Quick Course

Glucosamine and Chondroitin Sulfate with ASU — Joint Health Beyond NSAIDs

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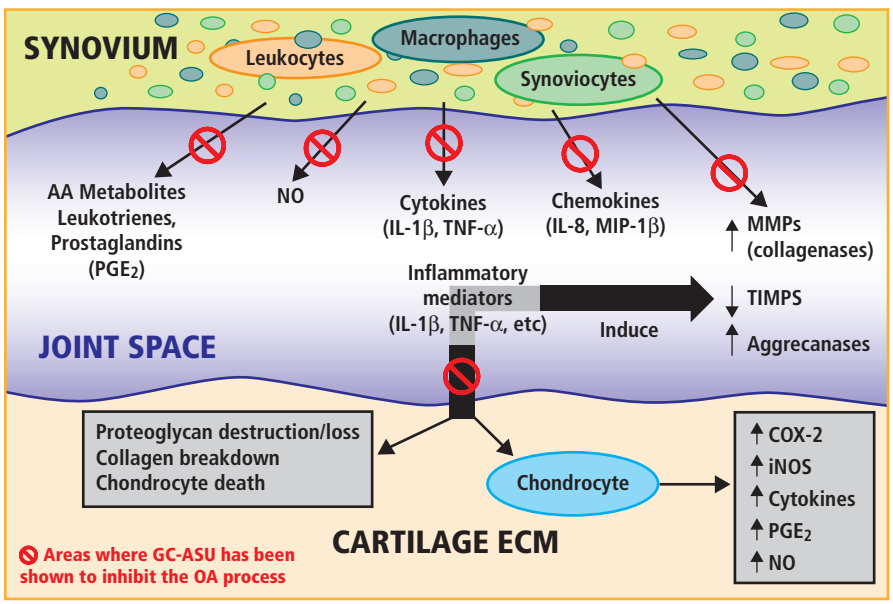
Although NSAIDs are the cornerstone of osteoarthritis (OA) treatment in dogs, pet owners and veterinarians have continued to seek management options with fewer side effects that can improve long-term quality of life for patients with OA. A more progressive approach to OA management may include NSAIDs, weight loss, controlled exercise and physical therapy, environmental modifications, and the use of disease-modifying chondroprotective agents such as oral glucosamine hydrochloride–chondroitin sulfate (GC) products. Incorporating GC into a multimodal management plan can improve long-term joint function for patients with OA.

A fairly recent addition to this family of agents is a GC product containing avocado/soybean unsaponifiables (ASU) and green tea polyphenols (Dasuquin®, Nutramax Laboratories, Inc., Edgewood, MD). This product is produced to the industry's highest quality standards. When administered to dogs and cats with OA, Dasuquin can serve as an important long-term option to help manage the chronic debilitating effects of this condition.



Some of the agents involved in the pathogenesis of OA are illustrated here. Early OA changes may begin with synovitis, or inflammation of the joint capsule. Synovitis causes an influx of leukocytes into the joint space and release of inflammatory mediators (e.g., prostaglandins and cytokines) into the joint cavity. These inflammatory mediators adversely affect chondrocytes and the extracellular matrix of the cartilage. In vitro research using chondrocytes and synovial cells has shown that ASU, glucosamine, and chondroitin sulfate inhibit the pathways indicated. Administration of these agents may therefore help support cartilage health. (MIP-1β = macrophage inhibitory protein-1β; MMPs = matrix metalloproteinases; NO = nitric oxide; PGE_2 = prostaglandin E_2; TIMPs = tissue inhibitors of matrix metalloproteinase.)

How Does GC Work?

Glucosamine is a glycosaminoglycan precursor used by chondrocytes, and chondroitin sulfate is the predominant glycosaminoglycan in the extracellular cartilage matrix. Administered together, these two agents act synergistically to modulate certain aspects of joint maintenance. They are also well absorbed after oral administration and have very limited side effects, even with long-term use.

Studies have demonstrated some of the benefits of GC use in dogs. Administration of GC to dogs before experimental induction of synovitis resulted in decreased synovitis, associated bone remodeling, and lameness.[1] Also, dogs with hip and elbow OA had improved pain scores and weight bearing after receiving GC,[2] and administration of GC to dogs with experimental cruciate ligament injury was associated with potentially beneficial alterations in cartilage matrix metabolism.[3]

What about ASU?

Avocado and soybean oils contain biologically active lipids known as ASU. These agents are thought to have antiinflammatory properties.[4] An in vitro study using bovine chondrocytes showed that ASU decreased

expression of the potent inflammatory mediators tumor necrosis factor–α (TNF-α), interleukin-1β (IL-1β), cyclooxygenase-2 (COX-2), and inducible nitric oxide synthase (iNOS) compared with chondrocytes incubated in control medium.[5] These inflammatory mediators have a role in cartilage degradation, proteoglycan destruction, and elsewhere in the pathogenesis of OA. ASU also stimulate synthesis of matrix components by increasing production of transforming growth factor–β (TGF-β), which is part of the extracellular matrix and is expressed by osteoblasts and chondrocytes. In a 2007 study, dogs given ASU for 3 months had higher levels of TGF-β in their joint fluid compared with control dogs.[6]

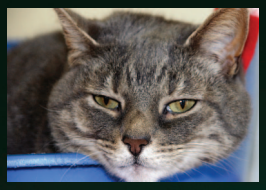
ASU have been shown to protect cartilage and/or improve joint function in several species,[7–10] and when combined with a GC product, ASU complement the actions of the other agents without increasing side effects.[10,11] In vitro studies also show a synergy between glucosamine and ASU, such that the combination of GC-ASU produces more favorable results than GC alone.[10]

Long-Term OA Management with GC-ASU

Because GC-ASU has very few side effects or contraindications and is convenient to administer, long-term administration is generally well accepted by pets and owners.

For severe OA pain, NSAIDs and/or alternative analgesic therapies are indicated to provide rapid pain relief and encourage mobility. But for mild to moderate pain or for longer-term control of OA pain and inflammation, appropriate nutraceuticals can complement other modalites, including intermittent NSAID therapy.[12] In many cases, GC-ASU can be instituted alone or in conjunction with other therapies throughout the course of disease management to support long-term improvements in joint health and quality of life.

GC-ASU IN FELINE OSTEOARTHRITIS



Although a recent study evaluated some methods for measuring pain in cats,[13] this process is more difficult than in dogs, and there are currently no validated methods for measuring OA pain in cats. This creates a challenge for veterinarians trying to assess level of discomfort and response to therapeutic measures. Additionally, NSAIDs aren't currently approved for treatment of OA pain in cats, so veterinarians trying to improve quality of life for these patients are somewhat limited by a lack of approved therapeutic options.

A study being performed by Dr. Mila Freire Gonzalez, a research fellow at North Carolina State University College of Veterinary Medicine, is indicating that cartilage degeneration is very common in cats. In addition, her team has found that as many as 60% of all cats show radiographic evidence of degenerative joint disease (DJD) somewhere in the skeleton. A significant number of those cats also have impaired mobility.

Fortunately, both GC and GC-ASU products are available for use in cats. Dr. Duncan Lascelles, director of the Comparative Pain Research Laboratory and the Integrated Pain Management Service at North Carolina State University College of Veterinary Medicine, employs various modalities for managing pain in cats, including physical therapy and nutraceuticals. He comments, "I've used Dasuquin extensively in cats, and it makes a marked difference. Over the past year, we have evaluated approximately 150 cats in detail for the presence of painful DJD. Many of those found to have painful DJD have received Dasuquin; I've seen these cats become more active with improved quality of life after taking Dasuquin." Although data on the use of GC-ASU products in cats are limited, an in vitro study showed inhibition of PGE_2 (an inflammatory mediator) in a model using feline chondrocytes.[14] These findings might infer an antiinflammatory effect in feline joint disorders, but Dr. Lascelles cautions that it would be inappropriate to assume a direct connection between in vitro effects on cartilage and overall clinical improvement. "We know these cats improve clinically, but we can't yet say why without more data," Lascelles says.

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