IncaCartilago™

The most potent chondroitin sulfate on the market

OPTIPURE® BRAND
Kenko International, Inc.

For years, chondroitin sulfate has been a top seller for joint support, frequently paired with glucosamine. Millions of Americans have relied on the cumulative support provided by chondroitin sulfate, and now IncaCartilago is a superior form of effective joint support – and bone support.

IncaCartilago™ chondroitin sulfate is the most potent on the market, with 45% guaranteed minimum of Total Chondroitin Sulfates, 10% minimum of Chondroitin Sulfate E, and 30% minimum Chondroitin Sulfates A & C.

TYPE	ORIGIN	STRUCTURE	SULFATION
A	Pig, Cow, Rooster	Carbon 4 of Glucuronic Acid - Acetylgalactosamine	R2
C	Shark	Carbon 6 of Glucuronic Acid - Acetylgalactosamine	R1
D	Eel	Carbon 2 of Glucuronic Acid and Carbon 4 of Acetylgalactosamine	toR1, R3
E	Squid	Carbon 4 and 6 of Glucuronic Acid - Acetylgalactosamine	R1, R2

IncaCartilago™: SuperStructure

Commercially sold chondroitins are typically derived from bovine and porcine sources and to a lesser but still significant percent, shark sources. Researchers in Japan have found a new source -- Humboldt Squid -- whose molecular profile has a superlative difference.

During our extensive research and development of Humboldt squid-derived chondroitin, our team found that to date, there had been no thorough investigation about the differentiations between chondroitins A, C and E, with the sole exception of where sulfation occurs. Humboldt squid-derived chondroitin sulfate (CS-E) is sulfated at carbons 4 and 6 of glucuronic acid—acetylgalactosamine; while that sourced from bovine, porcine (CS-A) or shark (CS-C) only exhibit onesite of sulfation.

Kenko's innovative use of two-dimensional electrophoresis has been able to consistently both identify and quantify chondroitin types in IncaCartilagoTM, which is truly groundbreaking.

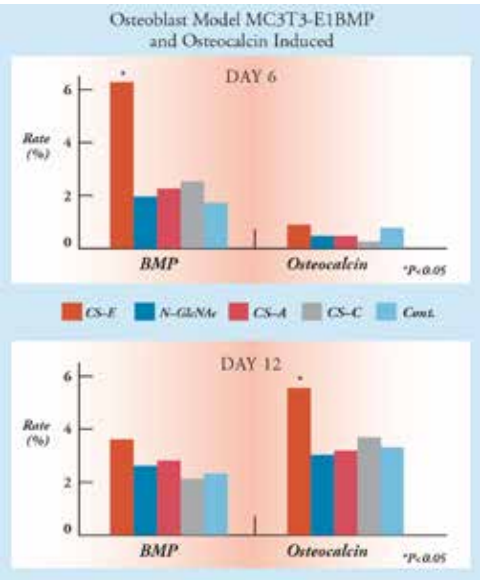
IncaCartilago™ is unique, as shown in assays, to be the only source known to have a full profile of active sulfates. IncaCartilago chondroitin sulfate is the most potent on the market, with 45% guaranteed minimum of Total Chondroitin Sulfates, 10% minimum of Chondroitin Sulfate E, and 30% minimum Chondroitin Sulfates A & C. Such high percentages provide the consumer with the ultimate protective benefit of each type of chondroitin sulfate, effectively supporting both bone and joint structures and functions—in one easy dosage form.

CSE Supports Bone Health

Unlike other chondroitin sulfate sources, the unique composition of IncaCartilago encourages osteoblast and osteocalcin formation, replication and expression.

Following conclusions of a preliminary study indicating that CS-E binds to MC3T3-E1 cells (i.e., specific animal-derived bone cells), a more in-depth investigation using MC3T3-E1 osteoblast cells compared various chondroitin sources. The study found that test sources CS-C (from shark), CS-D (from eel), heparin sulfate and heparin "had no positive or inhibitory effect on the growth of MC3T3-E1 cells;" however, CS-E (from Humboldt squid) "significantly enhanced the growth of the cells." CS-A, CS-C and CS-D produced no mineralization effect in cells seeded at low density. CS-E, however, actually enhanced the mineralization of the osteoblast cells.(1)

Favorable for joint health, testing demonstrated that CS-E enhanced collagen deposition by MC3T3-E1 cells, while CS-Aand CS-C did not show any similar net positive effect.(1)

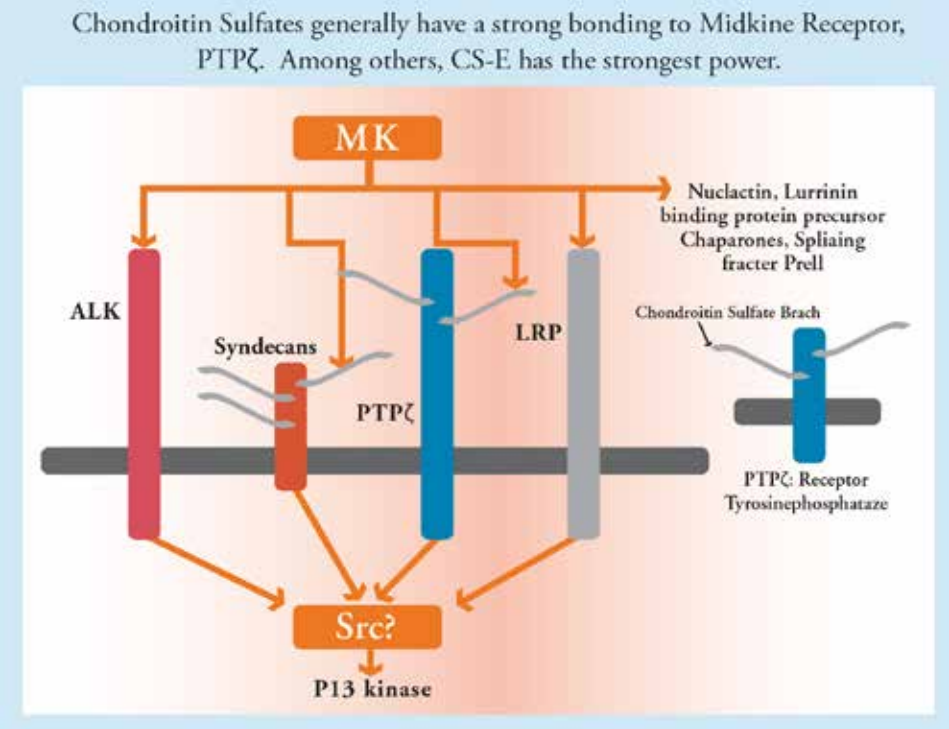


This study utilized fluorescence correlation spectroscopy, which illuminated for the first time that oversulfated CS, such as CS-E or CPS, binds to a specific bone morphogenetic protein called MP-4. These sulfated glycosaminoglycans (GAGs) bind directly to the BMP-4 molecule resulting in the enhancement of mineralization.

CS-E and CPS had strong affinity for BMP-4, whereas CS-D and monosulfated CS (CS-B or CS-C) did not.(1) The study authors assert that their findings support the concept that CS-E enhances mineralization induced by up-regulating BMP-4 activity. CS-E affects the phenotype of osteoblasts at the early stage of differentiation when osteoblasts secrete BMP-4.(1) More recent research ("Osteoblast Model MC3T3-E1 BMP and Osteocalcin-Induced") presented at the 64th meeting of Japanese Society for Nutrition and Food Science (2010) validates this activity. After six days in the assay, CS-E outperformed other chondroitin sources in accelerating bone morphogenetic protein activity nearly three times as much as its closest competitor, CS-C. After day 12, CS-E still outperformed other chondroitins in addition to showing an exceptional rate of osteocalcin formation and expressionby nearly 33% over its closest competitor, CS-C.

CS-E Supports Against Joint Pain

CS-E has been studied to show solid performance in supporting against joint pain, making it highly attractive as a dietary supplement for those who are leery of the side effects of NSAIDs. IncaCartilago™ is the first chondroitin shown in a particular study to affect the binding and action of midkines, the proliferation of which are responsible for pain sensation. Studies have shown distinct evidence that CS-E selectively binds to midkines (MK), which are specific proteins that enhance cell proliferation, cell migration, angiogenesis and fibronlysis, as well as are activated in inflamed areas to instigate the migration of inflamed cells. MK binds heparin Types of Chondroitin Sulfates to promote growth, survival and migration of various target cells and is involved in the etiology of inflammatory disease. Although typical chondroitin sulfates do generally bond well to a specific MK receptor (PTPz), CS-E was demonstrated in a study to exhibit the most potent and swift ability to do so, thus inhibiting the migration of inflamed cells.[2]



In this study, CS-E administered intraperitoneally significantly suppressed antibody-induced arthritis. MK are known to promote antibody-induced arthritis by spurring the migration of inflammatory leukocytes and osteoclast differentiation; CS-E had been previously shown to inhibit the migration of MK-dependent macrophages. The study authors concluded: "We found that intraperitoneally administered chondroitin sulfate E, but not chondroitin 4-sulfate [CS-A], inhibits the development of antibodyinduced arthritis."[2]

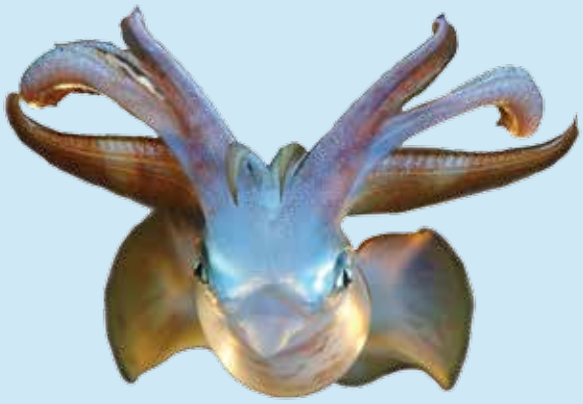
References
1. T. Mizayaki, et al., *"Oversulfated Chondroitin Sulfate-E Binds to BMP-4 and Enhances Osteoblast Differentiation,"* J. Cell. Physiol. 217 (3), 769–777 (2008).

2. H. Yamamoto, et al., *"Midkine as a Molecular Target: Comparison of Effects of Chondroitin Sulfate E and siRNA,"* Biochem. Biophys. Res. Commun. 351 (4), 915–919 (2006).

IncaCartilago™ is unique, as shown in assays, to be the only source known to have a full profile of active sulfates.

IncaCartilago™ chondroitin sulfate is the most potent on the market, with 60% guaranteed minimum of Total Chondroitin Sulfates, 40% minimum of Chondroitin Sulfate E, and 20% minimum Chondroitin Sulfates A & C.

Such high percentages provide the consumer with the ultimate protective benefit of each type of chondroitin sulfate, effectively supporting both bone and joint structures and functions—in one easy dosage form.



Humboldt squid

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