



Clinical Applications

- Promotes the Body's Processes of Tendon/Ligament Self-Repair*
- Supports Tendon/Ligament Function*
- Protects and Promotes Collagen Biosynthesis*
- Supports Tendon/Ligament Comfort*

*OrthoManage is an advanced formula designed to bolster tendon/ligament comfort and recovery. Whether repetitive use or something more acute is your challenge, preliminary research suggests that OrthoManage can support the stability, health, and proliferation of tendon and ligament cells and thereby promote the body's ability for self-repair. Let OrthoManage help you stay active.**

All 3rd Opinion Inc Formulas Meet or Exceed cGMP Quality Standards

Discussion

It is known that tendons and ligaments have a slower and more limited ability to self-repair than other tissues. However, healthy tendons and ligaments do indeed have an intrinsic capacity for repair, which is controlled by resident fibroblasts and their surrounding extracellular matrix (ECM).^[1] Fibroblasts (e.g., tenocytes) are responsible for producing the ECM and therefore the proteoglycans (protein/mucopolysaccharide complex) and collagen needed for tissue repair. The key is to stimulate this process. In vitro and in vivo research suggests OrthoManage does just that. This proprietary blend of type I collagen and mucopolysaccharides combined with vitamin C supports the structural and functional needs of tendons and ligaments.*

Type I Collagen and Mucopolysaccharides Adult tendons are comprised mainly of type-I collagen molecules that are hierarchically organized into structural units. The molecular structure and organization of tendon and ligament collagen fibrils are key determinants in the ability of these tissues to endure mechanical force and fuel self-repair.^[1] While collagen provides much of tendon/ligament structure and strength, mucopolysaccharides are said to provide the “glue” that holds them together and allows them to stretch, flex, bend, and maintain their resilience. Mucopolysaccharides—also known as glycosaminoglycans or GAGs—are a critical component of ECM and are important in maintaining structural integrity, lubrication, and spacing of collagen fibers. Furthermore, mucopolysaccharides have been shown to increase collagen and non-collagenous protein synthesis in cultures of bovine tenocytes and ligament cells.*^[2]

Vitamin C This vitamin helps maintain tendon/ligament structure and biomechanical properties by stimulating collagen biosynthesis.*^[3-5]

In Vitro IL-1beta (interleukin-1beta) is a cytokine associated with adverse tendon/ligament changes. The effect of OrthoManage in the presence of IL-1beta was studied in primary human tenocytes. Tenocyte cultures treated with 250, 500, and 1000 µg/ml of OrthoManage showed no signs of cytotoxicity or other negative effects on the viability of cells. The major findings were that this formula counteracted the negative effects of IL-1beta by: (1) protecting tenocytes from degenerative morphological changes, cellular degeneration, and apoptosis, (2) reversing the downregulation of collagen type I and beta 1-integrin receptor expression, (3) increasing tenomodulin production, and (4) causing a significant dose- and time-dependent increase in proliferation and viability of tenocytes. These results demonstrated that OrthoManage supports tenocyte viability and proliferation and type I collagen synthesis.^[1] Furthermore, the treated cells appeared healthy; displayed an abundant and well-organized ECM; and exhibited high levels of euchromatin, indicating that the cells were very active and had a high rate of protein (i.e., collagen) biosynthesis.^[1] In another in vitro test, human tenocytes incubated with OrthoManage for 10 days showed a strong stimulatory effect on cell proliferation that exceeded the proliferation seen in cells incubated with (IGF-1) insulin-like growth factor 1 (positive control).^[6] In addition, cells remained viable and showed large amounts of endoplasmic reticulum, which is needed for synthesis of ECM.*

In Vivo A prospective observational study performed by Nadal et al demonstrated the effects of OrthoManage on the health of epicondyles, plantar fascia, Achilles tendons, or supraspinatus tendons. Patients were selected on the basis of clinical assessment and ultrasound results. For three months, all of the patients received 20 to 30 physical therapy sessions and the study group received two caps/d of OrthoManage.^[7] Comfort, quality of life (SF-36), and physiotherapist assessments were performed before intervention began and also at 30-, 60-, and 90-day intervals during intervention. In every assessment, patients given OrthoManage showed numerical or statistically significant improvements after two to three months of supplementation compared to controls.^[7] Researchers concluded that supplementing with OrthoManage improved comfort level and biomechanical properties without adverse effects.*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.



Supplement Facts

Serving Size: 2 Capsules
Servings Per Container: 30

	Amount Per Serving	%Daily Value
Vitamin C (as ascorbic acid)	60 mg	100%
TENDOACTIVE® Proprietary Blend Mucopolysaccharides and Type I Collagen	520 mg	**

** Daily Value not established.

Other Ingredients: HPMC (capsule), microcrystalline cellulose, ascorbyl palmitate, silica, and medium-chain triglycerides.

TENDOACTIVE® is a registered trademark licensed by Bioiberica, S.A.

Directions

Take two capsules daily, or as directed by your healthcare practitioner.

Consult your healthcare practitioner prior to use. Do not use if tamper seal is damaged.

References

1. Shakibaei M, Buhrmann C, Mobasheri A. Anti-inflammatory and anti-catabolic effects of TENDOACTIVE® on human tenocytes in vitro. *Histol Histopathol.* 2011 Sep;26(9):1173-85. [PMID: 21751149]
2. Lippiello L. Collagen synthesis in tenocytes, ligament cells and chondrocytes exposed to a combination of glucosamine HCl and chondroitin sulfate. *Evid Based Complement Alternat Med.* 2007 Jun;4(2):219-24. [PMID: 17549239]
3. Grosso G, Bei R, Mistretta A, et al. Effects of vitamin C on health: a review of evidence. *Front Biosci.* 2013 Jun 1;18:1017-29. [PMID: 23747864]
4. Omeroğlu S, Peker T, Türközkan N, et al. High-dose vitamin C supplementation accelerates the Achilles tendon healing in healthy rats. *ArchOrthop Trauma Surg.* 2009 Feb;129(2):281-86. [PMID: 18309503]
5. Zanoni JN, Lucas NM, Trevizan AR, et al. Histological evaluation of the periodontal ligament from aged Wistar rats supplemented with ascorbic acid. *An Acad Bras Cienc.* 2013 Mar;85(1):327-35. [PMID: 23460436]
6. Shakibaei M, Csaki C, Mobasheri A. In vitro study of tendinopathy in humans: report on adhesion and proliferation assay, electron microscopy, immunofluorescence, and western blot analysis with Bioiberica compounds. Barcelona, Spain: Bioiberica, S.A.; 2006. [on file]
7. Nadal F, Bové T, Sanchís D, et al. Effectiveness of treatment of tendinitis and plantar fasciitis by Tendoactive™. [OARS abstract 473]. *Osteoarthritis Cartilage.* 2009 Sept; 17(suppl 1):S253.

Does Not Contain

Wheat, gluten, yeast, soy, dairy products, fish, shellfish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, or preservatives.

***These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.**

