dotFIT® Joint Flexibility Plus™ (Biocell Collagen II)

Goal

Osteoarthritis (OA) is a condition of degeneration of the protective covering at bone articular surfaces (cartilage). Age and injury are associated with an increased risk of development, with other lifestyle factors intervening (such as obesity). Because cartilage is used as a cushion between bone joints, its loss causes friction, pain and stiffness.

BioCell Collagen II is a patented dietary supplement containing low molecular weight undenatured type II collagen combined with hyaluronic acid (HA) and chondroitin sulfate (CS).

Type II collagen and collagen fragments (as found in Joint Support Formula) may act as signals to increase cartilage synthesis as well as provide lubrication to improve/maintain healthy joint tissue and function.

Rationale

Type II Collagen

The role of articular cartilage is to bear load, absorb shock and minimize wear between articulating joint surfaces. Chondrocytes, the cells of articular cartilage, do not directly contribute to these physical properties; only the extracellular matrix (ECM) plays a direct structural role. However, as the only cell type normally resident within articular cartilage, chondrocytes are responsible for the synthesis and maintenance of a viable extracellular matrix which is suitably adapted to cope with the physical pressures of its environment.

The health of articular cartilage, then, is dependent upon the maintenance of the ECM. The ECM is a macromolecular framework made of two main components, proteoglycans and collagens. Type II collagen is the predominant type in cartilage. Type II collagen forms a 3D fibrous network which provides tensile stiffness and strength to cartilage and provides the basic architecture to the tissue. Aggrecans (and other types of proteoglycans) are embedded within this fibrous network, providing compressibility and elasticity to the tissue.

Chondrocytes are responsible for the synthesis, organization and maintenance of the ECM. Communication between chondrocytes and the ECM determine degradation or synthesis. OA can alter the sensitivity of chondrocytes to regulatory signals. This leads to a progressive imbalance between degradation and synthesis/regeneration, leading to a marked decrease in the content of type II collagen in the ECM, eventually leading to cartilage damage. Type II collagen and collagen fragments are proposed to regulate metabolic activities in chondrocytes.

The theory behind supplementation is the role that collagen fragments have in regulating chondrocyte activity. The presence of collagen fragments (hydrolyzed) gives the appearance that ECM degradation has occurred. This stimulates the chondrocytes to increase ECM synthesis, in an attempt to "repair" the damaged structure. Several studies featuring in vitro and in vivo design have shown significant
improvement in the ECM as well as standard tests to assess pain, physical activity and quality of life in both animal and human models.

Animal studies in rats showed reduced articular cartilage degradation in an OA model with oral supplementation of chicken collagen type II. Obese-arthritic dogs given 4mg or 40mg doses of UC II (undenatured type II collagen from chicken sternum) for 90 days showed significant reductions in overall pain, pain during limb manipulation and lameness after physical activity. There was a dose dependant response. Additionally, after a 30 day withdrawal, all animal experienced a relapse and increases in pain measures.iii

In 2002, researchers in Germany explored the effect of type II collagen biosynthesis by bovine chondrocytes when cultured with different types and MW of collagen (type I and II hydrolyzed, type I and II native and collagen free wheat protein). Their results indicated a stimulatory effect on type II collagen biosynthesis and secretion by chondrocytes when cultured with hydrolyzed collagen, in a dose dependant manner. The researchers found that only hydrolyzed collagen, and primarily of lower MW (<10 kDa) was able to exert this influence. This illuminated a possible feedback mechanism for the regulation of collagen turnover in cartilage.iii a study in 2003 also showed that type II collagen increased the ECM content, as well as subtle differences in biochemical markers.iv

In 2000, Moskowitz reviewed the results of studies using collagen hydrolysates in the US, United Kindom and Germany. A significant impact on pain measures was noted; see Figure 1 and Figure 2. As with the GAIT study, the benefits seem to be greatest in those who suffer OA to a greater degree.v

The WOMAC* (Western Ontario and McMaster Universities) Index of Osteoarthritis

Figure 1 WOMAC scores were reduced 33% in the UC-II group vs. 14% with GS (UC-II = BioCell Collagen II).

*The WOMAC index is used to assess patients with osteoarthritis of the hip or knee using 24 parameters. It can be used to monitor the course of the disease or to determine the effectiveness of anti-rheumatic medications. In this study the WOMAC score measured the difficulty in physical function, stiffness and pain in the knee.
The VAS** (Visual Analogue Scale) Index of Osteoarthritis

Figure 2 VAS scores were decreased by 40% for UC-II vs. 15% for GS (UC-II = BioCell Collagen II).

A 2004 abstract looked at the efficacy of BioCell collagen specifically. In this RDBPCT, 16 subjects with OA of the knee or hand used BioCell 1000mg BID for two months. Adverse events were the same as placebo and were insignificant and not related to the study substances. The BioCell group experienced significant improvement in all WOMAC subscales and in total WOMAC score compared to placebo.\textsuperscript{vi}

In 2009, a clinical trial was presented that looked not only at the effectiveness of undenatured type II collagen (UC-II) on OA pain, but also compared it to glucosamine and chondroitin (GC) use. A daily dose of 40mg of UC-II was used, providing 10mg of bioactive undenatured type II collagen. WOMAC scores were reduced by 33% in the UC-II vs 14% with GC. VAS scores were decreased by 40% for UC-II vs 15% for GC. The Lequesne Score (used to determine the effect on pain during daily activities) was reduced by 20.1% for UC-II vs 5.9% for GC. Overall, the UC-II group experienced significant reductions in all measures of pain and pain during activities and did so to a significantly greater degree than GC supplementation.\textsuperscript{vii}

Additionally, there are several studies that have looked at the effects of UC-II on rheumatoid arthritis (RA), an autoimmune disorder. Results are promising and may be to an auto-antigen action, suppressing T cell activity and autoimmune responses.\textsuperscript{viii}

Ultimately, it appears that oral administration of UC-II is effective and appears to follow a dose response to symptoms of OA. The proposed mechanism of action is through increases undenatured type II collagen in the ECM signaling type II collagen synthesis by chondrocytes, leading to a more advantageous ECM environment- one that favors a better ration of synthesis vs degradation.

** A Visual Analogue Scale (VAS) is a measurement instrument that tries to measure a characteristic or attitude that is believed to range across a continuum of values and cannot easily be directly measured. An example of a VAS would be a numeric scale of 1 to 10 to represent severity of pain (1 being little to no pain and 10 representing excruciating pain).
Hyaluronic Acid

Hyaluronic acid (HA) is an anionic, non-sulfated glycosaminoglycan distributed widely throughout connective tissues and is one of the chief components of the extracellular matrix. It is a major component of the synovial fluid and contributes to the viscosity of the fluid. Along with lubricin, it is one of the fluid's main lubricating components.

HA is an important component of articular cartilage, where it is present as a coat around chondrocytes. When aggrecan monomers bind to hyaluronan in the presence of link protein, large highly negatively-charged aggregates form. These aggregates wick water and are responsible for the resilience of cartilage (its resistance to compression). In OA or joint degradation, HA levels are decreased.

The proposed mechanism of action would be to support a healthy ECM and provide the raw materials for joint health as well as bringing water to cartilage and aid in synovial fluid viscosity and protection/reaction to pressure and shock. Intra-articular injections with HA are quite common and have repeatedly shown improvement in symptoms of OA and joint degeneration. Effective absorption and uptake by oral supplementation of high MW hyaluronic acid has been shown in rats and dogs.

Chondroitin Sulfate

It is a necessary substrate for cartilage metabolism and assists in maintaining joint viscosity. In vitro studies show that chondroitin also inhibits enzymes that degrade cartilage. In recent reviews of chondroitin, the researchers concluded: the safety and tolerability of CS are confirmed, CS is effective, at least in part, for the treatment of OA and its therapeutic benefits occur through three main mechanisms: 1) stimulation of ECM production by chondrocytes; 2) suppression of inflammatory mediators; and 3) inhibition of cartilage degeneration. Its effects include benefits that are not achieved by current medicines and include chondroprotection and the prevention of joint space narrowing.
Summary

Purpose

Joint Flexibility Plus is a safe alternative to the more dangerous NSAIDS for the treatment of mild to moderate osteoarthritis and should be a strong consideration to those that suffer from OA. JFP would be targeted to those older adults who experience mild to severe joint pain due to the loss of cartilage that leads to OA.

- Joint Flexibility Plus is one component of the dotFIT longevity program which is made available to all program users and appears on the dotFIT website.
- Studies show that the ingredients in the new JSF may provide greater relief than glucosamine and chondroitin combined.
- The ingredients in Joint Flexibility Plus™ have been shown to support cartilage, joint and skin health.
- They have been clinically proven to be more than twice as effective as GS & CS in patients with moderate to severe osteoarthritis.
- Reduces symptoms of joint pain and increases functional capacity without the side effects of NSAIDS

Unique Features

- Contains the patented formula BioCell Collagen II
- Contains no other added ingredients so you may take other products (multivitamin, antioxidant) without worrying about reaching excessive nutrient levels that may be detrimental over time
- Dosages and compounds are in the amounts used in research that have shown to improve mobility, joint comfort, and knee-joint strength
- Formula considers use of other dotFIT products to help the user maintain a safe and optimal range of total nutrient intake
- Manufactured in an FDA-registered facility, in compliance with Good Manufacturing Practices (GMP’s)

Typical Use

- Individuals concerned with joint and cartilage health
- For overuse or age-related joint discomfort
- Take 1 capsule in the morning and 1 capsule at night before a meal with least 8 oz. of water.
- For optimal results, take 2 capsules in the morning and 2 capsule at night before a meal or as directed by your health care professional.
Precautions

The ingredients in the Joint Flexibility Plus are generally considered to be safe at the recommended dose.

Contraindications

The use of JSF is not recommended during pregnancy or lactation due to the absence of use data for these populations. No known contraindications exist at this time.

Adverse Reactions

Study participants who used BioCell 1000mg BID for two months experienced adverse events the same as placebo and were insignificant and not related to the study substances. No adverse events were reported in the literature for the other substances.

Upper Limit/Toxicity

There are no known overdoses of the BioCell ingredients either individually or as the formula.

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Supplement Reference Guide
This information is educational material for dotFIT Certified Fitness Professionals. This literature is not to be used to imply that dotFIT products may diagnose, treat, cure or prevent disease.

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