

# JOINTS ULTRA

*As we age, all too many of us experience the creaking and cracking of our joints as we "attempt" to make the same twists and turns we did when we were younger. Some might go through their day in pain and discomfort due to inflamed joints asking themselves, "Why don't I have the same elasticity in my tendons than I do in the waistline of my sweatpants?" When reality confronts us, we realize that there is little we can do against the inevitable. However, although cartilage deterioration will ensue to some degree as we age, it doesn't necessarily have to be as quick and painful as we might think. There are some nutrients found in plants and animals that surprisingly decrease inflammation and decay of joints. Viva Vitamins has prepared a formula that provides these very ingredients in a new product called Joints Ultra.*

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## Cartilage 101

Cartilage is dense connective tissue composed of *chondrocytes*, a unique class of cells that produce a large amount of extracellular matrix composed of collagen fibers, proteoglycan, and elastin fibers. There are three main classes of cartilage: elastic, hyaline, and fibrocartilage. Due to its avascularization (no blood vessels), cartilage is one of the body's slowest growth and repaired tissues. Chondrocytes are fed and nourished through the compression and flexion of the surrounding matrix, thus they are fed by passive diffusion. Hyaline cartilage is what sheaths the ends of bones and stretches over to form the articular blanket of joints. Endochondral ossification, the process in which bones grow, actually uses a hyaline cartilage intermediate. This is seen in infants all the way up to adolescence. Elastic cartilage contains mostly elastin within its matrix. This stiff but elastic tissue is found mainly in certain regions of the ear and epiglottis. Fibrocartilage has its matrix comprised mostly of a protein called Type I collagen, which provides incredible tensile strength and support. It is most ubiquitous in high and frequent stress areas such as intervertebral discs, the symphysis pubis, and the attachments of certain tendons and ligaments.

## What's in Joints Ultra?

Joints Ultra contains vitamins and minerals that have been hand picked due to their direct and indirect involvement in achieving maximum joint health. Joints Ultra starts out its formula with the ever so popular vitamin C. Vitamin C (the L-enantiomer of ascorbic acid), has been strategically placed into the formula due to two of its physiological benefits in tissue protection and repair. First, it is a well known and powerful anti-oxidant, thus preventing oxidative damage to cartilage matrices. Second, collagen cannot be synthesized in humans without vitamin C. It is the cofactor of the two crucial enzymes procollagen-lysine 5-dioxygenase, and procollagen-proline dioxygenase, which forms hydroxylysine and hydroxyproline, the two agents that allow crosslinking within collagen. There is also evidence of vitamin C's involvement in the reduction of pain from

osteoarthritis (Jensen NH, 2003), possibly due to its role as an inhibitor of proinflammatory prostaglandins (D M Pugh et al., 1975).

Vitamin A needs no introduction. Although a very popular supplement for maintaining the proper health of eye, immune system, skin, etc., this vitamin now has increasing evidence of reducing inflammation. It turns out that it does this by decreasing the amount of circulating monocyte chemoattractant protein-1 (Daniels S, 2006), which is responsible for one aspect of the inflammatory response. Vitamin E is a must have in any joint formula due to its amazing antioxidating and anti-inflammatory abilities. Studies show that tocopherols (in particular the  $\alpha$ -isoform) greatly reduce inflammation via reduction in the transcription of TNF- $\alpha$  and lipid peroxides (Devaraj S et al., 2007). Of all the minerals to select for reducing inflammation, zinc is one of our anti-inflammatory heroes. Zinc has the amazing ability to inhibit the nuclear factor kappa B (NFkB) leading to a reduction in the inflammation cascade (Kim CH et al., 2003). The ever so popular amino sugar, glucosamine is one of the most abundant monosaccharides in our bodies. It is prepared by the digestion of the exoskeletons of crustaceans and put into tablet or capsule form as sulfate or hydrochloride. The mechanisms of action of glucosamine have astounded scientists and have given rise to a wonderful array of different applications, most notably osteoarthritis. Glucosamine's benefits in osteoarthritis include, but are not limited to, its anti-inflammatory properties (Largo R, et al., 2003), propagation of proteoglycan synthesis (Bassleer C., et al., 1998), and catabolic decrease in chondrocyte activity, inhibiting proteolytic enzyme synthesis causing damage to cartilage matrix and causing death of articular chondrocytes (Dodge GR, et al., 2003, Chan PS, et al., 2005). Chondroitin and Shark Cartilage have been added to the Joints Ultra formula in a proprietary blend as well. The long-chained glycosaminoglycan characteristic of chondroitin is a crucial structural supporting factor of cartilage and contributes to cartilage's resistance to

compression and stress. When combined with glucosamine, the two form a powerhouse team in combating osteoarthritis. Supplemental chondroitin, usually from bovine or porcine sources, has demonstrated outstanding results for the treatment of osteoarthritis (Jordan KM. et al., 2003). In fact, in Europe it is used as an approved drug with evidence of its efficacy and safety backed by clinical trials for the successful treatment of osteoarthritis (Vergés J. et al., 2004). Shark cartilage is the strong, sturdy material that the skeleton of sharks is comprised of. Besides its composition of glycosaminoglycans, amino sugars involved in connective tissue rebuilding, and being one of the sources of commercially prepared chondroitin sulfate, there is a recent rise in studies that suggest its role in preventing certain cancers. One such study postulates shark cartilage having inhibitory effects on endothelial cell angiogenesis, metastasis, cell adhesion and MMP (matrix metalloprotease) activity (Bargahi A. et al., 2008). Collagen has a very unique ultrastructure such that it takes on a tri-dextro superhelix configuration in which the non-essential amino acid glycine comprises about a third of its residues. It is no wonder that Joints Ultra includes this amino acid in the formula. Moreover, glycine has been shown in recent studies to help prevent arthrosis<sup>1</sup>. An equimolar racemate of the essential amino acid has been included in the formula as well not only due to the beneficial effects of L-phenylalanine, but because of the D-enantiomer. D-phenylalanine has a very unique mechanism in which it acts as a pain killer in higher mammals. Studies show that D-phenylalanine actually increases the lifespan of enkephalins (pain regulators) by reducing their degradation via competitive inhibition of the enzyme carboxypeptidase A (Christianson DW et al., 1989). N-acetylated cysteine has also been strategically incorporated into the nutrient team due to its antiarthritic and anti-inflammatory properties. One study shows how NAC greatly reduces the production of reactive oxygen species inducing arthritis in Type II collagen (Kröger H et al., 1997). The non-essential amino acid proline has also been incorporated into the mix due to the ubiquitous amounts of it in collagen. Multiple hydroxylated proline residues in a row along helical strands within cartilage make up the predominant secondary structure in collagen. The conformational stability of collagen is significantly increased by the hydroxylation of these proline residues along the chain. In fact, ascorbic acid is the cofactor responsible for the enzyme prolyl hydroxylase, which is one of the reasons why vitamin C is placed as one of the first ingredients in the formula. Superoxide dismutase (SOD) is one of the most important and protective antioxidant enzymes in higher mammals. This enzyme's job is to perform the dismutation of the highly reactive and dangerous superoxide radical into the less reactive oxygen and hydrogen peroxide. In fact, mice that were found to be

deficient in this enzyme actually died within days after birth (Li Y et al., 1995). Highly reactive oxygen species like the superoxide pose major threats to oxidative attacks to cartilage.

Devil's claw has been chosen to be part of the formula due to its amazing ability to mimic the actions and pain relieving properties of the popular prescription medication Vioxx (S. Chrubasik et al., 2003) without the side effects. Curcumin (polyphenol which gives Turmeric its yellow color) is part of the Proprietary Herbal Support complex in Joint Ultra that demonstrates exemplary pain and inflammatory reducing abilities. Curcuminoids have been shown in studies to decrease the production of proinflammatory eicosanoids (Srivastava, KC et al., 1995) as well as inhibit the expression of nuclear factor kappa B (NFkB) in human models (Aggarwal BB et al., 2004).

Last but certainly not least, comes Pycnogenol. This flavonoid polymer, also called *proanthocyanadin*, has unmatched antioxidant capabilities that puts other antioxidants to shame. For example, pycnogenol has approximately 20 times the antioxidant power of vitamin C and about 50 times that of vitamin E (Shi, J. et al., 2003). It is for this reason that pycnogenol is one of the major players in the defense against oxidative stress to connective tissue.

## Purpose

Joints Ultra is a formula designed to help protect cartilage from inflammatory attack, oxidative stress, or any other factors involved in connective tissue degradation. Facing the reality that there is no magical supplement that will give you rubber band joints with the tensile strength of a pair of Goodyear tires, there are some ways that various biological sources can help us come close to it. As science is catching up with the times, researchers are now finding more and more nutrients that slow down the cartilage degradation process and greatly reduce inflammation. This is the very foundation in which Joints Ultra has built its formula upon.

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## References:

1. Glycine Supplement Helps Prevent Degenerative Diseases Such As Arthrosis Or Osteoporosis. *Bones / Orthopaedics*, 10 Aug 2007 - 7:00 PDT

Stephen Daniells; *More support for vitamin A against inflammation*. 06-Oct-2006

Sridevi Devaraj, Scott Leonard, Maret G. Traber and Ishwarlal Jialal; *Gamma-tocopherol supplementation alone and in combination with alpha-tocopherol alters biomarkers of oxidative stress and inflammation in subjects with metabolic syndrome*. *Free Radical Biology and Medicine*, Volume 44; Issue 6, 15 March 2008, pg. 1203-1208

Kim CH, Kim JH, Lee J, Ahn YS; *Zinc-induced NF-kappaB*

inhibition can be modulated by changes in the intracellular metallothionein level. *Toxicol Appl Pharmacol.* 2003 Jul 15;190(2):189-96.

Jensen NH; *Reduced pain from osteoarthritis in hip joint or knee joint during treatment with calcium ascorbate. A randomized, placebo-controlled cross-over trial in general practice.* *Ugeskr Laeger.* 2003 Jun 16;165(25):2563-6.

D M Pugh, S C Sharma, and C W Wilson; *Inhibitory effect of L-ascorbic acid on the yield of prostaglandin F from the guinea-pig uterine homogenates.* *Br J Pharmacol.* 1975 March; 53(3): 469

Largo R, et al. *Glucosamine inhibits IL-1beta-induced NFkappaB activation in human osteoarthritic chondrocytes.* *Osteoarthritis Cartilage.* 2003 Apr;11(4):290-8

Bassleer C., et al. *Stimulation of proteoglycan production by glucosamine sulfate in chondrocytes isolated from human osteoarthritic articular cartilage in vitro.* *Osteoarthritis Cartilage.* 1998 Nov;6(6):427-34.

Dodge GR, et al. *Glucosamine sulfate modulates the levels of aggrecan and matrix metalloproteinase-3 synthesized by cultured human osteoarthritic articular chondrocytes.* *Osteoarthritis Cart.* 2003 Jun;11(6):424-32.

Chan PS, et al. *Effect of glucosamine and chondroitin sulfate on regulation of gene expression of proteolytic enzymes and their inhibitors in interleukin-1-challenged bovine articular cartilage explants.* *Am J Vet Res.* 2005; 66 (11):1870-6.

Jordan KM, Arden NK. *EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT).* *Ann Rheum Dis,* 2003; 62:1145-1155

Vergés J, Castañeda-Hernández, G. *On the bioavailability of oral chondroitin sulfate formulations: proposed criteria for bioequivalence studies.* *Proc. West. Pharmacol. Soc.,* 2004; 47: 50-53

Bargahi A, Rabbani-Chadegani A; *Angiogenic inhibitor protein fractions derived from shark cartilage.* *Biosci Rep.* 2008 Feb;28(1):15-21.

Christianson DW, Mangani S, Shoham G, Lipscomb WN. *Binding of D-phenylalanine and D-tyrosine to carboxypeptidase A.* *Journal of Biological Chemistry* 1989 Aug 5;264(22):12849-53

Kröger H, Miesel R, Dietrich A, Ohde M, Altrichter S, Braun C, Ockenfels H; *Suppression of type II collagen-induced arthritis by N-acetyl-L-cysteine in mice.* *Gen Pharmacol.* 1997 Oct;29(4):671-4.

Li Y, Huang TT, Carlson EJ, Melov S, Ursell PC, Olson JL, Noble LJ, Yoshimura MP, Berger C, Chan PH, Wallace DC, Epstein CJ (December 1995). *Dilated cardiomyopathy and neonatal lethality in mutant mice lacking manganese superoxide dismutase.* *Nat. Genet.* 11 (4): 376-81

S. Chrubasik, A. Model, A. Black and S. Pollak; *A randomized double-blind pilot study comparing Doloteffin® and Vioxx® in the treatment of low back pain.* *Rheumatology* 2003; 42: 141-148

Srivastava, KC; Bordia A; Verma SK (April 1995). *Curcumin, a major component of the food spice turmeric (Curcuma longa), inhibits aggregation and alters eicosanoid metabolism in human blood platelets.* *Prostaglandins Leukot Essent Fatty Acids* 52 (4):

223-7.

Aggarwal BB, Shishodia S. *Suppression of the nuclear factor-kappaB activation pathway by spice-derived phytochemicals: reasoning for seasoning.* *Ann N Y Acad Sci.* 2004 Dec;1030:434-41

Shi, J. et al., (2003). *Polyphenolics in grape seeds-biochemistry and functionality.* *J Med Food.* 6(4):291-9.