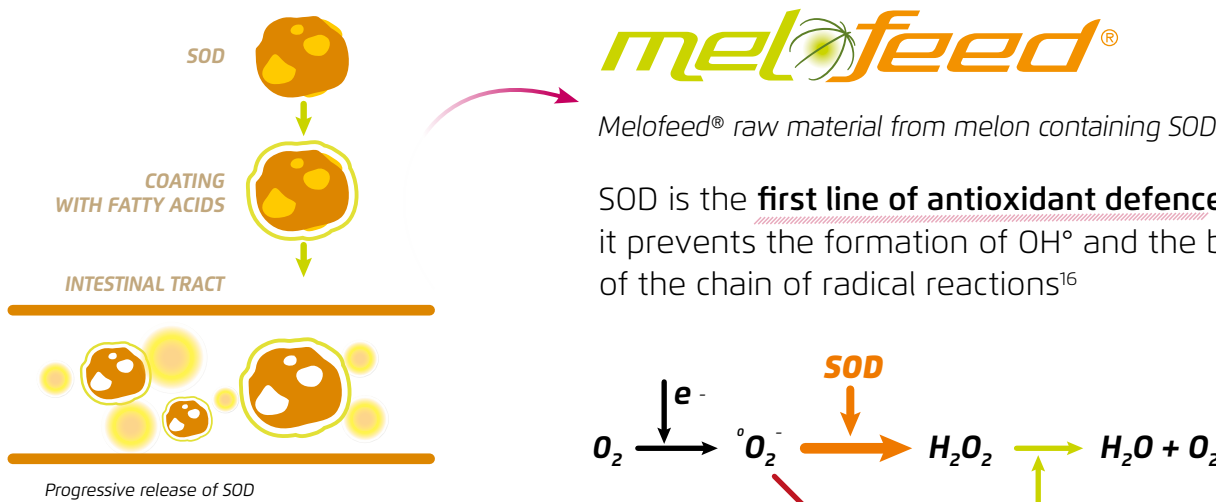


INFLAMMATION AND OXIDATIVE DAMAGE

Inflammation and oxidative damage are also present in lower urinary tract dysfunctions^{2,4,5,12,24}, particularly in oxalate calculosis⁶ and interstitial/idiopathic cystitis^{4,5,7,11,14}

SUPEROXIDE DISMUTASE FROM MELON



GREEN TEA CATECHINS

Antioxidant^{12,21,22,26,27,28} and anti-inflammatory action^{21,27,28} of green tea catechins (polyphenols)

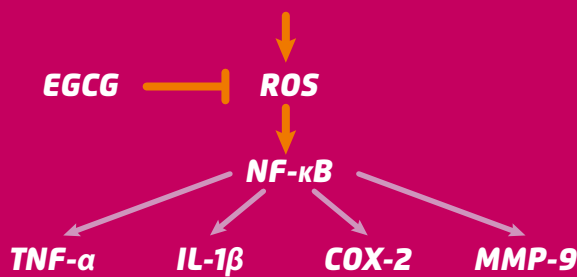


Fig. 1 Anti-inflammatory action of EGCG (main catechin of green tea). Free radicals generated by various extracellular inflammatory stimuli activate NF-κB, a transcriptional factor that stimulates the gene expression of pro-inflammatory proteins, including TNF-α, IL-1β, COX-2, and MMP-9. EGCG acts as an antioxidant in neutralizing ROS, attenuating its effects

by Ohishi mod

CystoCure®

FORTE

Contains Glucosamine and Cranberry pulp

COMPOSITION

Cystocure powder Maltodextrin, Glucosamine (Chitosamine) (from animal tissue) 25%, Yeast [Brewer's yeast], Cranberry pulp 3.0%, Sodium pyrophosphate, Lupine protein meal, Other fermentation products, Magnesium stearate, Vegetable oils and fats (Sunflower oil)

Cystocure tablets Glucosamine (Chitosamine) (from animal tissues) 25%, Dicalcium Phosphate, Yeast [Brewer's Yeast], Cranberry pulp 3%, Sodium Pyrophosphate, Mono and diglycerides of fatty acids esterified with organic acids (glyceryl dibehenate), Lupine protein meal, Magnesium stearate, Other fermentation products, Products obtained from vegetable processing (Melon) (*Melofeed), Vegetable oils and fats (Sunflower oil)

ADDITIVES PER KG

Cystocure powder Organoleptic additives: Camellia sinensis (L.) O. Kuntze: Tea extract CoE 451 mg 25,000 Anti-caking agents: Colloidal silica E 551b mg 5,000 Vitamins: Vitamin E 3a700 IU 8

Cystocure tablets Stabilizers: microcrystalline cellulose E 460 mg 515,000 Organoleptic additives: Camellia sinensis (L.) O. Kuntze: Tea extract CoE 451 25,000 mg Anti-caking agents: Colloidal silica E 551b mg 5,000 Vitamins: Vitamin E 3a700 IU 8

INSTRUCTIONS FOR PROPER USE

Cystocure powder Mix the powder to the usual food ration of moist food according to the following table. It is advisable to have an administration cycle of 15-30 days

Powder per day	
Initial Period	1 level scoop per 5 kg of b.w. twice a day
Maintenance	1 level scoop every 5 kg of b.w. 1 time per day

Cystocure tablets Administer directly or mix with the usual ration according to the following table. It is advisable to have an administration cycle of 15-30 days

Tablets per day	
Initial Period	period 1 tablet for every 20 kg of b.w. 2 times a day
Maintenance	1 tablet every 20 kg of b.w. 1 time a day

Cystocure Forte is a complementary food for dogs and cats

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THE NEW, MORE COMPLETE FORMULA
for the natural protection and well-being
of the lower urinary tract of dogs and cats



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Main dysfunctions of the lower urinary tract

DOGS³⁶

- Recurrent bacterial cystitis (E. coli approx. 50%)^{3,8,36}
- Urinary stones

CATS^{13,14,18,25,31,35,38}

- Idiopathic cystitis
- Urinary stones, urethral plugs
- Bacterial cystitis (cats >10 years up to 50%¹⁸) (E.coli 50%²⁵)

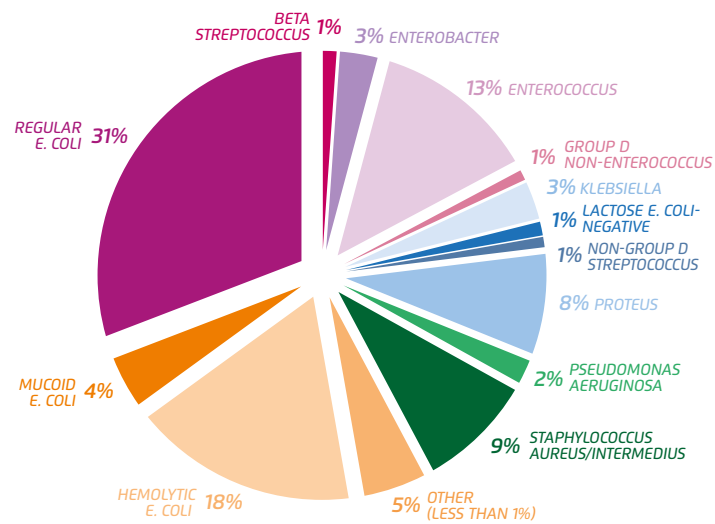


Fig. 1 Chew et al. 2010

Isolated bacteria	Total
E. coli	47
Enterococcus spp ^a	36
Staphylococcus felis	25
Proteus spp ^b	6
Enterobacter / Klebsiella spp ^c	4
Pseudomonas aeruginosa	2
Staphylococcus aureus	2
Staphylococcus intermedius	2
Streptococcus bovis	2
Total number of bacteria	126

Table 1 Isolated bacteria (n = 126) from 107 cats with infections of the lower urinary tract.
^aEnterococcus faecalis (n=34) and Enterococcus faecium (n=2)
^bProteus mirabilis (n=5) and an isolate identified as Proteus vulgaris
^cAn isolated strain identified as Enterobacter aerogenes, two isolates identified as Enterobacter cloacae and a subspecies of Klebsiella pneumoniae subspecies oxytoca from Lütser

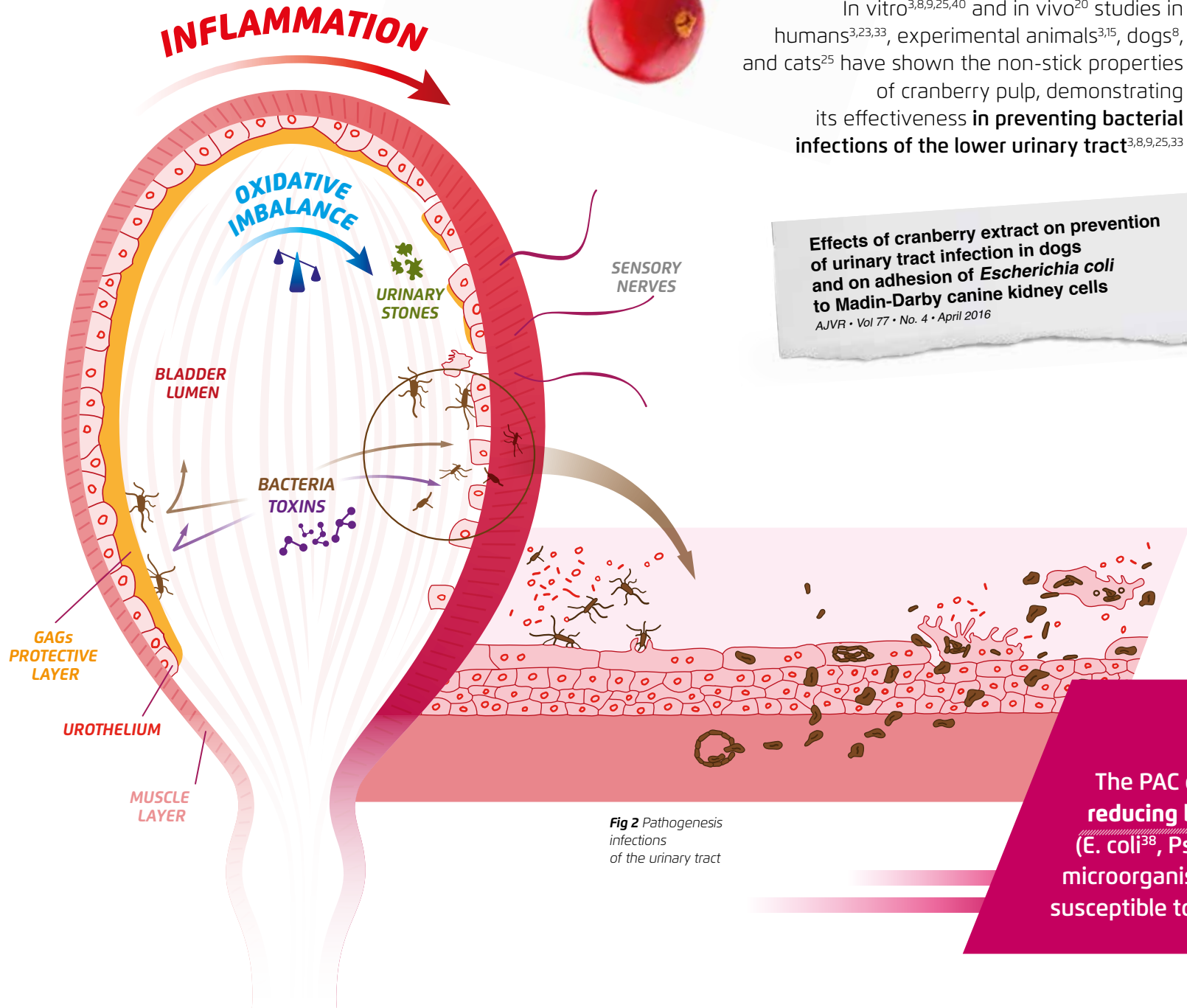


Fig 2 Pathogenesis infections of the urinary tract

CRANBERRY (Vaccinium Macrocarpon)



The **proanthocyanidins** contained in Cranberry pulp (mainly PAC type A) are able to **inhibit the adhesion capacity of pathogenic bacteria** with fimbrias (e.g. Escherichia coli)^{3,8,9,17,20,23,25,33,40} to the uroepithelium, altering fimbrias shape^{3,8,9,17} and reducing the bond strength to epithelial receptors^{3,8,9}

In vitro^{3,8,9,25,40} and in vivo²⁰ studies in humans^{3,23,33}, experimental animals^{3,15}, dogs⁸, and cats²⁵ have shown the non-stick properties of cranberry pulp, demonstrating its effectiveness in **preventing bacterial infections of the lower urinary tract**^{3,8,9,25,33}

Effects of cranberry extract on prevention of urinary tract infection in dogs and on adhesion of *Escherichia coli* to Madin-Darby canine kidney cells
AJVR • Vol 77 • No. 4 • April 2016

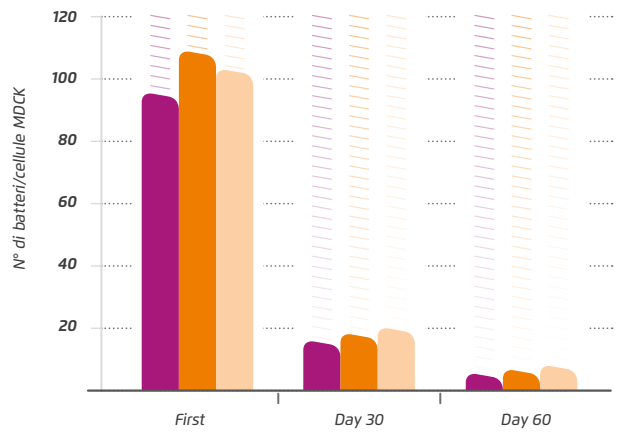
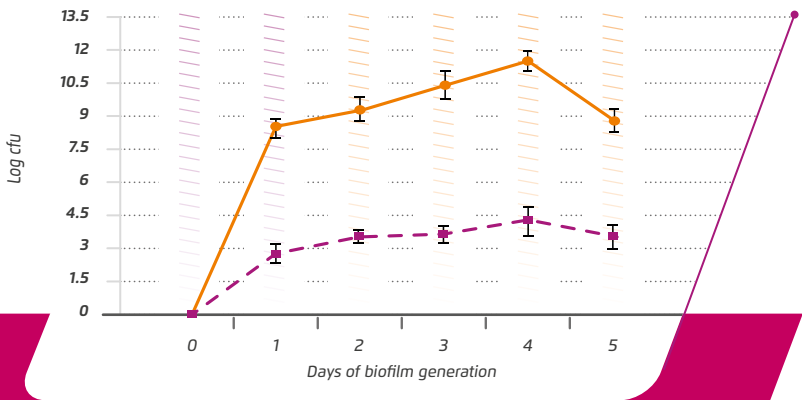


Fig. 3 SEM* mean of E. coli (strains C1-50, C2-48 and C3-48) adhering to MDCK cells after culture in urine samples obtained from 6 dogs before and after 30 and 60 days of administration of cranberry extract. *SEM: Standard Error of Mean *

From Chou



The PAC contained in cranberry pulp are also effective in **reducing biofilm formation** by urinary pathogenic bacteria^{3,39} (E. coli³⁸, Pseudomonas aeruginosa^{15,39}) and other pathogenic microorganisms (Candida albicans³²), making them more susceptible to normal antibiotic treatments^{15,39}

Fig. 4 From Harjai

THE URINARY EPITHELIUM

GLUCOSAMINE



Feline idiopathic cystitis, which accounts for more than 50% of cases of FLUTD (Feline Lower Urinary Tract Disease)^{5,7,13,14,18,34,35,36,37}, is a consequence of urothelium alterations and its functional properties of semipermeability^{5,7,14,18}. These alterations induce **neurogenic inflammation** at submucosa level (C fibres)^{7,14,18,29} with stimulation of the CNS and involvement of the hypothalamic-pituitary-adrenal axis^{7,29}.

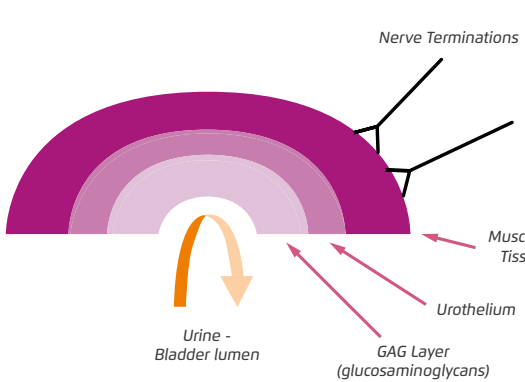


Fig. 6 Normal bladder with intact urothelium layer and glycosaminoglycans (GAG). Urothelium and GAGs act as natural barriers to protect the underlying layers and sensory nerves from urine-induced damage.

From Hostutler

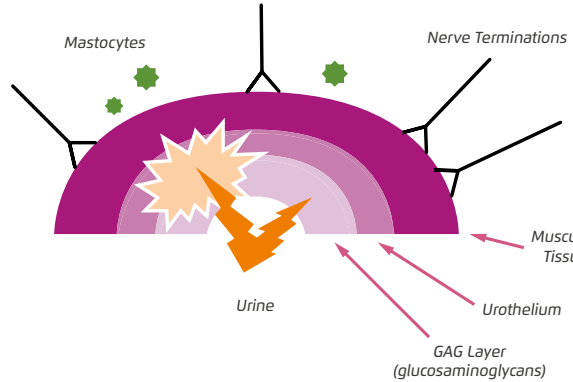


Fig. 5 Bladder pattern of cats with feline interstitial cystitis (FIC Feline Interstitial Cystitis). The loss of integrity of the glycosaminoglycans layer and of the urothelium is shown. The loss of integrity of these layers leads to sensory nerve stress, mast cell recall and activation, and changes in the central nervous system that determine the clinical signs observed in cats with FIC.

From Hostutler

Urothelium is naturally coated by a layer of GAGs that **protects against bacterial adhesion and contact with harmful substances** present in the urine^{7,13,14,18,19,29,30,31}. The loss of integrity of GAGs protective layer is at the origin of contact between sensitive nerve fibres and harmful constituents of urine^{13,14,18,19,29,30,31,37}.

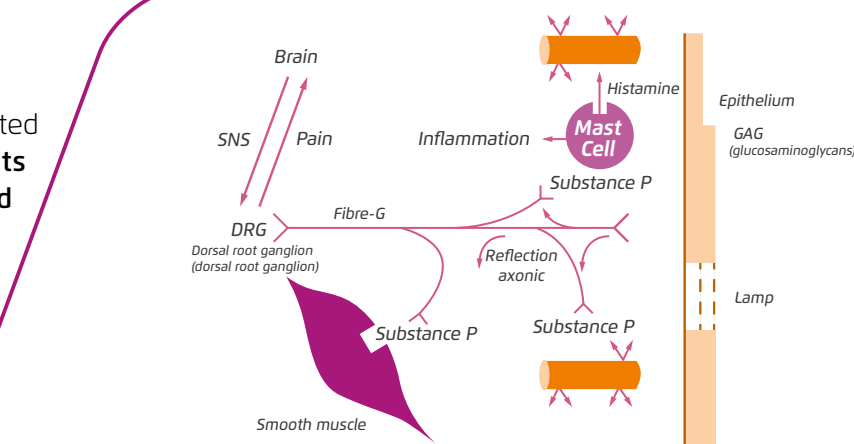


Fig. 7 From Chew, Senior

Glucosamine is able to contribute to the organic synthesis of GAGs^{19,29,31,37}, useful for maintaining urothelium integrity^{29,31,37}