A SCIENTIFIC PERSPECTIVE

LIQUID BIOCELL™

Liquid BioCell™ is a delicious liquid nutraceutical that promotes healthy aging and active joints.

It provides a unique and proprietary combination of science-substantiated ingredients and antioxidant-rich phytonutrients that synergistically support a healthier life. Only Liquid BioCell™ contains multi-patented Liquid BioCell™, containing constituents such as collagen, hyaluronic acid (HA), and chondroitin sulfate (CS), which are essential for healthy joints and skin. It is blended with exotic, antioxidant-rich fruits from around the globe, including blueberry, mangosteen, açai berry, noni, and pomegranate. The phytonutrients contained in the fruits possess multiple health-promoting, biological activities.

Maintaining active joints is essential for healthy aging. The key ingredient is Liquid BioCell™, a patented dietary supplement that supports joint and skin health. Its constituents, type II collagen (hydrolyzed), hyaluronic acid, and chondroitin sulfate (depolymerized) are proteins and glycosaminoglycans (GAGs) critical for the health of these tissues. Other key ingredients include are superfruits carefully selected from around the world to provide a variety of phytonutrients, including vitamins, flavonoids and polyphenols. The flavours are so unique, you will remember exactly where you were the first time Liquid BioCell™ touched your palate.

STUDIES

Liquid BioCell™ Life and Skin contain a number of health-promoting, functional ingredients. They include patented Liquid BioCell™, vitamin C, and a variety of superfruits known to contain antioxidants. Scientific studies on individual ingredients suggest that it can synergistically promote the overall health of aging people.

SAFETY

Liquid BioCell™ is well tolerated in humans. In a pilot clinical trial involving humans with joint health conditions, Liquid BioCell™ was well tolerated during the 8-week study period (1).

JOINTS

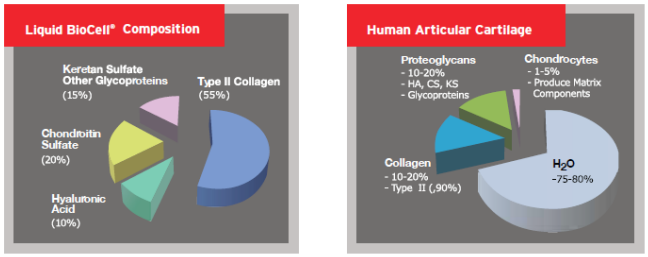
Studies support that the functional nutrients in Liquid BioCell™ can help improve joint health by providing structurally and functionally essential molecules.

There are many different types of collagen found in the body, and type II is the most abundant (>90% of collagens) in the cartilage of the synovial joint, the most common and movable joint (2). Type II collagen forms a fibrillar network to provide tensile strength to the cartilage. Proteoglycans (PGs) such as aggrecans are another key component of articular cartilage, and comprise a core protein linked with various GAGs such as HA and CS (3).

This diagram demonstrates how Liquid BioCell™ mirrors the joint composition.

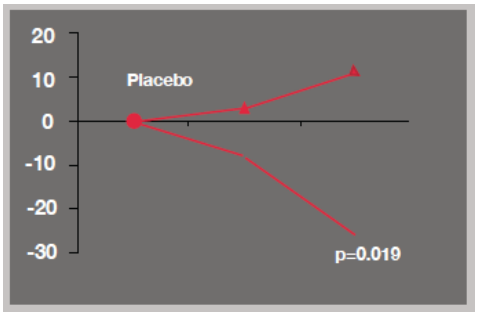
PGs are immobilized into the collagen fibrillar network to provide resistance to compression. The contents of these structural components and the integrity of the cartilage matrix decrease due to aging or degenerative conditions. Liquid BioCell™'s composition in terms of type II collagen and proteoglycans mirrors that of human articular cartilage and can support healthy joints by supplementing these molecules (Figure 1).

Figure 1. Comparison of composition of Liquid BioCell™ and human articular cartilage.



Multiple clinical studies demonstrate the safety and beneficial effects of collagen and GAGs toward various joint conditions (4; 5; 6). A double-blind, placebo-controlled trial of Liquid BioCell™ also revealed statistically significant efficiency in supporting joint health, leading to a decrease in difficulty carrying out physical activities (Figure 2) (1).

Figure 2. Reduced difficulty in physical activities 8-weeks after daily ingestion of Liquid BioCell™

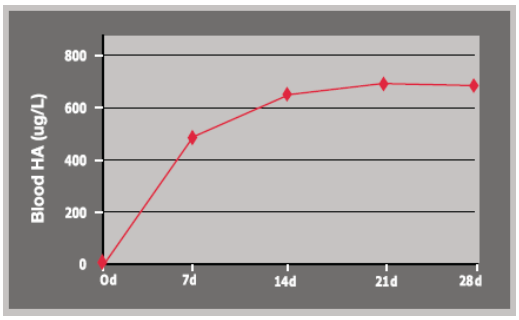


The p-value indicates the difference between Liquid BioCell™ and placebo

Recent studies suggest several possible mechanisms of action for the joint health benefits provided by Liquid BioCell™. First, it may support the cartilage matrix of collagen fibrillar network filled with proteoglycans by providing constituent molecules, and also supplement joint fluid by providing HA, which helps lubricate the joint (7). A review published in Current Medical Research and Opinion comprehensively analyzed collagen hydrolysate studies listed in the PubMed database (6). The authors stated, "According to published research, orally administered collagen hydrolysate has been shown to be absorbed intestinally and to accumulate in cartilage."

In order to ensure fast absorption and higher bioavailability, the three key constituents of Liquid BioCell® are proprietarily processed. Type II collagen is hydrolyzed to have an average molecular weight of 1.3 to 1.8 kDa, while chondroitin sulfate is depolymerized. In an HA bioavailability study, subjects taking Liquid BioCell™ (1500 mg/daily) for 28 days were shown to increase steady-state HA levels in their blood as much as 60-fold (Figure 3).

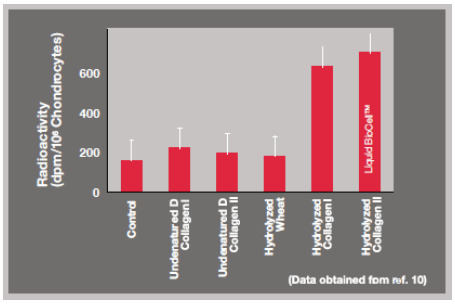
Figure 3. Increase in steady-state HA levels



60-fold increase in HA levels in the Human Blood by Liquid BioCell™

Second, a recent finding of the ability of hydrolyzed collagen, but not undenatured collagen, to stimulate novel biosynthesis of type II collagen from chondrocytes suggests that hydrolyzed collagen in Liquid BioCell™ may directly stimulate the only resident cells in the cartilage to produce its matrix components (Figure 4) (8). This would help maintain the tensile strength of cartilage, thereby supporting the shock absorption capability of the joint.

Figure 4. Hydrolyzed collagen in Liquid BioCell™ may directly stimulate the only resident cells in the cartilage to produce its matrix components

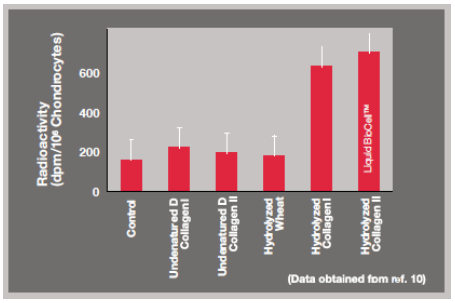


Novel biosynthesis of type II collagen by chondrocytes stimulated by Hydrolyzed Collagen

Joint support by Liquid BioCell™ is augmented by various fruit-derived phytonutrients with potent antioxidant activity. These phytochemicals contained in Liquid BioCell™ Life and Skin have been shown to have various health-promoting biological properties including antioxidant activity. Research suggests that antioxidants can support normal functions of chondrocytes, which appear to be affected by oxidative stress in the joints. First, nitrotyrosine, a marker of oxidative stress, is over-expressed in aging or degrading cartilage (9). This oxidative stress can lead to growth arrest and senescence of chondrocytes (10;11), a manifestation of the loss of their normal function, causing in turn deterioration in the structure and function of the cartilage (12). Second, lower antioxidative capacity was observed in degraded regions as compared with the intact regions from the same cartilage. Furthermore, treatment of chondrocytes with reactive oxygen species (ROS) induced genome instability and reduction of replicative capacity and GAG production, whereas treatment with antioxidants such as ascorbic acid (vitamin C) prevented the damaging effects (13).

These studies suggest that high contents of antioxidants such as vitamins, flavonoids, and polyphenols in Liquid BioCell™ Life may help neutralize these damaging effects of oxidative stress in aging joints. Taken together, a variety of naturally-occurring antioxidants abundantly contained in Liquid BioCell™ Life can support joint health by neutraliing oxidative stress, in synergy with Liquid BioCell® in supporting normal functions of chondrocytes and cartilage matrix they produce.

Figure 5. Dose-dependent inhibition of hyaluronidase



Dose-dependent inhibition of hyaluronidase by Liquid BioCell™

SKIN

The skin, the largest organ in the body, is the epidermis and the dermis. The dermis shares key structural components with the joint, including hyaluronic acid (HA), chondroitin sulfate (CS) and collagen (types I and III vs type II in the joint). Thus, Liquid BioCell™ Life helps support healthy and younger-looking skin through the provision of structurally-essential molecules to the dermis and through protection against oxidative damage closely associated with intrinsic and extrinsic skin aging.

HA, a key component of Liquid BioCell™, is found in virtually all tissues including the skin and bodily fluids (14). Approximately one-third of HA is turned over daily by coordinated action of HA synthesis and hyaluronidases (15). HA in the skin is a major component of the dermal extracellular matrix and responsible for hydration, nutrient exchange, protection against free radical damage, and regulation of cell differentiation and motility (16). As we grow older, the contents of dermal structural components decrease, resulting in disorganization or collapse of the extracellular network in the dermis (17). The molecular weight of HA also decreases, aggravating the loss of its water-retaining capability.

Studies suggest that Liquid BioCell™ can help maintain volume, density, and turgidity of the skin in several ways. First, Liquid BioCell™ harbors a unique biological activity which differentiates it from other dietary ingredients.

Second, a bioavailability study (Figure 3) suggests that a 60-fold increase in blood HA levels from daily intake of Liquid BioCell™ provides a pool available for the maintenance of adequate HA levels in the skin. Photoaging processes are similar to those of intrinsic, chronological aging. Dai et al (2007) showed that during photoaging, the total cell number and percentage of proliferating fibroblasts in the papillary dermis decreased in concomitance with the loss of HA from the dermis (18). It may alleviate the effects of photoaging by supplementing HA.

Third, the HA of Liquid BioCell™ may help skin in a more fundamental way. Greco et al reported that during wound healing, HA stimulated the proliferation of dermal fibroblasts responsible for biosynthesis of collagen, elastin and GAGs including HA (19; 20). Enhanced bioavailability of HA and inhibition of hyaluronidase would increase HA levels in the skin, which is postulated to stimulate dermal fibroblasts to synthesize skin collagens and other extracellular components.

Hyaluronic acid and collagen are naturally-occurring elements in human skin tissue and are vital for maintaining skin. Used safely and effectively worldwide for years, HA can be described as a "space filler" because it provides the moisture-filled cushioning in between our cells, while collagen provides the connective framework to uphold the skin tissue's integrity. HA is especially abundant in youthful skin, where it binds to water and provides volume — thereby plumping out the appearance of wrinkles and adding resiliency to skin.

Healthy aging requires an effective measure against oxidative stress in the skin because insufficient removal of reactive oxygen species (ROS) initiates or accelerates both natural and extrinsic skin aging processes by damaging DNA, proteins and cellular membrane (21;10). Our body has endogenous defense mechanisms, including enzymatic (superoxide dismutase and catalase, etc.) and nonenzymatic molecules (vitamins and glutathione) (22). As one ages, however, these defense mechanisms weaken while the load of oxidative stress increases, which will accelerate skin aging. Thus, additional and constant supply of antioxidants is essential.

As shown in Table 1, 13 fruits contained in Liquid BioCell™ Life provide a variety of antioxidants, such as vitamins and polyphenols that can help neutralize ROS arising from normal cellular metabolism and from exogenous factors, such as UV exposure, cigarette smoking, and alcohol consumption (25; 26).

◀ Actual results from subjects who took 2 oz., twice daily for 12 weeks in a clinical trial. Results may vary.

Table 1.

Fruits	Phytochemical Compounds
Blueberry	Anthocyanins, flavonols, proanthocyanidins, resveratrol
Red Grapes	Anthocyanins, resveratrol, flavonoids
Strawberry	Anthocyanins, ellagic acid
Apple	Quercetin, chlorogenic acid, epicatechin, procyanidin B2
Pomegranate	Punicalagins, catechins, anthocyanins, quercetin
Mangosteen	Mangostins
Açai Berry	Carotenoids, anthocyanins, flavonoids
Jujube	Triterpenes, cyclopeptide alkaloids, flavonoids
Lycium (Goji berry)	LBP (Lycium Barbarum polysaccharide)
Nopal	Prickly Pear Pectin
Maqui	Anthocyanins, flavonols
Noni	Lignans, flavonoids, catechins
Cranberry	Proanthocyanidins

◀ Phytonutrients in Liquid BioCell® Life possess a wide range of biological activities

Vitamin C is a powerful antioxidant that can only be obtained from food. Sunlight and environmental pollution can deplete vitamin C in the skin, causing lipid peroxidation of epidermal layers (24).

Vitamin C plays another important role in maintaining healthy skin, as a co-factor required for collagen biosynthesis from dermal fibroblasts (25). Liquid BioCell™ Life and Skin offers a continuous supply of vitamin C, together with structural molecules such as HA essential to skin health, which can help neutralize the detrimental effects of sun exposure and associated aging process.

The antioxidant capacity of Liquid BioCell™ Life is fortified further by carefully selected fruits from around the globe that harbour science-substantiated phytonutrients. For example, punicalagins and its hydrolysis product ellagic acid, the most abundant polyphenolic compound in pomegranate, have been shown to have potent antioxidant capacity (26). Studies also show that pomegranate extract restores enzymatic antioxidant defense mechanisms, including catalase, peroxidase and superoxide dismutase, which might explain pomegranate-induced amelioration of UVA-mediated damages and protection against the adverse effects of UVB radiation in human epidermal keratinocytes (27; 28). Similarly, anthocyanin-rich blueberry extract was shown to dampen UVB-mediated toxicity in human dermal fibroblasts through blocking NF-ÎB and p53 activation and through suppressing ROS-mediated expression of matrix--metalloproteinases (MMPs) that could degrade skin collagen (29). These results support that polyphenolic compound-rich pomegranate, blueberry and other fruits in Liquid BioCell™ Life and Skin may be highly protective against UV induced skin photoaging, as well as chronological aging.

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* Liquid BioCell™ is the exclusive highly bioavailable liquid form of BioCell Collagen® TF

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