ProThera® and Klaire Labs®
UPDATE
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Joint ReVitalizer™: Promoting Joint Health with Type II Collagen

Glucosamine and chondroitin have long been the most popular supplements for supporting joint health. Research suggests that supplementation with glucosamine, a precursor to glycosaminoglycan, and chondroitin, the most abundant glycosaminoglycan, can play a significant role in chondroprotection by providing nutritional building blocks for the synthesis and repair of cartilage. Numerous products containing isolated forms of glucosamine (as hydrochloride or sulfate) and/or chondroitin sulfate have been marketed to support joint function. While these supplements can provide valuable support for joints and connective tissues, they do not specifically address some of the other nutritional needs of joint structures.

Researchers are finding that another nutrient, type II collagen, may provide more comprehensive sustenance for joint health. Extracts of type II collagen, the main form of collagen in articular cartilage of joint structures, contain the amino acids found in human cartilage that are required for the synthesis and repair of connective tissue throughout the body. Current research shows that supplementation with type II collagen may help to reduce collagen destruction, have an anti-inflammatory effect, and improve joint stiffness, thereby increasing mobility and flexibility. BioCell Collagen® developed by BioCell Technologies is a highly efficacious and absorbable form of type II collagen produced through a patented manufacturing process that hydrolyzes cartilage components to form more easily absorbed, low molecular weight compounds. This all-natural ingredient contains a physiologic matrix of hydrolyzed collagen type II, hyaluronic acid, and chondroitin sulfate, all of which are highly bioavailable. BioCell Collagen® is a primary ingredient in Klaire Labs® Joint ReVitalizer™ formulation provided together with MSM® and vitamin C to protect connective tissues, promote cartilage synthesis, and support wound healing.

Collagen Hydrolysate May Stimulate Type II Collagen Growth

Articular cartilage is a complex, protective gel-like tissue surrounded by a fibrous membrane that covers the ends of bones. It allows the bones in a joint to move smoothly, without causing damage, by helping to reduce friction during movement. It also serves as a shock absorber during joint loading and motion. The ability of cartilage to withstand mechanical stress depends largely upon the interactions between the various components of its extracellular matrix that is made up of water, ground substance, and collagen, the most abundant protein in the human body. Collagen connects, supports, and strengthens body tissues of the skin, tendons, muscles, cartilage, bones, and even teeth. There are more than 28 types of collagen structures in the body, but 90 percent of collagen falls into four main categories: types I, II, III, and IV. Ninety percent of collagen in the body is type I; however, type II collagen is the primary structural component of articular cartilage. Its fibers provide the strength of articular cartilage and securely attach cartilage to bone.

Hydrolyzed collagen, also called collagen hydrolysate, is produced from collagen found in the bones, skin, and connective tissue of animals by breaking down the molecular bonds between individual collagen strands. Hydrolyzed gelatin products, a type of collagen hydrolysate, have long been used in pharmaceuticals and foods. Several studies strongly indicate collagen hydrolysate supplementation may reduce articular cartilage degradation, and may even lead to regeneration. In one study, the effect of hydrolyzed collagen on the metabolism of mature articular chondrocytes was investigated using a cell culture model of mature bovine chondrocytes. The culture medium was supplemented with collagen (denatured) hydrolysate. The control cells were treated with native (undenatured) type I and type II collagen, as well as a collagen-free wheat protein hydrolysate. Biosynthesis of type II collagen was then compared among the cells.

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The results, demonstrated by immunocytochemical detection, clearly indicated that the presence of extracellular collagen hydrolysate led to a dose-dependent increase in type II collagen secretion; whereas, the native collagens as well as the collagen-free hydrolysate of wheat proteins failed to stimulate the production of type II collagen in chondrocytes. The results also showed that only the smaller collagen fragments with a molecular weight of less than 10 kDa seemed to exert a positive influence on the biosynthesis of type II collagen in chondrocytes.

It is most likely that collagen hydrolysate might improve and maintain the extracellular matrix by increasing type II collagen secretion. This is supported by several clinical investigations. One investigation showed that human ingestion of hydrolyzed collagen led to the appearance of various collagen-derived peptides in the blood, with Pro-Hyp (proline, hydroxyproline) being a major form. In another study, mice fed with Pro-Hyp were protected from cartilage degradation under osteoarthritis-inducing conditions. Thus, collagen hydrolysate might be of particular importance for the nutrition of cartilage tissue in conditions where cartilage is under considerable stress, and might help reduce degenerative alterations in the extracellular matrix.

Another study, conducted on surgically induced, osteoarthritic rats showed that oral administration of chicken type II collagen delayed the degradation of articular cartilage. The data obtained in this study suggests that chicken type II collagen exhibits a protective effect on osteoarthritic cartilage at least in part by reducing the increased synthesis of MMP-13, MMP-9, and cathepsin K, three major proteases involved in the degradation of articular cartilage during osteoarthritis. It also confirmed the notion that MMP-13, MMP-9 and cathepsin K are present in increased amounts in osteoarthritic cartilage. The exact mechanism remains unclear, but it is interesting to note that oral administration of chicken type II collagen could effectively reduce cartilage damage.

A recent comparative study of type II collagen and glucosamine/chondroitin showed greater benefit for type II collagen. In this study, 52 subjects with osteoarthritis of the knee were randomized to take type II collagen extract or a glucosamine/chondroitin combination for 90 days. Accepted standardized WOMAC questionnaires and the Lequesne's functional index, as well as VAS scores were used to compare the two groups. The results indicate that subjects taking type II collagen had significantly greater symptom improvement than subjects taking glucosamine/chondroitin. WOMAC scores, which measure the difficulty in physical function, stiffness and pain in the knee, were reduced by 33% in the group taking type II collagen, as compared to only 14% in the glucosamine/chondroitin group. VAS scores reflected a similar result.

Treatment with collagen type II led to a 40% decrease in pain after 90 days as compared to only 15.4% with treatment of glucosamine/chondroitin. The Lequesne's functional index, which is used to determine the effect of different treatments on pain during daily activities, showed a reduction by 20.1% with treatment with type II collagen as compared to 5.9% with glucosamine/chondroitin. The improvement in daily activities resulted in an improvement in the overall quality of life for the subjects receiving collagen type II supplementation. Animal studies of type II collagen have indicated a reduction in pain with little adverse effects on arthritic conditions as well as a reduction in inflammation and collagen breakdown.

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BioCell Collagen® Supplies Highly Bioavailable Type II Collagen

BioCell Technologies has developed a highly efficacious and absorbable form of type II collagen. This supplement ingredient contains naturally occurring levels of hydrolyzed type II collagen protein (60-65%), depolymerized chondroitin sulfate (20%), hylaluronic acid (10%), and cartilage matrix glycoproteins. In addition to glycosaminoglycans, BioCell Collagen® contains a natural mixture of amino acids including lysine and proline that are essential for collagen synthesis. Unlike many traditional joint supplements that derive glucosamine from shellfish shells and chondroitin from bovine cartilage, BioCell Collagen® provides glucosamine and chondroitin derived entirely from pure chicken sternal cartilage, one of the richest natural sources of glucosamine, chondroitin, hyaluronic acid, and other chondroprotective nutrients. The composition of BioCell Collagen® mirrors that of human articular cartilage, providing comprehensive support for active joints.

Although collagen is rich in chondroprotective nutrients, it offers minimal benefit in its native (undenatured) state because the collagen molecules are too large to be absorbed by the body. To enhance bioavailability and absorption into the bloodstream, BioCell Collagen® is produced through a patented manufacturing process that hydrolyzes the cartilage components to form more easily absorbed, low molecular weight compounds. The natural ratio of nutrients present in cartilage remains intact but the forms are modified so that they can be readily used in the body to sustain connective tissues, promote cartilage synthesis, support wound healing, and even improve the overall appearance of the skin. One human bioavailability study conducted showed that hyaluronic acid levels increased ten-fold after BioCell Collagen® ingestion. Hyaluronic acid plays dual roles for the joint, one as an essential structural component of the cartilage and second as a major lubrication agent in the synovial fluid. BioCell Collagen® thus offers a unique profile of naturally occurring nutritional elements which are important in maintaining healthy cartilage and joint structures.

Human Clinical Trials of BioCell Collagen®

Three human clinical trials have been performed, showing that daily ingestion of BioCell Collagen® led to the reduction of chronic symptoms associated with various joint conditions, primarily osteoarthritis. One trial enrolled 89 subjects who were experiencing pain caused by joint discomfort. The subjects ingested 2 grams daily of BioCell Collagen® for 45 days. Out of 89 subjects, 80 (89%) experienced a degree of improved joint comfort. In contrast, only one subject who took a placebo had improved joint comfort. No adverse events associated with BioCell Collagen® were reported. A second, randomized, double-blind, placebo-controlled trial enrolled 16 subjects who had joint discomfort. The safety and efficacy of BioCell Collagen® in managing joint discomfort was investigated by using the WOMAC index. The subjects ingested 2 grams daily of BioCell Collagen® for 8 weeks. Compared to placebo, BioCell Collagen® significantly reduced joint discomfort as much as 40% at the end of the study. No adverse events associated with BioCell Collagen® were reported. The study details were presented at the international conference of Experimental Biology, 2004, Washington, DC. Finally, a third randomized, double-blind and placebo-controlled trial enrolled 80 subjects who had joint discomfort. The safety and efficacy of BioCell Collagen® in managing joint discomfort was investigated again by using the WOMAC index. The subjects ingested 2 grams daily of BioCell Collagen® for 10 weeks. Compared to placebo, BioCell Collagen® significantly reduced joint discomfort, confirming the earlier trial discussed above. No adverse events associated with BioCell Collagen® were reported. The study outcome is submitted for publication in a peer-reviewed journal.

In addition to its benefits for joints, recent data suggests potential benefits of BioCell Collagen® for skin health. A recently completed human skin study on BioCell Collagen® showed a significant increase in collagen content in the skin dermis. BioCell Collagen® appears to stimulate dermal fibroblasts responsible for production of skin collagen, which is comprised primarily of collagen types I and III. The unique biological properties of BioCell Collagen® may thus promote both healthy joints and more youthful-looking skin.

Joint ReVitalizer™ Combines BioCell Collagen®, MSM®, and Vitamin C

Joint ReVitalizer™ capsules combine three key nutritional ingredients to provide a full complement of collagen building block materials needed to support healthy cartilage biosynthesis and joint lubrication. BioCell Collagen® supplies a naturally occurring matrix of type II collagen, hyaluronic acid, glucosamine sulfate, chondroitin sulfate, and proteins found in cartilage. Methylsulfonylmethane (MSM®) provides a bioavailable source of organically bound sulfur, important for connective tissue formation. Vitamin C, essential for collagen synthesis, is also included.

Four capsules of Joint ReVitalizer™ supply 2,000 mg of BioCell Collagen® providing approximately 1,200 mg of collagen type II protein (amino acids), 400 mg of chondroitin sulfate, and 200 mg of hyaluronic acid along with naturally occurring cartilage matrix glycoproteins. In addition to glycosaminoglycans, BioCell Collagen® contains a natural mixture of amino acids including lysine and proline essential for collagen synthesis.

Methylsulfonylmethane (MSM®) is a naturally occurring organic compound containing 34% elemental sulfur, an essential mineral required for at least 150 compounds within the body, including tissues, enzymes, hormones, antibodies, and antioxidants. Sulfur is critical to the formation of collagen in healthy joints, ligaments, and tendons, as synthesis of most glycosaminoglycans requires the addition of sulfur. In fact, the concentration of sulfur in arthritic cartilage has been shown to be about one-third the level of normal cartilage. Sulfur is also responsible for the flexible bond between the cells, including those that make up the skin, and acts to block undesirable chemical and physical cross-linking of collagen associated with tough, aging skin. MSM® is added to Joint ReVitalizer™ to complement the sulfur naturally present in BioCell Collagen® and to help ensure adequate bioavailable sulfur for optimal joint and ligament health. Four capsules supply 1,000 mg of MSM®.

Vitamin C, or ascorbic acid, serves multiple functions in the overall health of connective tissue. It functions as an essential cofactor for the synthesis of collagen and other organic components of the intracellular matrix. As an enzymatic cofactor, ascorbic acid is required for hydroxylation of proline and lysine residues in the synthesis of procollagen, a precursor molecule which undergoes subsequent conversion to collagen. Ascorbic acid also functions synergistically with MSM® to maintain connective tissue health of joints, skin, and the cardiovascular system.

Suggested Use of Joint ReVitalizer™

Joint ReVitalizer™ is intended to provide nutritionally meaningful amounts of easily

absorbed and readily available nutrient materials in the suggested use of two capsules, twice daily. These nutrient materials help maintain cell structure and function and support the health of the body's connective tissues, particularly articular cartilage. This formulation is especially beneficial for individuals with damaged cartilage who may not synthesize adequate amounts of glycosaminoglycans needed for repair and maintenance of healthy connective tissue. It may also be helpful for those who have not obtained satisfactory benefit from use of glucosamine and/or chondroitin taken alone.

References and further information available on request.