



**A CLINICALLY TESTED INGREDIENT FOR JOINT,
SKIN AND CONNECTIVE TISSUE HEALTH**



WhitePaper
BioCell Technology, LLC

Abstract

The aging process promotes physiological and structural changes that affect how our bodies look and feel. The magnitude of these changes in any one of us depends upon the extent to which connective tissues in our joints, skin, tendons, ligaments, bones, eyes, and blood vessels, have been weakened with age. The health of our connective tissue is commonly attributed to the depletion of its core structural components collagen and supporting glycosaminoglycans (GAGs: hyaluronic acid, chondroitin sulfate, etc.), which may aid in the preservation of younger looking skin and healthy joints if replenished. This white paper discusses scientific research on BioCell Collagen®: a patented dietary ingredient that contains a highly bioavailable, naturally occurring matrix of hydrolyzed type II collagen (60%), chondroitin sulfate (20%), and hyaluronic acid (HA) (10%). Multiple human clinical studies have demonstrated that BioCell Collagen is a healthy aging ingredient that promotes joint health and skin beauty. Recent studies also implicate BioCell Collagen as aiding in the protection and recovery of musculoskeletal tissue during sports activity.

A comprehensive approach to healthy aging

There are many internal and external factors that influence the pace and effects of aging. The progression of aging is linked to steady deterioration of the extracellular matrix (ECM) in connective tissue, which results from decreased synthesis and increased degradation of molecules essential for connective tissue integrity. Since collagen and GAGs such as chondroitin sulfate and hyaluronic acid (HA) are the major molecular constituents of the ECM, their replenishment could help counteract effects of aging that include feelings of malaise or tiredness, proness to injury, and declining facial skin condition. BioCell Collagen comprehensively addresses the loss of both collagen and GAGs, while also having established a record of proven safety, efficacy, and bioavailability substantiated by human clinical studies.

The unique molecular nature of BioCell Collagen®

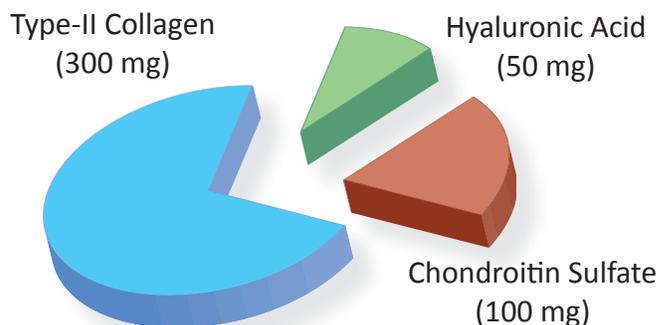


Figure 1. Patented molecular composition (500 mg).

BioCell Collagen is derived exclusively from chicken sternal cartilage, which is a rich source of collagen type II, hyaluronic acid, and chondroitin sulfate, mirroring the fundamental composition of human articular cartilage (Figure 1). Cartilage is an ideal source of these cartilaginous building blocks because it is free from blood supplies; meaning it does not contain blood, lymphatic vessels, or capillaries like other collagen-rich animal parts (e.g. hides, bones, skin and scales). The importance of this fact lies in not just a lack of contaminating proteins, but also the ability to avoid bacterial, viral, steroidal, and antibiotic contaminants that are endemically carried within our blood circulatory system. Type II Collagen is further ideal because it is predominantly found in cartilage naturally, which contains both hyaluronic acid and chondroitin sulfate. It has also been shown clinically that ingestion of BioCell Collagen boosts levels of all three major collagen types (I, II, & III).

BioCell Collagen is manufactured via a patented procedure that includes filtration, purification, concentration, hydrolysis, and sterilization, to ensure consistent quality and safety. This patented process removes impurities from the chicken sternal cartilage and remarkably reduces the size of all of its molecules, making them highly absorbable and fast-acting. The composition and synergy among BioCell Collagen's three molecular constituents are unique and cannot be found naturally in any other collagen ingredients.

BioCell Collagen is affirmed GRAS (Generally Recognized as Safe), non-GMO, and gluten free. It offers a comprehensive approach to healthy aging by providing the nutritional building blocks of macromolecular collagen and GAGs essential for the proper structure and function of various connective tissues.

Bioavailability

The native forms of collagen and GAGs are too large to be absorbed by our bodies. However, a patented BioOptimized™ hydrolysis manufacturing process reduces them into very low molecular weight forms to ensure fast and effective absorption into the small intestine. A bioavailability study in human subjects showed that ingestion of BioCell Collagen (1500 mg/day) elevated blood HA levels by sixty times at steady state when compared to the baseline levels (Figure 2).

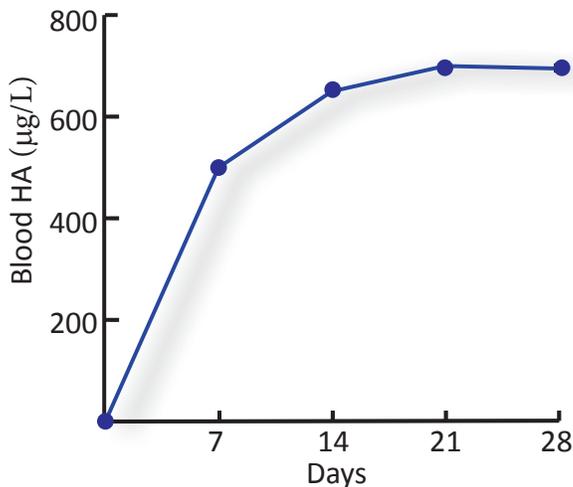


Figure 2. HA bioavailability at steady state.

Joint health studies

Synovial joints, the most common and active joints in the body, contain articular cartilage and synovial fluid. Collagen type II, chondroitin sulfate, and HA are required for healthy cartilage function. HA is also an essential lubricating molecule in the synovial fluid. Both the aging process and repeated strenuous sport activity cause the synovial joint to deteriorate, which can lead to chronic discomfort and mobility restriction. The synergy of the natural joint structure constituents found in BioCell Collagen (Figure 3) can then promote healthy joints.

Mirroring the molecular composition of human cartilage, BioCell Collagen provides effective replenishment of collagen type II, chondroitin sulfate, and HA.

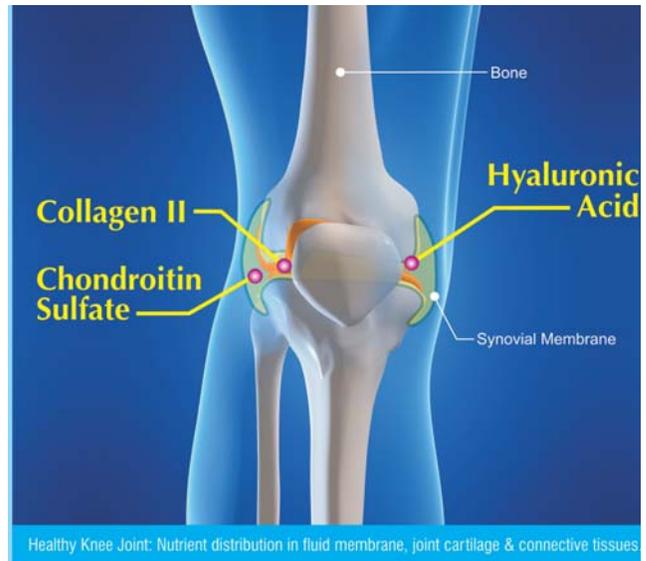


Figure 3. BioCell Collagen provides simultaneous support for type II collagen and GAGs.

Figure 4 shows the outcome of a human clinical study, which enrolled 89 subjects suffering from pain caused by various joint-related conditions including joint discomfort. The subjects ingested 2 grams of BioCell Collagen daily for 45 days. There was a continuous increase in the number of subjects who reported increases in joint comfort.

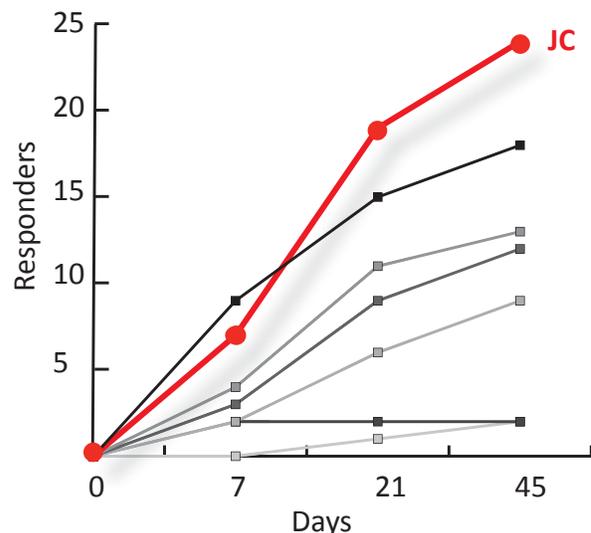


Figure 4. 89 % responders experienced increased joint comfort (JC)

The second human clinical study examined 16 subjects with self-diagnosed joint discomfort. Figure 5 shows the results of this randomized, double-blind, placebo-controlled trial (RCT). When compared to the placebo, ingestion of 2 grams of BioCell Collagen daily for 8 weeks significantly led to an increase in joint comfort related symptoms by as much as 40% (Figure 5). There was no adverse event associated with BioCell Collagen during this study, which was presented at the 2004 international conference of Experimental Biology in Washington DC.

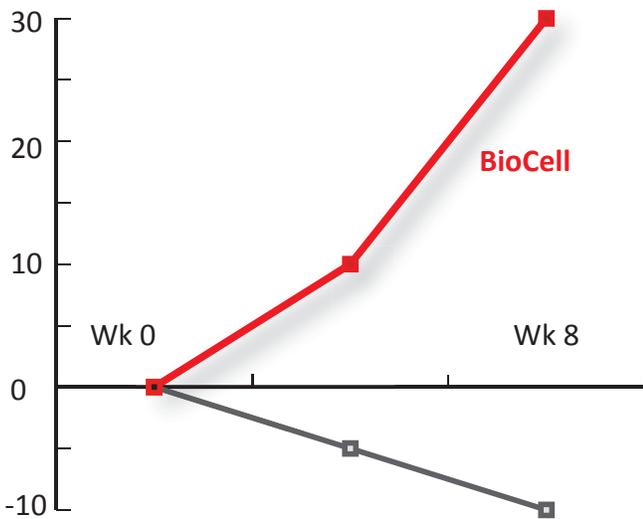


Figure 5. Percent reporting an increase in joint comfort **BioCell** vs. Placebo.

A confirmatory RCT enrolled 80 subjects experiencing advanced degrees of joint discomfort. Again, BioCell Collagen was significantly more effective than the placebo, at both measurement points (Day 35 and Day 70), in promoting joint health as evaluated by WOMAC score. 71% of subjects in the BioCell Collagen group experienced at least a 30% decrease in joint discomfort. When more stringent criteria (i.e., min 40% decrease in symptoms) was applied, more than 50% of subjects in the BioCell Collagen group experienced improvement in comfort, compared to only 13% in the placebo group. There was no adverse event associated with BioCell Collagen.

This study was published in the Journal of Agricultural and Food Chemistry

(<http://www.ncbi.nlm.nih.gov/pubmed/22486722>).

Study on skin beauty

Maintaining the integrity of the skin dermis' extracellular matrix (ECM) is crucial for youthful appearance. Collagen and GAGs are key molecules essential for healthy structure and function of the dermal matrix. Both the natural and photo-aging processes entail the degradation of the skin's collagen (types I & III) and HA, causing the dermal layer to deteriorate and to exhibit visible effects of aging such as wrinkles, fine lines, skin dehydration, and scaling (Figure 6). However, it is possible to counteract these effects and revitalize the skin with BioCell Collagen supplementation, by boosting collagen production in the skin.

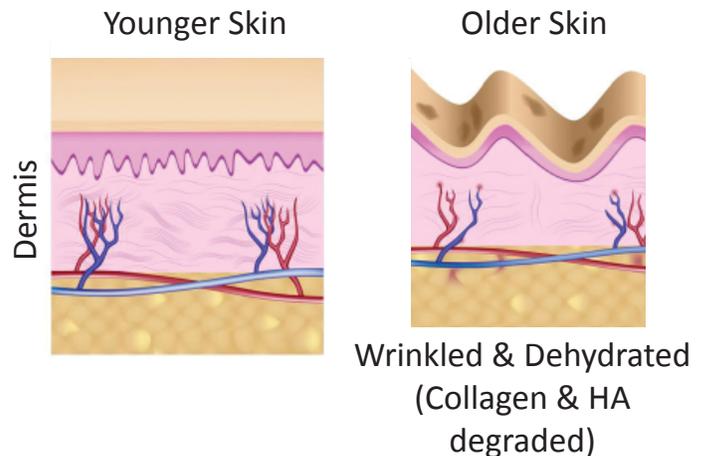


Figure 6. Deterioration of dermal ECM in aged skin.

A human study enrolled 26 subjects who displayed visible signs of natural (chronological) and photo-aging in the face. The study found that daily ingestion of 1 gram of BioCell Collagen for 12 weeks led to a significant reduction of facial lines and wrinkles (-13%), and dryness and skin scaling (-76%) (Figure 7). The content of collagen (type I/III) in the dermis increased by 3.5%, while blood microcirculation in the dermis increased by 15%.

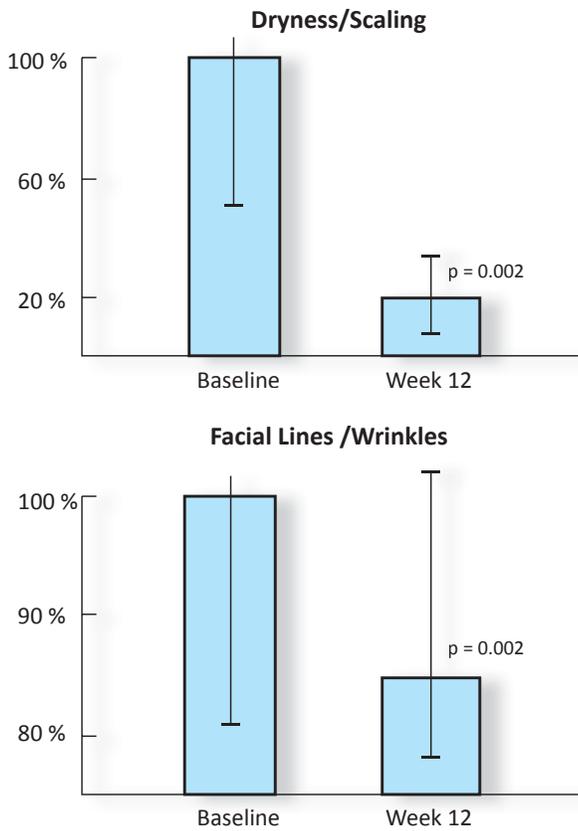


Figure 7. Reduction of facial aging signs

Figure 8 shows before and after images of subjects who participated in the study. This data suggests that BioCell Collagen can combat the appearance of facial aging. There was no adverse event associated with BioCell Collagen. This study was published in the Journal of Clinical Investigation in Aging (<http://www.ncbi.nlm.nih.gov/pubmed/22956862>).



Figure 8. Reduction of facial aging signs

Study on sports nutrition application

The ECM of muscle, tendon, and ligament tissue is sensitive to exercise-induced mechanical stimuli. Studies have shown that exercise-induced muscle damage involves connective tissue elements such as collagen, GAG-containing proteoglycans (PG), and myofibrils. A pilot RCT was conducted to assess the potential impact of BioCell Collagen on functional indices and molecular biomarkers of recovery from intense exercise. Eight healthy, recreationally active subjects ingested either 3g of BioCell Collagen or placebo daily over a 6-week period, prior to an upper body resistance exercise challenge (UBC) on day 43 and a re-challenge on day 46. Supplementation with BioCell Collagen attenuated an increase in serum markers for muscle tissue damage resulting from UBC, creatine kinase (CK), lactate dehydrogenase (LDH), and C-reactive protein (CRP). In terms of performance, the number of bench press repetitions to failure was higher (in percentage terms) in the BioCell Collagen group. This proof-of-concept study suggests that BioCell Collagen may favorably impact key biochemical markers of connective and skeletal muscle tissue damage, and enhance stress resilience following intense resistance exercise. This study was published in Integrative Medicine (Encinitas) (<http://www.ncbi.nlm.nih.gov/pubmed/26770145>).

Conclusions

Multiple human clinical studies have demonstrated that BioCell Collagen is bioavailable, safe, and effective in promoting joint comfort and mobility as well as skin beauty. These studies, together with the recent study on sports nutrition applications, demonstrate that BioCell Collagen provides a unique and comprehensive nutraceutical solution for rejuvenating healthy connective tissue throughout the body.

References

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About BioCell Technology

BioCell Technology, LLC, is in the business of researching, developing, branding, and distributing innovative, science based raw material ingredients that have applications in health and beauty. The company is headquartered in Newport Beach, California USA and operates facilities in Anaheim, California, and Elmshorn, Germany. The company's executive management team is composed of industry veterans and scientists with decades of experience. Founded in 1997, the company's goal is to provide non-invasive, economically feasible, long-term solutions that improve quality of life for people all over the globe. As a steward of quality and integrity, BioCell Technology believes that licensing is the best way to ensure the quality, safety, and efficacy of the innovative finished products that contain their branded ingredients in the market. The company's products are rooted in quality and science and were developed with sustainability in mind. The company does not sell finished products, but rather licenses its branded ingredients to leading consumer packaged goods companies for use in their finished products. Each of the branded ingredients have a trademarked logo of authenticity that is proudly displayed on the labels of finished products licensed by BioCell Technology and marketed by leading consumer packaged goods companies under their own brand names or formulas.

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