Dynamic Chiropractic

VITAMINS / SUPPLEMENTS

Glucosamine, Part I: Basic Science

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This is first part of a three-part series on glucosamine. Although we have covered glucosamine in this column previously, there continues to be a great deal of interest from both doctors and patients. This month, we will discuss in question and answer form the basic science of glucosamine.

Q: What exactly is glucosamine?

A: Glucosamine can be defined two ways depending on your point of view. Oral preparations of glucosamine in the health-food store or doctor's office are classified as a chondroprotective nutraceutical. In the body, glucosamine is an amino monosaccharide produced by chondrocyte cells and used to make glycosaminoglycans and proteoglycans. It is water soluble and well-absorbed in the small intestine. Glucosamine has an affinity for articular cartilage, which is well adapted for its active uptake. Many scientists feel that glucosamine is the most important and rate-limiting substance for the synthesis of healthy cartilage.

Q: What are glycosaminoglycans?

A: Glycosaminoglycans (GAGs), formerly known as mucopolysaccharides, are long chains of modified disaccharides. They are the main component of proteoglycans which, along with chondrocyte cells and collagen, make up cartilage. There are six types of GAGS, four of which are involved in connective tissues. These are hyaluronan; chondroitin sulfate; keratan sulfate; and, to a lesser extent, dermatan sulfate.

Q: What is glucosamine's role in GAGs?

A: Glucosamine makes up 50% of the hyaluronan and keratan sulfate GAG molecules. It is the immediate precursor and is converted in one easy step to galactosamine, which makes up 50% of the chondroitin sulfate and dermatan sulfate GAG molecules. Without adequate glucosamine, GAG synthesis would essentially shut down. In turn, this would cause proteoglycan synthesis to also cease.

Q: What are proteoglycans?

A: Proteoglycans (PGs), along with collagen and chondrocyte cells, make up cartilage. Long molecules of the GAG hyaluronan form the back bone of PGs. From this back bone branch out proteins. From these proteins branch out the three sulfur-containing GAGs, chondroitin sulfate, keratan sulfate, and dermatan sulfate. The sulfur gives them a negative charge which attracts water. This causes PGs to have a gel-like consistency and the ability to fill space in three dimensions. Intertwined collagen fibers give them body. If PGs are not synthesized in adequate amounts, then normal cartilage function is impaired and breakdown is accelerated.

Q: What are chondrocytes?

A: As previously mentioned, chondrocytes (along with PGs and GAGs) make up cartilage. They are

cells that are involved in both anabolism and catabolism of PGs and collagen. In other words, they are responsible for the synthesis, maintenance, and regeneration of cartilage.

Chondrocytes make GAGs two ways. The first way is with glucose and amino acids. A glucose molecule will undergo phosphorylation and epimerization reactions. This modified sugar then receives an amino group donated from glutamine. A synthetase reaction forms the molecule glucosamine 6 phosphate, which then undergoes additional reactions in GAG synthesis.

The second way chondrocytes produce GAGs is by using exogenous or preformed glucosamine from supplemental or dietary sources. When the preformed glucosamine enters the chondrocyte, a phosphorylation reaction occurs forming glucosamine 6 phosphate.

Q: How does glucosamine work?

A: Glucosamine has numerous effects on the health of cartilage. There must be adequate glucosamine, whether from supplements, internal production, or dietary sources (gristle) in order for cartilage to be healthy. Glucosamine stimulates GAG and PG production.[1]

Glucosamine accomplishes this in two ways. The first is by acting as a raw material for the chondrocytes. When glucosamine is available for chondrocytes, they are able to produce connective tissue faster because they can skip three chemical reactions, needing only a phosphorylation reaction to make glucosamine 6 phosphate.

The second way glucosamine appears to work is as a stimulating agent. As chondrocytes increase GAG production from supplemental glucosamine, fibrotic articular tissues begin to heal. This improves the diffusion of glucose and amino acids through joint capsules and synovial membranes, providing the once-starved chondrocytes with the raw materials necessary (sugar and amino acids) to stimulate the synthesis of GAGs and PGs.

Glucosamine may have an effect on the biochemistry of nonsteroidal anti-inflammatory drugs. Many people with arthritis take nonsteroidal anti-inflammatories to reduce inflammation and pain, as well as prevent excessive adhesions. However, NSAIDs accomplish these functions at a high cost. In addition to being very hard on the stomach, intestines, and, in some cases, liver and kidneys, NSAIDs also inhibit the production of GAGs, which means that even though a patient may have a reduction in pain, their body's ability to heal itself is impaired. This explains why many patients with arthritis who take anti-inflammatories have symptomatic relief with they use them, but never seem to get better. In animal cartilage culture studies, glucosamine was able to partially reverse the effects some nonsteroidals have on inhibiting GAG and collagen synthesis.[1]

Glucosamine also appears to inhibit lysosomal enzymes used for cartilage catabolism, including collagenase and phospholipase A2.[2] These effects give glucosamine anti-inflammatory properties with a nontraditional action; that is, prostaglandin biochemistry is completely undisturbed. Finally, in animal studies, glucosamine blocks the generation of intra-articular superoxide radicles.[3]

In conclusion, even though glucosamine is not an analgesic, antioxidant, or anti-inflammatory in the classic sense, it possesses these properties due to its ability to normalize cartilage biochemistry which in turn stimulates the healing process. The net result -- more healthy cartilage, and healthy cartilage does not cause pain.

Next month, we will continue our discussion of glucosamine, focusing on the various forms available to the clinician.

References

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3. Setnikar, et al. Antereactive properties of glucosamine sulfate. Arzneimittel Forschung, 41:157-161, 1991.

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