



# LIQUID BIOCELL™ EQUINE

## A Scientific Perspective

### Liquid BioCell™ Equine A comprehensive joint health solution

Horses under strenuous training and fitness work, experience a great deal of stress on joints that may lead to deterioration of articular cartilage with high incidence of lesions (1). Aging-associated wear and tear of the joint and its surrounding connective tissues is an additional degenerative physiological burden, even in leisure horses. Liquid BioCell™ Equine's formulation is made with natural ingredients, that replenishes the vital components of articular cartilage in the synovial joint of a horse's body. It helps maintain the health and resiliency of joints and connective tissues, and ease discomfort associated with a horse's daily exercise or athletic lifestyle.

### The liquid power of Liquid BioCell™: A patented, clinically-researched, veterinarian-approved nutraceutical

The key ingredient of Liquid BioCell™ Equine synergistically supports the healthy joints of horses throughout life. It contains highly bioavailable Liquid BioCell™, a naturally-occurring matrix containing hydrolyzed collagen type II, low molecular weight (LMW) hyaluronic acid (HA), and chondroitin sulfate, which are essential for healthy joints, skin, and other connective tissues.

### Safety Studies

Several toxicology studies, including a 14-day acute study and a 90-day sub-chronic study, demonstrated that Liquid BioCell™ was well tolerated up to over 30 times the recommended dose of 30 mg/kg body weight per day (2). In three clinical trials involving humans with joint discomfort, it was also well tolerated during the study periods (3; 4; 5). Liquid BioCell™ has acquired a GRAS (generally recognized as safe) affirmation, and since 1997 billions of Liquid BioCell™ servings have been safely consumed worldwide.

### Joint Health

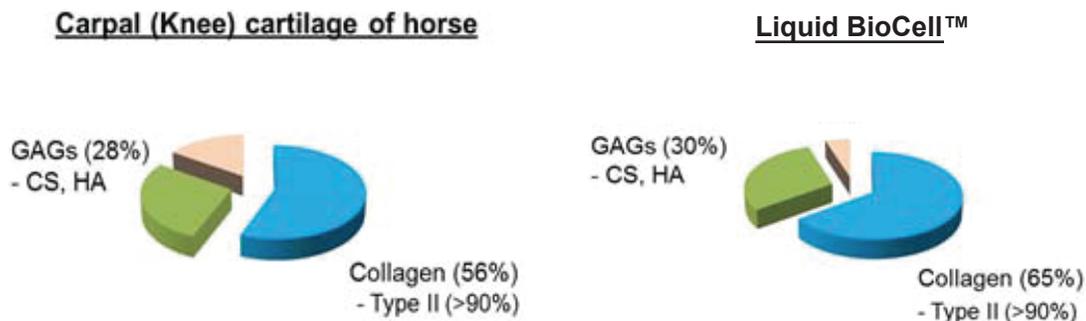
The efficiency of Liquid BioCell™ and its mechanism of action have been studied in a series of preclinical and multiple clinical trials. These studies suggest that Liquid BioCell™ improves joint health by providing multi-layered mechanisms, including potential cartilage regeneration as well as replenishment of both collagen type II and glycosaminoglycans (GAGs).

Liquid BioCell™'s innovative technology and exceptional scientific substantiation was recognized by the prestigious award, "Joint Health Ingredient of the Year (2011)" by Frost & Sullivan.

## Multiple Mechanisms of Action

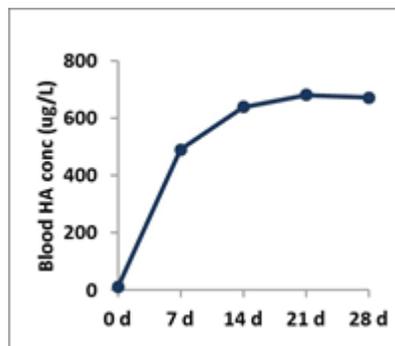
### 1. Comprehensive support of both collagen type II and GAGs

There are many different types of collagen found in the body and type II is the most abundant (>90% of collagen) in the cartilage of the synovial joint, the most common and movable joint (6). Collagen type II forms a fibrillar network to provide tensile strength to the cartilage. Proteoglycans (PGs) such as aggrecans are another key component, consisting of a core protein linked with various GAGs such as HA and CS (7). PGs are immobilized into the collagen fibrillar network to provide resistance to compressive or shearing forces. The content of these structural components and the integrity of the cartilage matrix deteriorates due to aging, repeated strenuous activity, or degenerative conditions. Derived from the articular cartilage of chicken sternum, molecular composition of collagen type II and GAGs of Liquid BioCell™ is similar to that of the articular cartilage in horses' synovial joints (8), enabling this unique ingredient to provide a comprehensive support for healthier joints with the essential molecules.



### 2. Patented Bio-Optimization™ process for efficient absorption

Liquid BioCell™ is produced by using a patented hydrolysis process which optimizes the molecule size of collagen, HA, and chondroitin sulfate for fast and effective absorption. For example, a bioavailability study in human subjects showed that consumption of Liquid BioCell™ led to an increase in blood HA levels by 60-fold (9). Another absorption study showed that more than 90% of hydrolyzed collagen was quickly absorbed via the small intestine into the bloodstream and interestingly these collagen-derived peptides are accumulated into connective tissues such as joint cartilage (10).



HA Bioavailability study subjects taking Liquid BioCell™ for 28 days increased blood HA levels by 60-fold.



### 3. Stimulation of the chondrocytes by hydrolyzed collagen type II

Liquid BioCell™ is not only bioavailable, but biologically active. The chondrocytes, residing exclusively in the cartilage, are responsible for the biosynthesis of collagen type II, HA, and chondroitin sulfate. Hydrolyzed collagen type II, a major constituent of Liquid BioCell™, was shown to stimulate the chondrocytes to synthesize collagen type II, which is specific to the cartilage (11). This biological activity of chondrocyte stimulation is highly intriguing because

it suggests that ingestion of Liquid BioCell<sup>™</sup> may help rebuild or regenerate worn-down cartilage of the horse via restoration of the normal function of chondrocytes. In contrast, undenatured or unhydrolyzed native forms of collagen failed to stimulate the chondrocyte, suggesting potential regeneration of the cartilage might be unique to hydrolyzed collagen.

#### 4. Multiple support for the amount and integrity of HA for better joint lubrication

HA, found in virtually all tissues, plays two important roles in the joint. First, it acts as a key structural molecule to make healthy cartilage. Second, HA serves as a major lubricating molecule of the synovial fluid. Liquid BioCell<sup>™</sup> is nature's premier source of this versatile molecule, as well as collagen type II. In addition to providing remarkably bioavailable Low-Molecular Weight (LMW) HA, Liquid BioCell<sup>™</sup> can support the amount and integrity of HA in a unique fashion, as hydrolyzed collagen-derived peptides were shown to stimulate the synovial cells to produce HA (12).

#### Multiple clinical studies

Four human clinical trials were performed, three on joint health and one on skin beauty from within. First, a randomized, double-blinded, and placebo-controlled trial enrolling 80 subjects investigated the safety and efficacy of Liquid BioCell<sup>™</sup> in managing various joint discomforts (5).

#### Implication of Liquid BioCell<sup>™</sup> for other connective tissues

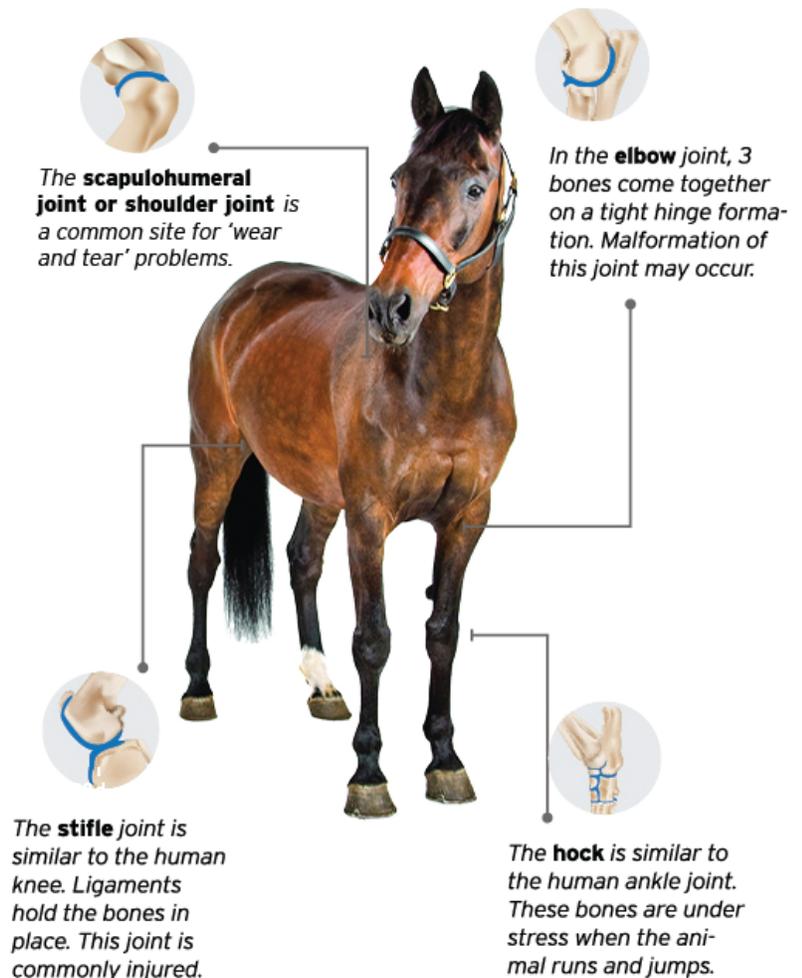
The connective tissue is found throughout the body, including not only cartilage, but ligaments, tendons, bone, blood, and adipose tissue. Among these diverse tissues, collagen type I and GAGs are the major structural molecules for ligaments and tendons, and synthesized by fibroblasts in ligaments and by tenocytes (elongated fibroblast-like cells) in tendons, respectively (13). The molecular nature of Liquid BioCell<sup>™</sup> and the capability of hydrolyzed collagen-derived peptides to stimulate fibroblasts in the connective tissue imply that ingestion of Liquid BioCell<sup>™</sup> may be beneficial to ligament and tendon health as well. Interestingly, a human skin study of Liquid BioCell<sup>™</sup> demonstrated that its daily intake increased the content of collagen type I, together with enhanced blood circulation (14).

#### The flavor

Liquid BioCell<sup>™</sup> Equine contains the proteins and fats horses love, and their bodies need. Natural rosemary flavor makes it a treat for horses.

#### Dosage Recommendation

Body Weight lbs	KG	Serving Size	Servings Per Container
<800	<365	20 cc	45
800-1099	635-500	30 cc	30
1100-1399	500-636	40 cc	22.5
1400-1699	636-773	50 cc	18
1700-2000+	773-909+	60 cc	15



## Conclusion

Joint health is important at all stages of a horse's life—from a pony to a senior horse. When a horse's joints aren't performing optimally, health and behavioral problems can result. Liquid BioCell™ Equine is a clinically substantiated and veterinarian-approved nutraceutical, designed to meet the demanding needs of athletic performance and complete joint support for horses of all breeds, providing the essential nutrients for a long, happy and active life.

## References

1. Exercise affects the mechanical properties and histological appearance of equine articular cartilage. Murray et al. 1999. J Orthop Res. 17(5):725-31.
2. Acute and subchronic oral toxicity studies in rats of a hydrolyzed chicken sternal cartilage preparation. Schauss et al. 2007, Food Chem Toxicol, pp. 45: 315-321.
3. Effects of collagen type II for subjective pain relief: a report of human clinical trial. Buckman et al. 1999.
4. A randomized double-blind clinical pilot trial evaluating the safety and efficacy of hydrolyzed collagen type II (BioCell Collagen II®) in adults with osteoarthritis. Sheldon et al. 2003, Miami Research Associates.
5. Effect of the novel low molecular weight hydrolyzed chicken sternal cartilage extract, BioCell Collagen, on improving osteoarthritis-related symptoms: a randomized, double-blind, placebo-controlled trial. Schauss et al., J Agric Food Chem. 2012 60(16):4096-101.
6. Articular cartilage: structure, injuries and review of management. Bhosale et al. 2008, Brit Med Bull, pp. 87: 77-95.
7. Aggrecan, aging, and assembly in articular cartilage. Dudhia. 2005, Cell Mol Life Sci, pp. 62: 2241-2256.
8. Biochemical analysis of normal articular cartilage in horses. Vachon et al. 1990. Am J Vet Res. 51(12):1905-11.
9. Clinical study shows hyaluronic acid in BioCell Collagen® found to have significant absorption and bioavailability: A report by Judy et al., SIBR. 2004.
10. Oral administration of 14C-labeled gelatin hydrolysate leads to an accumulation of radioactivity in cartilage of mice (C57/BL). Oesser et al. 1999. J Nutr 129:1891-1895.
11. Stimulation of type II collagen biosynthesis and secretion in bovine chondrocytes cultured with degraded collagen. Oesser et al. 2003, Cell Tissue Res, pp. 399: 393-399.
12. Effects of Pro-Hyp, a collagen hydrolysate-derived peptide, on hyaluronic acid synthesis using in-vitro cultured synovium cells and oral ingestion of collagen hydrolysates in a guinea pig model. Ohara et al. 2010. Biosci Biotechnol Biochem. 74(10): 100193-14.
13. Collagen structure of tendon relates to function. Franchi et al. 2007. Scientific World Journal. 7:404-420.
14. Ingestion of BioCell Collagen®, a novel hydrolyzed chicken sternal cartilage extract; enhanced blood microcirculation and reduced facial aging signs. Schwartz et al. 2012. Clin Interv Aging. 7:267-73.

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

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