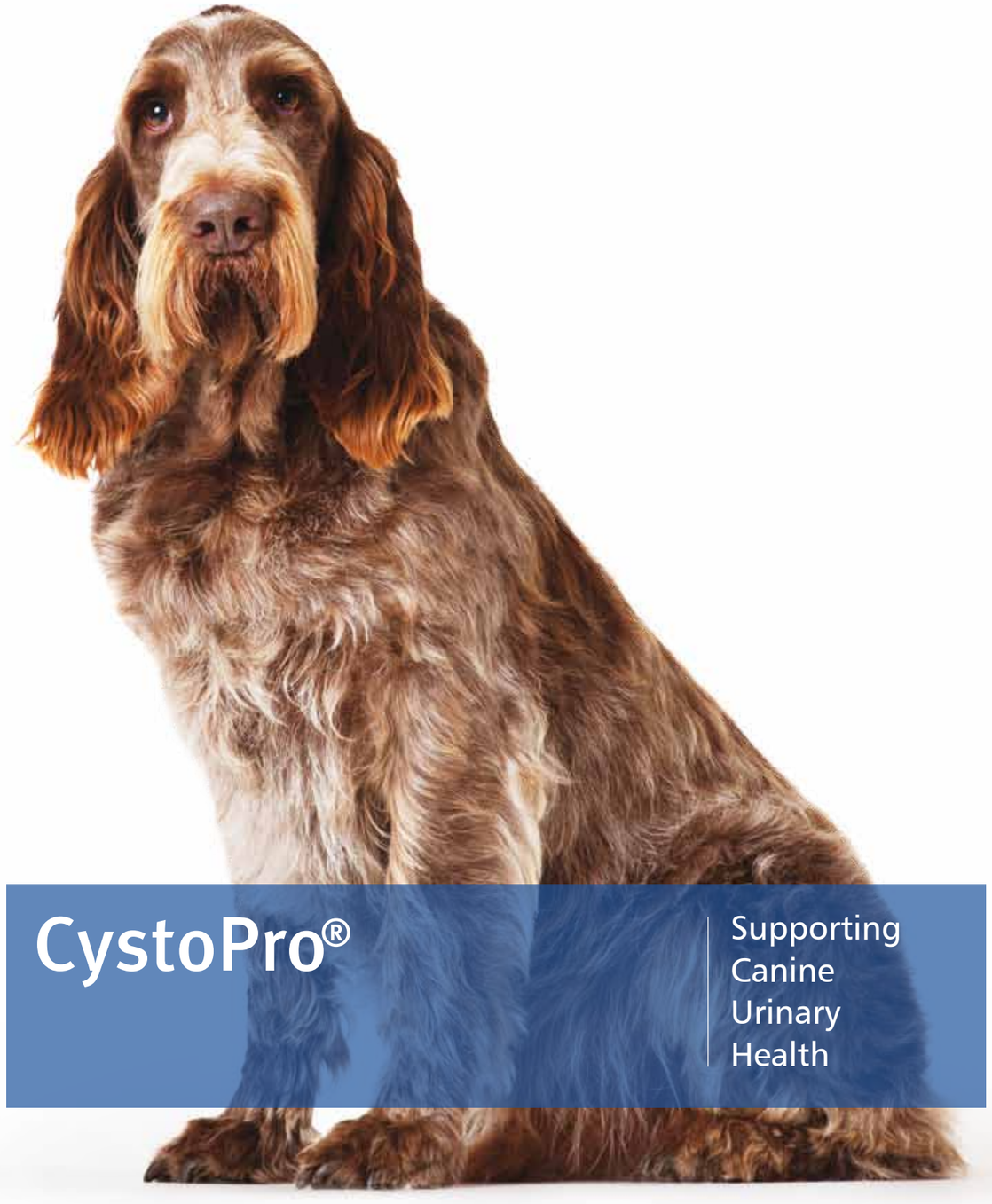

CystoPro®

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Canine Urinary Tract Infections

A urinary tract infection (UTI) involves adherence, multiplication, and persistence of an infectious agent within the urogenital system.

Infections may involve commensal bacterial organisms normally present in the distal urogenital tract, or may result from ascending infections by faecal or cutaneous organisms. Less commonly, infections may be iatrogenic or haematological in origin.

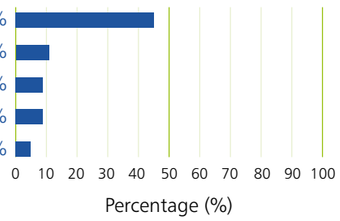
Bacterial UTIs affect 14% of all dogs during their lifetime[1], and are more common in females[2,3,4].

Dogs with diabetes mellitus, hyperadrenocorticism (Cushing's Disease) or treated chronically with steroids have more bacterial UTIs than normal dogs and have a higher percentage of *E.coli* UTIs[5].

The first step in infection is attachment of the bacteria to the bladder urothelium followed by colonisation and proliferation. Specific types of fimbriae (P-fimbriae) on *E.coli* facilitate this adhesion.

E.coli is the most common canine urinary tract pathogen accounting for approximately 33-50% of canine UTI cases[4,6,7].

Bacterial isolate	Percentage of total isolates[4]
Escherichia coli	44.1%
Staphylococcus spp.	11.6%
Proteus spp.	9.3%
Klebsiella spp.	9.1%
Streptococcus spp.	5.4%



A single bacterial pathogen is isolated from approximately 75% of bacterial UTIs in dogs, 20% of UTIs are caused by two co-infecting species, and approximately 5% are caused by three species[4].

Use of indwelling urinary catheters in hospitalised dogs resulted in 55% developing a UTI[8].

Clinical Signs and Treatment

Clinical Signs

Dogs with a UTI may or may not be symptomatic. Clinical signs associated with a UTI are variable and depend on the virulence and number of uropathogens, presence of concurrent disease, health of the immune system, duration of infection, and site(s) of infection.

Clinical signs may include:

- Pollakiuria
- Stranguria
- Dysuria
- Haematuria
- Inappropriate urination

Owners can also report urinary incontinence between urinations and an offensive odour to the urine.

A large proportion of canine patients with a UTI exhibit minimal clinical signs.

Treatment

Antimicrobials are often the treatment of choice for UTIs and should be based on culture and sensitivity of a urine sample collected via cystocentesis.

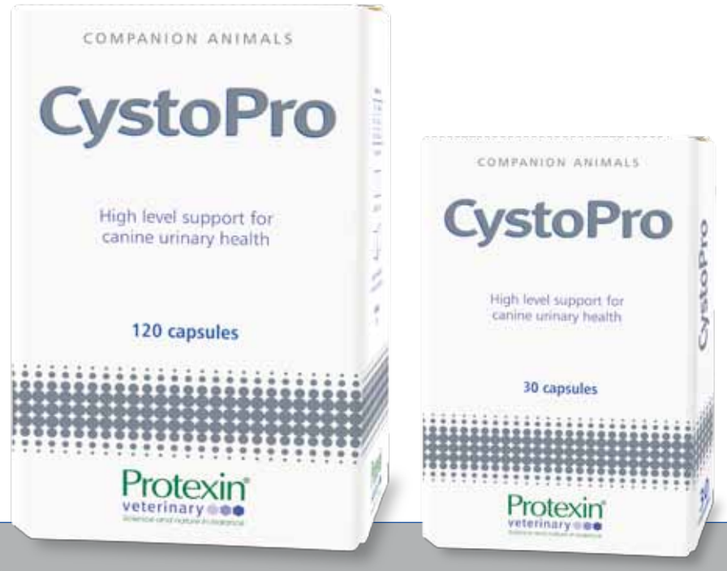
E.coli is becoming increasingly resistant to antibiotics. The rate of bacterial resistance is greatest in dogs with recurrent *E.coli* infections.

Reasons for failure of treatment can include:

- Inappropriate drug, dose, or duration of therapy. Owner compliance is critical
- Failure of the drug to reach sufficient concentrations in urine despite drug administration
- Presence of nidus of infection (urolithiasis, neoplasia)
- Anatomical defect

Introducing CystoPro

High Level Support for Canine Urinary Health.



Ingredients

Proanthocyanidins (PACs)

Proanthocyanidins are naturally occurring powerful antioxidants extracted from the North American cranberry. PACs inhibit the ability of *E.coli* to attach to the urothelium, thereby preventing bacterial adherence, colonisation and infection.

Probiotic

The EU-registered strain *Enterococcus faecium* (NCIMB 10415) E1707 acts to reduce pathogenic bacteria within the gastrointestinal tract thereby reducing the risk of ascending UTIs of faecal origin.

Mannan-oligosaccharide

Created from purified yeast cell walls, Mannan-oligosaccharide (MOS), binds *E.coli* and upregulates the innate immune system by attracting phagocytes to opsonise the bacteria. MOS is commonly used as a prebiotic to support intestinal microflora.

N-acetyl D-glucosamine

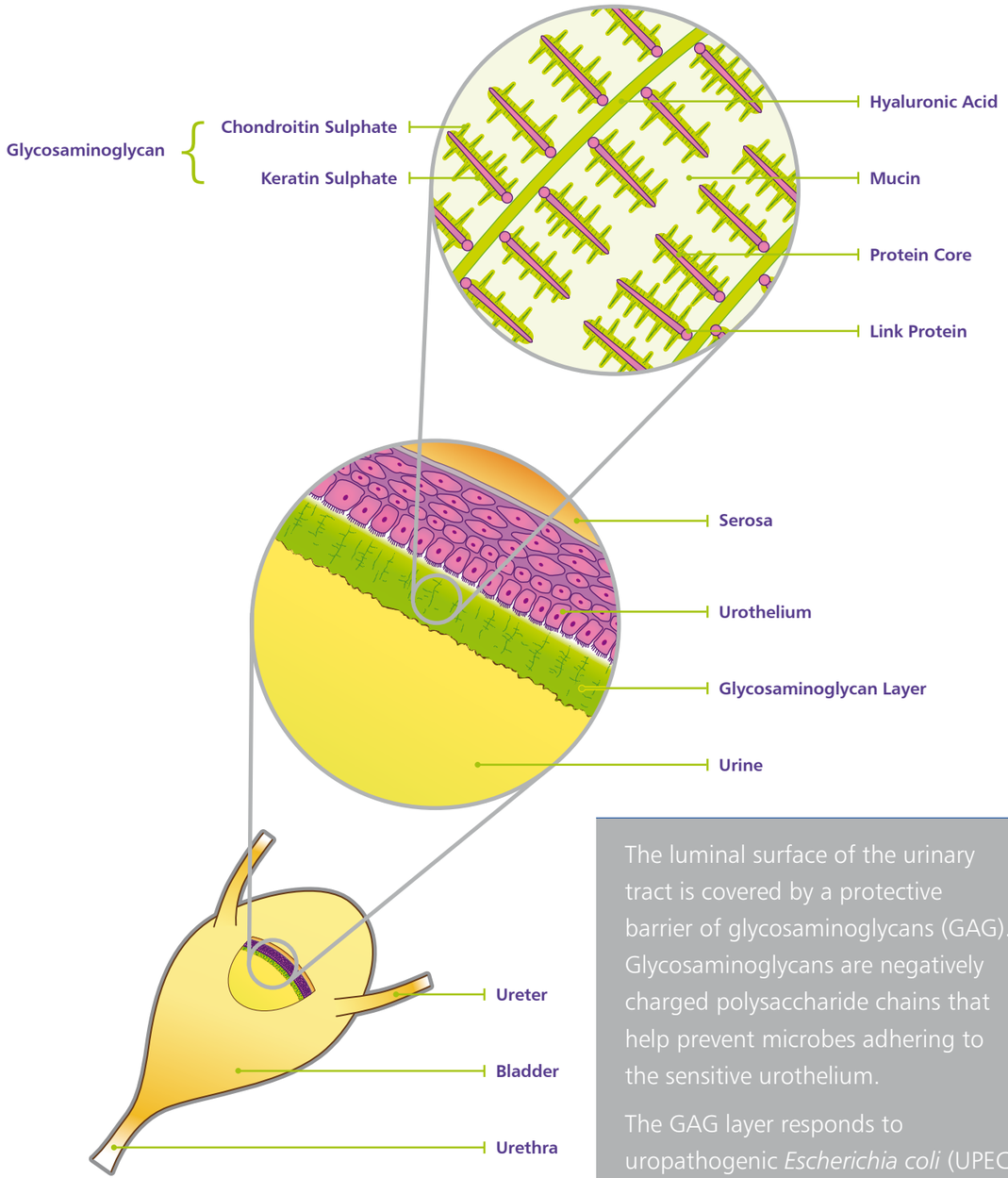
N-acetyl D-glucosamine is a precursor to Chondroitin sulphate and Keratin sulphate which make up the Glycosaminoglycan (GAG) layer that lines and protects the sensitive bladder urothelium.

A strong, resilient GAG layer prevents bacteria from adhering to the urothelial cells.

Artificial Chicken Flavour

For enhanced palatability.

The Glycosaminoglycan (GAG) Layer of the Bladder



The luminal surface of the urinary tract is covered by a protective barrier of glycosaminoglycans (GAG). Glycosaminoglycans are negatively charged polysaccharide chains that help prevent microbes adhering to the sensitive urothelium.

The GAG layer responds to uropathogenic *Escherichia coli* (UPEC) infection by increasing in thickness to reinforce its defensive properties.

Proanthocyanidins

Proanthocyanidins (PACs) are a class of biologically active flavonoids and are one of the most potent antioxidants in nature. PACs reduce the ability of *E.coli* bacteria to establish infection in the lower urinary tract[9].

PACs are sourced from the North American cranberry, *Vaccinium macrocarpon*, and they are unique in that they contain A-type linkage versus the B-type linkage found in many other PACs. This linkage is believed to contribute to the anti-adhesion activity of the PACs.

Attachment of the P-fimbriated *E.coli* to the bladder urothelium[15], followed by colonisation and proliferation (Figure 1).

Figure 1

PACs work by inhibiting the adhesion of P-fimbriated *E.coli* to the urothelium (Figure 2). By preventing the bacterial attachment to the urothelium of the lower urinary tract, the bacteria fail to colonise and are instead voided in the urine (Figure 3).

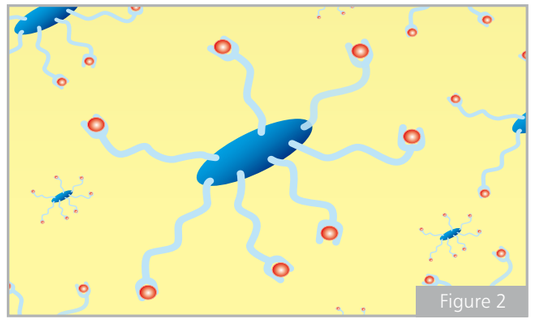


Figure 2

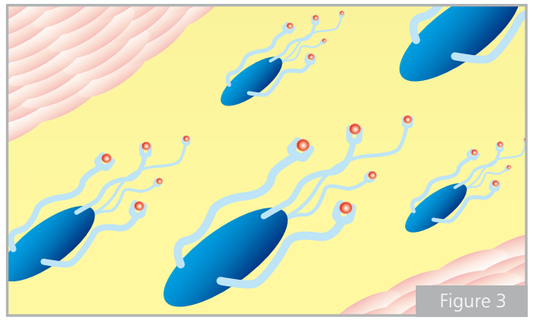


Figure 3

PACs have been shown to have an effect on biofilm formation within the bladder. PAC administration for 1 week resulted in a reduction of urothelial biofilm formation as compared with water consumption[10].

What is a biofilm?

A biofilm is a collection of bacteria adhering to each other (and/or to a surface) and are frequently within a self-produced matrix of extracellular material consisting of DNA, proteins and polysaccharides. This matrix provides protection to the bacteria and may aid in protecting them from antibiotics.

Proanthocyanidins

PACs administered to canine patients at 1mg/kg bodyweight daily for 3 weeks exhibited significant *ex vivo* anti-adhesion activity against *E.coli*[11].

Six male beagle dogs (3-8 years old) were given a standardised cranberry extract (1mg/kg PACs) daily for 21 days. Urine samples were collected on days 1, 3, 5, 7 and 21 and tested in an *ex vivo* assay for the ability to agglutinate human red blood cells (HRBC) specific for P-fimbriated *E.coli*.

The results of the study demonstrate that PACs reduce the ability of *E.coli* to adhere to and colonise the urinary tract.

Mean daily anti-adhesion activity against *E.coli*