JointComplex

Code: FE0082 – 30 vegetable capsules

Joint**Complex** is a synergic formula with Internal Eggshell Membrane (ESM®) and standardised extracts of boswellia, devil's claw, turmeric and piperine.

ESM®, Eggshell Membrane, is obtained via a natural process using water, by mechanical action, washing and drying, and does not undergo any further treatment that would cause the hydrolysis of the collagen it contains. ESM® is the inner eggshell membrane with the highest collagen content on the market; it is a 100% natural, non-hydrolysed collagen.

In contrast to other eggshell membrane manufacturers, who receive eggshells from different geographical areas, which can lead to increased microbial contamination during storage, the eggs are received directly from the poultry farms. Once the shell is separated from the contents of the egg, it is immediately processed, thus reducing the risk of microbial contamination to the minimum.

The inner membrane of the eggshell is obtained by mechanical action and subsequent washing and crushing. This process is natural, which means that ESM® is a 100% natural ingredient.

ESM® egg membrane contains approximately 35% non-hydrolysed collagen (Types I, V and X), about 6% glycosaminoglycans chondroitin sulphate, hyaluronic acid and keratan and dermatan sulphates and about 3.5% lysozyme.

Ingredients: ESM® (internal **egg**shell membrane), *Boswellia serrata* raisin extract, turmeric extract (*Curcuma longa*), devil's claw root extract (*Harpagophytum procumbens*), anticaking agents (magnesium salts of fatty acids and silicon dioxide), flavour (piperine from black pepper, *Piper nigrum*), vegetable capsule (glacing agent: hydroxypropylmethylcellulose; humectant: purified water).

Nutricional information:	**2 capsules (1 396 mg)**
ESM® (internal **egg**shell membrane	500 mg
Boswellia serrata (45% boswellic acid)	260 mg
Devil's claw (*Harpagophytum procumbens*) (10% harpagosides)	160 mg
Turmeric (*Curcuma longa*) (95% curcuminoids*)	200 mg
Piperine (from black pepper, *Piper nigrum*)	4 mg

* providing curcumin I, demethoxycurcumin, and bisdemethoxycurcumin.

ESM® is a registered trademark of Torolis S.L.

Size and format:
30 vegetable capsules

Recommended daily dose:
1 capsule twice daily.
Do not exceed the recommended daily dose.

Indications and uses:
Different studies have shown that **JointComplex** is helpful in inflammatory processes of the joints that may be accompanied by pain and stiffness. It helps re-establish cartilage and connective tissue.

Cautions:
Consult a health-care practitioner prior to use this product if you are allergic to eggs, if you are pregnant or breast-feeding, if you are treated with medication (anticoagulants or antiplatelet), or if you have a special medical condition (ulcers or gallstones).

JointComplex is a synergic formula aimed at relieving joint pain and inflammation naturally and re-establishing healthy cartilage and connective tissue. It offers an innovative nutrient called ESM® which contributes to healthy development and movement of cartilage and synovial fluid. *Boswellia serrata* extract actively inhibits the production of the signalling molecule that causes inflammation. Harpagophytum helps inhibit inflammatory cell signalling. Curcumin also acts on enzymes (COX-1 and COX-2) that are among the underlying causes of joint pain and inflammation. Black pepper increases the bioavailability of curcumin.

JointComplex can be a catalyst for restoring a healthy and active lifestyle as it allows for carrying out daily activities without pain.

ESM ® (Internal Eggshell Membrane): A powerful source of glycosaminoglycans (GAGs) of natural origin, with essential proteins for maintaining healthy cartilage and synovial fluid. ESM® is also a **natural source of glucosamine, chondroitin and hyaluronic acid**. Hyaluronic acid is abundant in synovial fluid, the lubricant-filled membrane surrounding joints that absorbs shock in the bones, ligaments, tendons and muscles, protecting them from friction which causes pain and restricts movement.

Studies have been carried out prior to human trials on the safety of ESM®[1], its anti-inflammatory activity[2] and the mechanism of action of this anti-inflammatory activity[3].

In a randomized, double-blind, placebo-controlled clinical trial assessing the safety and efficacy of Internal Eggshell Membrane® for the treatment of pain and stiffness in osteoarthritis of the knee, there was a 15.9% reduction in pain, and a 12.8% reduction in stiffness **after only 10 days** at a daily dose of 500 mg. Specifically, pain and stiffness of the knee are the most common complaints from those who suffer from joint pain from arthritis[4,5].

Composition:

Protein	94%
Colagen (Types I,V,X)	35%
Elastin	4-5%
Chondroitin sulfate	2%
Hyaluronic acid	2%
Glucosamine	2%
Dermatan and keratan sulphate	1%
Growth factor TGF-β, IGF-1	
Amino acids:	
-Methionine -Cysteine	-Lysine -Tyiptophan
Other substances:	
- Calcitonin - Ovocalixin - Ovotransferrin	- Ovocleidin - Desmosine - Isodesmosine

In 2018, a randomized double-blind clinical trial-controlled respect to placebo was conducted at the UCAM (Catholic University San Antonio, Murcia) in 80 patients diagnosed with osteoarthritis to analyse the efficacy of ESM® on joint pain during a period of 8 weeks of treatment.

The parameters assessed were: The subjective perception of pain (VAS scale), functional capacity variable (WOMAC questionnaire), assessment of strength and joint rotation angle, and sleep quality variable (Pittsburgh Test).

After 8 weeks of study, participants treated with ESM® showed a reduction in joint pain compared to subjects in the placebo group. This pain reduction was accompanied by an improvement in strength as a result of reduced functional limitation associated with the joint inflammatory process.

Although the groups treated with 300 and 500 mg of ESM®, respectively, showed an improvement in all parameters evaluated, the group that consumed 500 mg was the one that presented the most significant results in terms of improvement, so we can affirm that the functional improvement of the subjects is dose-dependent.

Taking ESM® for 8 weeks improved functional capacity and quality of life in patients diagnosed with grade I to III osteoarthritis. Furthermore, it tended to improve sleep quality due to reduced joint pain.

Finally, daily consumption of ESM® for 8 weeks did not cause any adverse events in any of the subjects in the two egg membrane treatment groups, so it can be concluded that ESM® is safe to use.

The conclusions would be as follows:

- ESM® has a positive effect on mobility in people suffering from joint pain.
- ESM® has been shown to have a dose-dependent anti-inflammatory efficacy depending on the severity of the joint pain and mobility limitation of the individual.
- ESM® increases collagen synthesis by skin fibroblasts.

BOSWELLIA (*Boswellia serrata*): The resin of Boswellia Serrata contains boswellic acid as its active principle. This acid has great anti-inflammatory activity as it inhibits an enzyme that transforms arachidonic acid into leukotrienes, which mediate inflammation, and it has anti-arthritic activity induced by collagen[6]. *Boswellia serrata* significantly reduces the degradation of glycosaminoglycans (main components of connective tissue), so it inhibits the degeneration of joint surfaces. Boswellic acid also decreases the activity of leukocyte elastase, an enzyme that is significantly involved in the physiopathology of pulmonary emphysema, chronic bronchitis and cystic fibrosis[6,7].

Animal trials have shown that boswellic acid works well with glucosamine (a component of ESM®) to relieve arthritis, showing positive effects on pain and stiffness of the knee[6,7].

HARPAGOPHYTUM (*Harpagophytum procumbens*): possesses analgesic and anti-inflammatory properties which are attributed to its high concentration of iridoid glycosides (harpagosides), whose main function is to inhibit the release of cell signalling proteins (cytokines such as IL1-β, TNF-β) which contribute to the inflammatory process[8]. Upon inhibiting the release of these mediators, devil's claw inhibits the catabolic processes that cause degradation of joint cartilage, reestablishing the balance between catabolic and anabolic processes in the extracellular matrix of the joints. [8,9].

CURCUMIN (95% of curcuminoids): This is a polyphenol compound, a cucuminoid which is responsible for the pigment of turmeric (*Curcuma longa*). Among its many other properties, curcumin is well known for its anti-inflammatory effect since it safely tackles COX-1 and COX-2, which are among the underlying causes of chronic pain and inflammation. It inhibits the release of inflammatory mediators (type 2 prostaglandins, thromboxanes and eicosanoids) providing similar benefits to those of cortisone, but without the toxicity[10].

BLACK PEPPER (95% piperine): Piperine is the critical marker compound of black pepper that has been shown in clinical trials to increase the bioavailability of curcumin by up to 2,000%[11].

References:
1) Ruff KJ, et al. Safety evaluation of a natural eggshell membrane-derived product. *Food and chemical toxicology*. 2012; 50(3):604-611.
2) Benson KF, et al. Effects of natural eggshell membrane (NEM) on cytokine production in cultures of peripheral blood mononuclear cells: increased suppression of tumor necrosis factor-α levels after in vitro digestion. *Journal of medicinal food*. 2012; 15(4):360-368.
3) Ruff KJ & DeVore DP. Reduction of pro-inflammatory cytokines in rats following 7-day oral supplementation with a proprietary eggshell membrane-derived product. *Modern Research in Inflammation*. 2014; 3(1):19-25.
4) Ruff KJ, et al. Eggshell membrane in the treatment of pain and stiffness from osteoarthritis of the knee: a randomized, multicenter, double-blind, placebo-controlled clinical study. *Clinical Rheumatology.* 2009; 28(8): 907–914.
5) Ruff KJ, et al. Eggshell membrane: A possible new natural therapeutic for joint and connective tissue disorders. Results from two open-label human clinical Studies. *Journal of Clinical Interventions in Aging*. 2009; 4: 235-240.
6) Sontakke S, et al. Open, randomized, controlled clinical trial of *Boswellia serrata* extract as compared to valdecoxid in osteoarthritis of knee. *Indian Journal of Pharmacology.* 2007; 39(1): 27–29.
7) Singh S, et al. Boswellic acids and glucosamine show synergistic effect in preclinical anti-inflammatory study in rats. *Bioorganic & Medicinal Chemistry Letters.* 2007; 17(13): 3706–3711.
8) Garcia-Garcia P, et al. Propiedades antiinflamatorias de *Harpagophytum procumbens*: ¿Usos tradicionales o evidencia científica? *Revista de Fitoterapia*. 2004; 4(2); 155-156.
9) Crespo Gil ME and Navarro Moll MC. La raíz de harpagofito en el tratamiento de afecciones reumáticas. *Revista de Fitoterapia*. 2012; 12(1): 5-14.
10) Ramsewak RS, et al. Cytotoxicity, antioxidant and antiinflammatory activities of Curcumins I–III from *Curcuma longa*. *Phytomedicine.* 2000; 7(4): 303-308.
11) Shoba G, et al. Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. *Planta Medica.* 1998; 64(4):353–356.