SynovX® RECOVERY

Ultra-Pure Joint Support*

Available in 120 vegetarian capsules

DISCUSSION

Nourishing and maintaining the connective tissue (cartilage) in our joints are essential to maintaining flexibility, exercising comfortably, and recovering effectively. Three high-quality ingredients are combined in SynovX Recovery to promote joint health and assist with recovery from temporary joint discomfort due to occasional overexertion or intensive activity.*

CS b-Bioactive® Chondroitin sulfate (CS) is the most abundant glycosaminoglycan (GAG) in the body. GAGs are the principal components of cartilage and synovial fluid. CS is thought to enhance joint health by supporting endogenous synthesis and preventing degradation of other joint GAGs. Oral administration of CS (800-1200 mg/d) has proven to positively influence brain response to patellar pressure, joint space width, joint comfort, and fluid accumulation.[1-5] SynovX Recovery provides 1200 mg of CS in the recommended four-capsule-per-day dosage.*

The pharmaceutical grade, low-molecular–weight CS in CS b-Bioactive has demonstrated higher bioavailability[6] and greater biological activity[7] than other CS sources. CS b-Bioactive is the reference CS for the European Union Pharmacopoeia, and it was selected by the US National Institutes of Health for their glucosamine/chondroitin trial.[8] In fact, most of the clinical research performed using CS has employed CS b-Bioactive; and in all clinical trials and over 10 years of pharmacovigilance, CS b-Bioactive has shown an excellent safety profile.*

In a landmark study, the comparable efficacy of 1200 mg/d of CS b-Bioactive versus standard intervention was tested. In this multicenter, randomized, double-blind, controlled and comparative study, 194 subjects were studied for a two-year period. According to quantitative magnetic resonance, subjects supplemented with CS b-Bioactive showed slower progression of cartilage volume loss in the first year when compared to subjects on standard intervention. Furthermore, both interventions were found to be equally effective on comfort, function, ease of movement, and fluid accumulation.*[9]

CLINICAL APPLICATIONS

- Supports Joint Structure and Function*
- Supports Proteoglycan Synthesis for Healthy Connective Tissue*
- Helps Protect Cartilage Cells*
- Contributes to Muscle Recovery Following Exercise*

SynovX® Recovery *features methylsulfonylmethane (MSM) blended with naturally occurring, clinically researched glucosamine sulfate and chondroitin sulfate. Combined, these three ingredients provide targeted support for healthy joint structure and function.**

A comprehensive review published by Cochrane in 2015 included 43 randomized controlled trials including 4962 participants treated with chondroitin sulfate; 4148 participants given placebo or another control were included. The review revealed that chondroitin (alone or in combination with glucosamine) was better than placebo for supporting joint comfort in short-term studies.*[10]

Glucosamine Sulfate Glucosamine is a naturally occurring amino saccharide (glucose with a nitrogen-containing amino group attached) that is a principle substrate for cartilage synthesis.[11] Research suggests that glucosamine stimulates chondrocytes (cartilage cells), supports GAG synthesis, incorporates sulfur into cartilage tissue, induces hyaluronic acid (HA) production, and modulates prostaglandin (e.g., PGE2) synthesis.[12-14] Prostaglandins (specialized hormone-like fatty acids produced in the body) regulate a wide variety of bodily functions, including cytokine production and balance. Glucosamine sulfate was found to inhibit the release of PGE2, the activity of NF-kappaB, and the synthesis of COX-2 enzymes in human chondrocytes.*[15]

Most of the scientific research done on glucosamine has been performed using glucosamine sulfate. Oral doses of 1500 mg/d have shown clinical benefits in joint mobility and comfort.[12,16] Four capsules per day of SynovX Recovery provide 1500 mg of glucosamine sulfate. It is postulated that even lower doses may nourish joint tissues, especially in combination with chondroitin sulfate.*

Several studies have confirmed that the benefits of combining glucosamine sulfate with chondroitin sulfate outweigh taking either alone.[17-19] During a randomized, double-blind, placebo-controlled clinical trial that followed 605 participants for two years, all study groups who had received glucosamine sulfate (1500 mg/d), chondroitin sulfate (800 mg/d), or a combination of the two experienced an improvement in joint comfort. However, only the group that received a combination of glucosamine sulfate and chondroitin sulfate experienced a significant improvement in joint space.*[20]

A phase IV, multicenter, randomized, double-blind, non-inferiority trial (n = 606) compared the effects of chondroitin sulfate plus glucosamine hydrochloride—1200 mg and 1500 mg, respectively—versus a standard intervention. At six months, both interventions produced equivalent effects on knee comfort (50% improvement),

ease of movement (~48% improvement), functional limitation (~45.95% improvement), and joint fluid accumulation (~50% improvement).*[21]

Methylsulfonylmethane (MSM) As an organosulfur compound, MSM is thought to primarily benefit joint tissues by delivering sulfur. Sulfur helps maintain the strength and structure of connective tissue by forming cross-linkages through disulfide bonds—such as those found in GAGs.[22] One joint study shows that glucosamine and MSM achieve better results when combined than when administered individually.*[23] Research suggests that MSM may reduce joint tissue damage triggered by free radicals and support muscle recovery after exercise through its antioxidant capacity. Though relatively high doses of MSM were used in exercise studies, the one gram provided in two servings of SynovX Recovery can contribute to MSM dosing for exercise recovery.*[24-26]

SynovX® Recovery Supplement Facts

Serving Size: 2 Capsules VEGETARIAN CAPS

	Amount Per Serving	%Daily Value
Glucosamine Sulfate (as glucosamine sulfate sodium chloride)	750 mg	**
Chondroitin Sulfate (as chondroitin sulfate sodium)[S1]	600 mg	**
Methylsulfonylmethane (MSM)	475 mg	**

** Daily Value not established.

Other Ingredients: Capsule (hypromellose and water), ascorbyl palmitate, medium-chain triglyceride oil, and silica.
Contains: Crustacean shellfish (shrimp and crab).

DIRECTIONS: Take two capsules twice daily, or as directed by your healthcare professional.

Consult your healthcare practitioner prior to use. Individuals taking warfarin or other medication should discuss potential interactions with their healthcare practitioner. Do not use if tamper seal is damaged.

STORAGE: Keep closed in a cool, dry place out of reach of children.

FORMULATED TO EXCLUDE: Wheat, gluten, corn, yeast, soy, dairy products, fish, peanuts, tree nuts, egg, ingredients derived from genetically modified organisms (GMOs), artificial colors, artificial sweeteners, and artificial preservatives.

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REFERENCES

1. Kahan A, Uebelhart D, De Vathaire F, et al. Long-term effects of chondroitins 4 and 6 sulfate on knee osteoarthritis: the study on osteoarthritis progression prevention, a two-year, randomized, double-blind, placebo-controlled trial. *Arthritis Rheum.* 2009 Feb;60(2):524-33. [PMID: 19180484]
2. Möller I, Pérez M, Monfort J, et al. Effectiveness of chondroitin sulphate in patients with concomitant knee osteoarthritis and psoriasis: a randomized, double-blind, placebo-controlled study. *Osteoarthritis Cartilage.* 2010 Jun;18 Suppl 1:S32-40. [PMID: 20399899]
3. Wildi LM, Raynauld JP, Martel-Pelletier J, et al. Chondroitin sulphate reduces both cartilage volume loss and bone marrow lesions in knee osteoarthritis patients starting as early as 6 months after initiation of therapy: a randomised, double-blind, placebo-controlled pilot study using MRI. *Ann Rheum Dis.* 2011 Jun;70(6):982-89. [PMID: 21367761]
4. Hochberg MC, Clegg DO. Potential effects of chondroitin sulfate on joint swelling: a GAIT report. *Osteoarthritis Cartilage.* 2008;16 Suppl 3:S22-24. [PMID: 18768335]
5. Monfort J, Pujot J, Contreras-Rodriguez O, et al. Effects of chondroitin sulfate on brain response to painful stimulation in knee osteoarthritis patients. *Ann Rheum Dis.* 2014;73:82. doi:10.1136/annrheumdis-2014-eular.4908.
6. Adebowale A, Du J, Liang Z, et al. The bioavailability and pharmacokinetics of glucosamine hydrochloride and low molecular weight chondroitin sulfate after single and multiple doses to beagle dogs. *Biopharm Drug Dispos.* 2002 Sep;23(6):217-25. [PMID: 12214321]
7. Tat SK, Pelletier JP, Mineau F, et al. Variable effects of 3 different chondroitin sulfate compounds on human osteoarthritic cartilage/chondrocytes: relevance of purity and production process. *J Rheumatol.* 2010 Mar;37(3):656-64. [PMID: 20110528]
8. Barnhill JG, Fye CL, Williams W, et al. Chondroitin product selection for the glucosamine/chondroitin arthritis intervention trial. *J Am Pharm Assoc.* 2006 Jan-Feb;46(1):14-24. [PMID: 16529337]
9. Pelletier JP, Raynauld JP, and Beaulieu A, et al. In a two-year double-blind randomized controlled multicenter study, chondroitin sulfate was significantly superior to celecoxib at reducing cartilage loss with similar efficacy at reducing disease symptoms in knee osteoarthritis patients [abstract]. *Arthritis Rheumatol.* 2015; 67 (suppl 10). http://acrabstracts.org/abstract/in-a-two-year-double-blind-randomized-controlled-multicenter-study-chondroitin-sulfate-was-significantly-superior-to-celecoxib-at-reducing-cartilage-loss-with-similar-efficacy-at-reducing-disease-sym/. Accessed January 8, 2016.
10. Singh JA, Noorbaloochi S, MacDonald R, et al. Chondroitin for osteoarthritis. *Cochrane Database Syst Rev.* 2015 Jan 28;1:CD005614. [PMID: 25629804]
11. Glucosamine. Natural Medicines. https://naturalmedicines.therapeuticresearch.com/databases/food,-herbs-supplements/professional.aspx?productid=807. Accessed January 13. 2016.
12. Kelly GS. The role of glucosamine sulfate and chondroitin sulfates in the treatment of degenerative joint disease. *Altern Med Rev.* 1998 Feb;3(1):27-39. Review. [PMID: 9600024]
13. Igarashi M, Kaga I, Takamori Y, et al. Effects of glucosamine derivatives and uronic acids on the production of glycosaminoglycans by human synovial cells and chondrocytes. *Int J Mol Med.* 2011 Jun;27(6):821-27. [PMID: 21455564]
14. Kapoor M, Mineau F, Fahmi H, et al. Glucosamine sulfate reduces prostaglandin E(2) production in osteoarthritic chondrocytes through inhibition of microsomal PGE synthase-1. *J Rheumatol.* 2012 Mar;39(3):635-44. [PMID: 22089456]
15. Largo R, Alvarez-Soria MA, Díez-Ortego I, et al. Glucosamine inhibits IL-1beta-induced NFkappaB activation in human osteoarthritic chondrocytes. *Osteoarthritis Cartilage.* 2003 Apr;11(4):290-98. [PMID: 12681956]
16. Selvan T, Rajiah K, Nainar MS, et al. A clinical study on glucosamine sulfate versus combination of glucosamine sulfate and NSAIDs in mild to moderate knee osteoarthritis. *Scientific World Journal.* 2012;2012:902676. [PMID: 22577354]
17. Tat SK, Pelletier JP, Vergés J, et al. Chondroitin and glucosamine sulfate in combination decrease the pro-resorptive properties of human osteoarthritis subchondral bone osteoblasts: a basic science study. *Arthritis Res Ther.* 2007;9(6):R117. [PMID: 17996099]
18. Lippiello L, Woodward J, Karpman R, et al. In vivo chondroprotection and metabolic synergy of glucosamine and chondroitin sulfate. *Clin Orthop Relat Res.* 2000 Dec;(381):229-40. [PMID: 11127660]
19. Clegg DO, Reda DJ, Harris CL, et al. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. *N Engl J Med.* 2006 Feb 23;354(8):795-808. [PMID: 16495392]
20. Fransen M, Agaliotis M, Nairn L, et al. Glucosamine and chondroitin for knee osteoarthritis: a double-blind randomised placebo-controlled clinical trial evaluating single and combination regimens. *Ann Rheum Dis.* 2015 May;74(5):851-58. [PMID: 24395557]
21. Hochberg MC, Martel-Pelletier J, Monfort J, et al. Combined chondroitin sulfate and glucosamine for painful knee osteoarthritis: a multicentre, randomised, double-blind, non-inferiority trial versus celecoxib. *Ann Rheum Dis.* 2016 Jan;75(1):37-44. [PMID: 25589511]
22. Methylsulfonylmethane (MSM). Monograph. *Altern Med Rev.* 2003 Nov;8(4):438-41. [PMID: 14653770]
23. Usha PR, Naidu MU. Randomised, double-blind, parallel, placebo-controlled study of oral glucosamine, methylsulfonylmethane and their combination in osteoarthritis. *Clin Drug Investig.* 2004;24(6):353-63. [PMID: 17516722]
24. Brien S, Prescott P, Lewith G. Meta-analysis of the related nutritional supplements dimethyl sulfoxide and methylsulfonylmethane in the treatment of osteoarthritis of the knee. *Evid Based Complement Alternat Med.* 2011;2011:528403. [PMID: 19474240]
25. Kalman DS, Feldman S, Scheinberg AR, et al. Influence of methylsulfonylmethane on markers of exercise recovery and performance in healthy men: a pilot study. *J Int Soc Sports Nutr.* 2012 Sep 27;9(1):46. [PMID: 23013531]
26. Barmaki S, Bohlooli S, Khoshkhahesh F, et al. Effect of methylsulfonylmethane supplementation on exercise - Induced muscle damage and total antioxidant capacity. *J Sports Med Phys Fitness.* 2012 Apr;52(2):170-74. [PMID: 22525653]

Additional references available upon request

All XYMOGEN® Formulas Meet or Exceed cGMP Quality Standards.

***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.**

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