

# Mode of action of nutritional therapies for managing degenerative joint disease

**NORMAL articular cartilage is composed of chondrocytes surrounded by an extracellular matrix, comprised of water, collagen and proteoglycans.**

Collagen functions to provide tensile strength and structure to the extracellular matrix. Proteoglycans consist of a protein core, with side chains of heteropolysaccharides called glycosaminoglycans (GAGs) (i.e. chondroitin sulphate and keratin sulphate).

Proteoglycans form large aggregates by associating with hyaluronic acid and provide resilience and flexibility to the connective tissue matrix (see diagram).

Cartilage is able to repair itself by increasing the synthesis of the extracellular matrix (collagen and proteoglycans). This constant and on-going synthesising process, especially when osteoarthritis is present, creates an increased demand for the building blocks of collagen and the proteoglycans.

Because of the undesirable side-effects that can occur with long-term use of corticosteroids and some non-steroidal anti-inflammatory drugs (NSAIDs), and because of the detrimental effects these drugs have on chondrocyte and matrix homeostasis, attention has recently focused on alternative modes of therapy for the management of osteoarthritis.

A new class of nutritionally based products, that are based on heteropolysaccharides and that act differently from the previously described anti-inflammatory agents have become

synovium and/or subchondral blood vessels.

To date, no single compound can exert all these chondrometabolic effects. The two most commonly used chondroprotective agents are glucosamine salts and chondroitin sulphate. They

Along with keratin sulphate, they are the major glycosaminoglycans found in cartilage.

*In vitro*, chondroitin sulphate is an effective and direct inhibitor of degradative enzymes. As a result of a shift from an anabolic to a catabolic state, chondrocytes

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act synergistically to maintain healthy cartilage through their chondrometabolic effects.

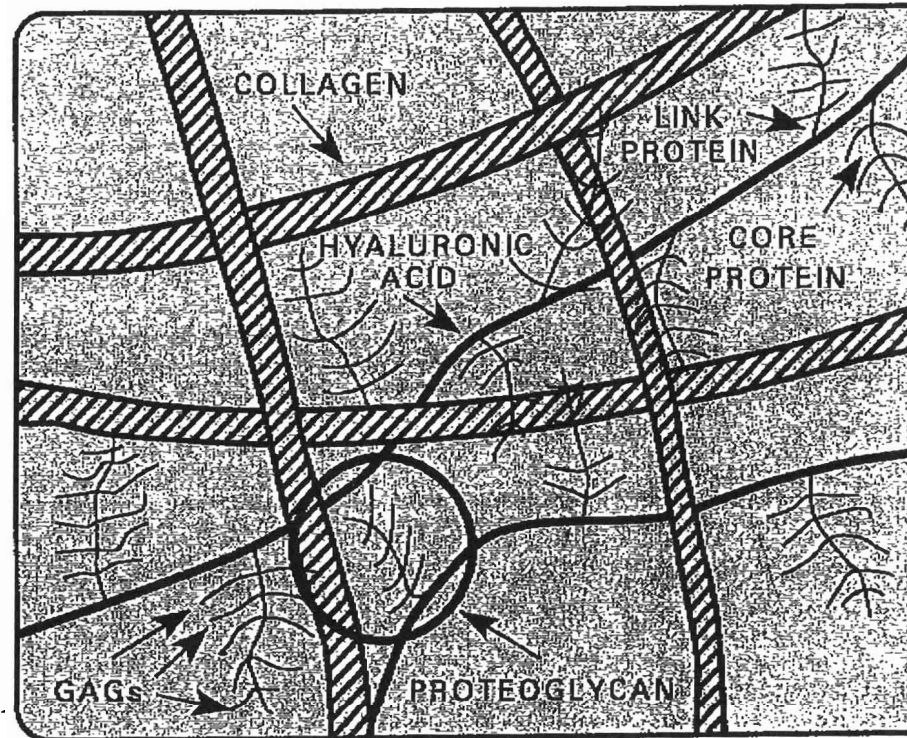
Glucosamine is the major building block of glycosaminoglycans and is a key regulator in glycosaminoglycan biosynthesis. Glucosamine is readily absorbed orally and shows special tropism for the cartilaginous tissue, where it is readily incorporated into the proteoglycan molecules of the cartilage matrix.

Glucosamine has been shown to stimulate glycosaminoglycan and proteoglycan, in chondrocytes and fibroblasts. Furthermore, it was shown to provide natural protection against the cartilage-damaging effects of NSAIDs. Chondrocytes obtain

are the major source of degradative enzymes within the osteoarthritic joint; chondroitin sulphate is beneficial in directly inhibiting this enzyme destruction of proteoglycan and hyaluronic acid.

In long-term clinical trials of injectable chondroitin sulphate, the course of osteoarthritis was greatly slowed, joint function improved, joint pain and analgesic usage reduced, and clinical signs of increased mobility were apparent.

Chondroitin sulphate is readily bioavailable as intact chains, monomer sub-units, and the spectrum of intermediate chain lengths. Inhibition of enzymes that degrade cartilage is accom-



recently reported chondro-stabilising effect on articular cartilage.

Both glucosamine salts and chondroitin sulphate, therefore, have proven bioavailability and clinical benefits. Glucosamine salts stimulate glycosaminoglycan synthesis whilst chondroitin sulphate inhibits degradative enzymes. The combination of these two compounds provides a unique synergistic effect due to their overlapping and unique functions.

Other co-factors can play a significant role in chondro-protection. For example, manganese supplementation was suggested to be helpful in chronic degenerative joint diseases. This

Cosequin (imported by Xeipon Ltd, PO Box 46, Retford, Notts DN22 7WD; telephone 0973 655007), which is a patented combination of glucosamine, purified chondroitin sulphate and manganese ascorbate, the natural biologic approach to the protection of joint tissues

and management of arthritis looks very promising. An extensive list of referees for this article is available on request; it can be obtained by sending a stamped address envelope to: Caroline Prymak, 129 Selby Road, West Bridgford, Nottingham NG2 7BB.

## WHAT'S AHEAD THIS YEAR

6th-9th March:  
Crufts  
NEC, Birmingham

8th-12th March:  
British Veterinary Association

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