



FORMULATED BY DAVID HAASE, MD

Clinical Applications

- Supports Joint Mobility and Comfort*
- Supports Healthy Synovial Fluid*
- Supports Joint Integrity and Function**

*Hopalong™ is a breakthrough formula designed for active adults who don't want to slow down or reduce their ability to perform athletic tasks—from walking to extreme sports. It promotes healthy joint fluid and synovial membranes, supports joint mobility, and helps support cytokine and eicosanoid balance. Keep the fluid in your joints healthy just as you would change the oil in your car to get more mileage. Let Hopalong™ help you stay active and perform well!**

All Creating Health Formulas Meet or Exceed cGMP Quality Standards

Discussion

Hopalong™ provides primary support for joint lubrication and comfort in the face of aging, normal wear and tear, and robust physical activity. This unique formula addresses the health of the total joint, including articular cartilage (highly specialized connective tissue), the synovial membrane (a thin layer of tissue that contains synoviocytes), and the synovial fluid (the fluid that lubricates the joint). Providing early support for the joint's cartilage matrix can tip the balance in favor of anabolism (building up) versus catabolism (breaking down). A proprietary blend of ingredients makes Hopalong™ the early "go-to" formula for healthy joint maintenance.*

Hyal-Joint® This proprietary complex is rich in high-molecular-weight hyaluronic acid, along with polysaccharides and collagen. Hyaluronic acid (HA), the principal component of Hyal-Joint, is a lubricating substance produced naturally in the body.^[1] It is found in abundance in the synovial fluid and extracellular matrix of joints where it reduces friction between cartilage surfaces and helps maintain cytokine balance. Hyaluronic acid helps maintain the quality of the synovial fluid and the integrity of the synovial membrane, both key factors in the health of the joint itself. Oral HA is absorbed in the small intestine and has yielded positive results in human, animal, and cell studies.^[2,3] Cell studies suggest that high-molecular-weight HA has a positive effect on cytokine balance due to downregulation of IL-8, iNOS, aggrecanase-2, and TNF-alpha gene expression.^[4] In vitro efficacy studies found Hyal-Joint to be two to four times more effective than fermented HA in stimulating the synthesis of endogenous HA and improving the concentration and viscous properties of joint fluid.*^[5-7]

Research on Hyal-Joint has yielded positive outcomes.^[8-14] A randomized, double-blind, placebo-controlled trial indicated that oral Hyal-Joint (80 mg/d) resulted in significant improvements in WOMAC (Western Ontario and McMaster Universities Osteoarthritis) scores compared to baseline, with a greater magnitude of improvement in physical function and total symptoms when compared to placebo. Hyal-Joint was found to improve several markers of quality of life in the study as well.^[2] Oral supplementation with Hyal-Joint resulted in a decrease in synovial effusion and occasional pain when compared to other treatment.^[9] Several other human studies showed varied positive effects of Hyal-Joint supplementation at 80 mg/d for three months.^[9-11] The observed benefits included improved joint mechanics, increased muscle strength and function, increased joint comfort and mobility, and reduced fluid accumulation. In one study, pre- and post-intervention peripheral blood samples taken in a subset of patients showed that supplementation improved gene expression related to GAG metabolism and extracellular matrix remodeling.*^[11] Animal studies have yielded promising results suggesting that Hyal-Joint supports joint tissue at the cellular level^[12] and reduces synovial effusion.^[13] Hyal-Joint was found to lower levels of prostaglandin E2 (PGE2) in human fibroblasts cells which, in turn, supports eicosanoid balance in the body.*^[14]

Hesperidin A citrus bioflavonoid that has been studied for its effect on cytokine balance, hesperidin (HES) is often combined with other therapeutic agents.^[15] Research suggests that oral HES can support joint health; when administered, it significantly improved all clinical parameters measured,^[16] suppressed clinical scores, and improved histological features in the animal model.^[17] Hesperidin administration was associated with the suppression of T-lymphocyte proliferation and IL-2 production; downregulation of IL-1, IL-6, and TNF-alpha; and amelioration of pathological changes in a targeted rat population.*^[18]

Xanthohumol Hops are used traditionally to promote relaxation and healthy mood.^[19] However, current research suggests that hop extract, particularly xanthohumol (XN), helps support eicosanoid and cytokine balance and joint health.^[20-23] Specifically, XN was found to be superior to other hops-derived compounds (including isoxanthohumol) for inhibiting hyaluronic acid export, inhibiting proteoglycan and collagen loss, and supporting cytokine balance in bovine chondrocytes.^[21] XN appears to suppress production of nitric oxide, IL-1 α , and TNF- α ; induce nuclear translocation of Nrf2; and increase cellular glutathione.^[24] Furthermore, XN appears to confer additional support for cytokine balance by downregulating cellular toll-like receptor 4 (TLR4) protein content.^[25] Hopalong™ contains a concentrated extract of xanthohumol.*

*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: 1 Capsule
Servings Per Container: 60

	Amount Per Serving	%Daily Value
SynovX Performance Proprietary Blend	490 mg	**
Hesperidin (from <i>Citrus sinensis</i>) (fruit), Hyal-Joint® (proprietary natural complex rich in high-molecular-weight hyaluronic acid, other polysaccharides, and collagen), and xanthohumol (from <i>Humulus lupulus</i>) (hop cones)		
** Daily Value not established.		

Other Ingredients: HPMC (capsule), dicalcium phosphate, ascorbyl palmitate, silica, and medium-chain-triglyceride oil.

Hyal-Joint® Hyal-Joint® is a registered trademark
licensed by Bioiberica, S.A.

Directions

Take one capsule twice daily, or as directed by your healthcare practitioner.

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

References

1. Natural Medicines. Hyaluronic Acid. <https://naturalmedicines.therapeuticresearch.com/databases/health-wellness/professional.aspx?productid=1062>. Accessed January 11, 2016.
2. Kalman DS, Heimer M, Valdeon A, et al. Effect of a natural extract of chicken combs with a high content of hyaluronic acid (Hyal-Joint) on pain relief and quality of life in subjects with knee osteoarthritis: a pilot randomized double-blind placebo-controlled trial. *Nutr J*. 2008 Jan 21;7:3. [PMID: 18208600]
3. Bergin BJ, Pierce SW, Bramlage LR, et al. Oral hyaluronan gel reduces post operative tarsocrural effusion in the yearling Thoroughbred. *Equine Vet J*. 2006 Jul;38(4):375-8. [PMID: 16866209]
4. Wang CT, Lin YT, Chiang BL, et al. High molecular weight hyaluronic acid down-regulates the gene expression of osteoarthritis-associated cytokines and enzymes in fibroblast-like synoviocytes from patients with early osteoarthritis. *Osteoarthritis Cartilage*. 2006 Dec;14(12):1237-47. [PMID: 16806998]
5. Torrent A, Ruhí R, Theodosakis J, et al. Comparative efficacy of IB0004, extracted hyaluronic acid (HA) and fermented HA on the synthesis of endogenous HA by human synoviocytes. *Osteoarthritis Cartilage*. 2009;17(Suppl 1):S278-S279. [on file]
6. Bioiberica. Hyal-Joint. http://www.hyal-joint.com/Information_on_the_ingredient.html. Accessed January 11, 2016.
7. Torrent A, Ruhí R, Theodosakis J, et al. Comparison of the efficacy of two products sold as orally-administered hyaluronic acid supplements, IB0004 and ID386 on the endogenous in vitro synthesis of hyaluronic acid by human synoviocytes. *Osteoarthritis Cartilage*. 2009;17(Suppl 1):S277-S278.
8. Möller I, Martínez-Puig D, Chetrit C. Oral Administration of a natural extract rich in hyaluronic acid for the treatment of knee OA with synovitis: a retrospective cohort study. *Clin Nutr Suppl*. 2009;4(2):171. <http://download.journals.elsevierhealth.com/pdfs/journals/1744-1161/PIIS1744116109703941.pdf>. Accessed January 11, 2016.
9. Martínez-Puig D, Möller I, Fernández C, et al. Efficacy of oral administration of yoghurt supplemented with a preparation containing hyaluronic acid (Mobilee™) in adults with mild joint discomfort: a randomized, double-blind, placebo-controlled intervention study. *Mediterr J Nutr Metab*. 2013;6:63-68.
10. Solà R, Valls RM, Martorell I, et al. A low-fat yoghurt supplemented with a rooster comb extract on muscle joint function in adults with mild knee pain: a randomized, double blind, parallel, placebo-controlled, clinical trial of efficacy. *Food Funct*. 2015 Nov 4;6(11):3531-39. [PMID: 26302034]
11. Sánchez J, Bonet ML, Keijer J, et al. Blood cells transcriptomics as source of potential biomarkers of articular health improvement: effects of oral intake of a rooster combs extract rich in hyaluronic acid. *Genes Nutr*. 2014 Sep;9(5):417. [PMID: 25024048]
12. Castillo V, Bendele AM, Li K, et al. Effects of oral administration of Hyal-Joint® in 17 day rat developing type II collagen arthritis. *Osteoarthritis and Cartilage*. 2010 Oct;18(Suppl 2):S244-S245. doi:10.1016/S1063-4584(10)60572-9.
13. Carmona JU, Argüelles D, Deulofeu R, et al. Effect of the administration of an oral hyaluronan formulation on clinical and biochemical parameters in young horses with osteochondrosis. *Vet Comp Orthop Traumatol*. 2009;22(6):455-9. [PMID: 19876524]
14. Torrent A, Ruhí R, Martínez C, et al. Anti-inflammatory activity and absorption of a natural rooster comb extract (Hyal-Joint®). *Osteoarthritis and Cartilage*. 2010 Oct;18(Suppl 2):S246-S247. doi:10.1016/S1063-4584(10)60577-8.
15. Natural Medicines. Hesperidin. <https://naturalmedicines.therapeuticresearch.com/databases/health-wellness/professional.aspx?productid=1033>. Accessed January 13, 2016.
16. Umar S, Kumar A, Sajad M, et al. Hesperidin inhibits collagen-induced arthritis possibly through suppression of free radical load and reduction in neutrophil activation and infiltration. *Rheumatol Int*. 2013 Mar;33(3):657-63. [PMID: 22527139]
17. Kawaguchi K, Maruyama H, Kometani T, et al. Suppression of collagen-induced arthritis by oral administration of the citrus flavonoid hesperidin. *Planta Med*. 2006 Apr;72(5):477-9. [PMID: 16557465]
18. Li R, Li J, Cai L, et al. Suppression of adjuvant arthritis by hesperidin in rats and its mechanisms. *J Pharm Pharmacol*. 2008 Feb;60(2):221-8. [PMID: 18237470]
19. Natural Medicines. Hops. <https://naturalmedicines.therapeuticresearch.com/databases/food-herbs-supplements/professional.aspx?productid=856>. Accessed January 13, 2016.
20. Hougee S, Faber J, Sanders A, et al. Selective inhibition of COX-2 by a standardized CO2 extract of Humulus lupulus in vitro and its activity in a mouse model of zymosan-induced arthritis. *Planta Med*. 2006 Feb;72(3):228-33. [PMID: 16534727]
21. Stracke D, Schulz T, Prehm P. Inhibitors of hyaluronan export from hops prevent osteoarthritic reactions. *Mol Nutr Food Res*. 2011 Mar;55(3):485-94. [PMID: 20848398]
22. Gao X, Deeb D, Liu Y, et al. Immunomodulatory activity of xanthohumol: inhibition of T cell proliferation, cell-mediated cytotoxicity and Th1 cytokine production through suppression of NF-kappaB. *Immunopharmacol Immunotoxicol*. 2009;31(3):477-84. [PMID: 19555200]
23. Cho YC, Kim HJ, Kim YJ, et al. Differential anti-inflammatory pathway by xanthohumol in IFN-gamma and LPS-activated macrophages. *Int Immunopharmacol*. 2008 Apr;8(4):567-73. [PMID: 18328448]
24. Lee IS, Lim J, Gal J, et al. Anti-inflammatory activity of xanthohumol involves heme oxygenase-1 induction via NRF2-ARE signaling in microglial BV2 cells. *Neurochem Int*. 2011 Feb;58(2):153-60. [PMID: 21093515]
25. Peluso MR, Miranda CL, Hobbs DJ, et al. Xanthohumol and related prenylated flavonoids inhibit inflammatory cytokine production in LPS-activated THP-1 monocytes: structure-activity relationships and in silico binding to myeloid differentiation protein-2 (MD-2). *Planta Med*. 2010 Oct;76(14):1536-43. [PMID: 20309792]

Does Not Contain

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

Manufactured For Creating Health
556 Fire Station Rd, Suite B
Clarksville, TN 37043
www.creatinghealth.com

DRS-275
REV. 01/21/16