

## ABSTRACT

**Introduction and Objectives:** Painful bladder syndrome/interstitial cystitis (PBS/IC) is a disorder of the urinary bladder characterized by suprapubic/pelvic pain along with urgency and frequency of urination. PBS/IC occurs primarily in women and symptoms are exacerbated by stress, ovulatory hormones and certain foods. PBS/IC pathogenesis is unknown, but the most consistent findings involve some dysfunction of the bladder glycosaminoglycan (GAG) protective layer and a high number of activated bladder mast cells. There is no curative therapy. Hydrodistension, intravesical administration of dimethylsulfoxide (DMSO), as well as oral pentosanpolysulfate (PPS), amitriptyline and hydroxyzine have had variable success.

**Methods:** A dietary supplement, CystoProtek®, was formulated to contain (per soft gel capsule) the natural GAG building block glucosamine sulfate (140 mg), as well as the GAG components chondroitin sulfate (150 mg) and sodium hyaluronate (10 mg) to provide urothelial protection, together with the flavonoid quercetin (130 mg) and the quercetin glycoside rutin (20 mg), which have anti-inflammatory, anti-oxidant and cytoprotective properties, while they also inhibit mast cell release of pro-inflammatory molecules. The active ingredients were mixed in olive kernel oil that increases their absorption and supplies its own content of protective polyphenols, especially luteolin.

**Results:** Female patients with PBS/IC (n=269, mean age 52.34±13.04 years) who had failed other forms of therapy took CystoProtek® (2 capsules in am and 2 pm) for 11.22±8.12 months (n=262). Global assessment scale (0=least, 10=worst) was reduced from 7.49±2.00 (n=263) to 3.66±2.38 (n=258, p=0.0001, non-parametric Mann-Whitney U test), a 51.2% inhibition. There was stomach upset in less than 1% of subjects, especially those with concurrent irritable bowel syndrome (IBS).

**Conclusions:** These results indicate that CystoProtek® is beneficial and well tolerated in PBS/IC; it could also be given together with other oral medications. A prospective clinical study would be useful in order to also investigate any additional benefit for those patients with comorbid atopic diseases.

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## BACKGROUND

- Interstitial cystitis (IC) is a bladder syndrome mostly present in women with symptoms of urinary urgency, frequency, nocturia and suprapubic/pelvic pain.
- The prevalence of IC was estimated at about 60 cases/100,000 women.
- IC pathogenesis is unknown, but the most consistent findings involve some dysfunction of the bladder glycosaminoglycan (GAG) protective layer and a high number of activated bladder mast cells.
- There is no effective therapy even through intravesical administration of dimethylsulfoxide (DMSO) or oral pentosanpolysulfate (PPS) have had variable success.
- A dietary supplement, CystoProtek®, was formulated with the natural GAG components chondroitin sulfate and sodium hyaluronate to provide urothelial cytoprotection, together with the flavonoid quercetin that has anti-inflammatory properties and inhibits activation of mast cells.

## OBJECTIVE OF THIS STUDY

To study the effect of the dietary supplement, CystoProtek®, on global response of PBS/IC patients.

# A RETROSPECTIVE OPEN LABEL STUDY OF CYSTOPROTEK® IN PAINFUL BLADDER SYNDROME/INTERSTITIAL CYSTITIS (PBS/IC)

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**Table 1. Characteristics of olive kernel extract**

- Low acidity and special filtration from the island of Crete, Greece
- Provides greater solubility and absorption of chondroitin sulfate and quercetin
- Unsaturated fatty acids provide fluidity of biological membranes
- Antioxidants protect against peroxidation and other free radicals
- Polyphenols have anti-inflammatory actions
- Contains a natural cyclo-oxygenase inhibitor
- Helps heal damaged mucosal surface

**Table 2. Effect of olive kernel extract (OKE) on absorption of chondroitin sulfate in rats**

Conditions	Absorption (%)
CS alone	3.9 ± 1.2
CS+OKE	14.3 ± 2.9

+ Chondroitin sulfate (CS) was tritiated (3H) at New England Nuclear (specific activity = 4.3 mCi/ml); 2.5 mCi 3H-chondroitin sulfate was given orally to rats with or without mixing in OKE; plasma radioactivity was measure 8 hr later using a beta-counter. \*p<0,05 (n=5)

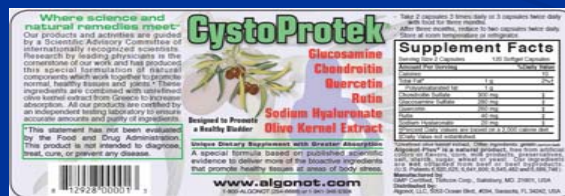
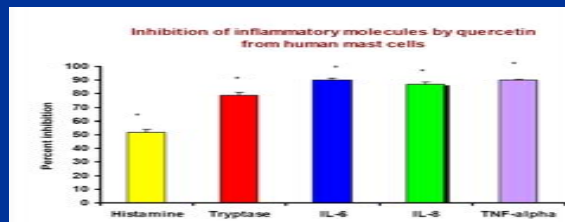


Table 3. Amount, purity and source of CystoProtek® ingredients				
Ingredients	Amount per capsule	Source	Purity	Country of origin
Glucosamine sulfate	140 mg	Cell fish chitin	>95%	China
Chondroitin sulfate	150 mg	Shark cartilage	>90%	China
Sodium hyaluronate	10 mg	Chicken combs	>98%	Japan
Quercetin dihydrate	130 mg	Saphora plant	>99%	Chile
Rutin	20 mg	Saphora plant	>99%	Chile
Olive kernel extract	45% w/v	Olive seeds	100%	Greece

## RESULTS

PBS/IC female patients (n=269) diagnosed by the NIDDK criteria who had failed all forms of therapy took four softgel CystoProtek® capsules per day for 11.2 ± 8.1 months. Global assessment scale was reduced from 7.49 ± 2.0 (n=263) to 3.66 ± 2.38 (n=258; p = 0.0001, using non-parametric Mann-Whitney U test), 51.2% inhibition.

Table 4. Comparison of some nutraceuticals containing Quercetin				
Ingredients	Benefits	CystoProtek®§	Quercetin	CystoQ®
Glucosamine	Mucosal GAG layer part	280 mg	None	None
Chondroitin sulfate	Mucosal GAG layer part, mast cell inhibitor	300 mg	None	None
Hyaluronate Na	Mucosal GAG layer part	20 mg	None	None
Quercetin dihydrate, Rutin	Mast cell inhibitor anti-oxidant, anti-inflammatory	260 mg 40 mg	300 mg None	500 mg (?) None
Olive Kernel Extract	Anti-oxidant, Cytoprotective, Anti-inflammatory	900 mg	None	None
Manufacturer		Algonot, LLC 1-800-Algonot algonot.com	NutriCology, Inc. 510-487-8526 nutricology.com	Farr Labs, LLC 1-877-284-3976 cystoq.com

# Per 2 softgel capsules; § Other ingredients, sources and purity not disclosed

## CONCLUSIONS

These results indicate that CystoProtek® is beneficial and well tolerated in IC. It could also be given together with other oral medications. A prospective clinical study would be useful.

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