Recommending Nutraceuticals for Joint Health

You have asked...

How do I know which supplements to recommend for my patients to help ensure joint health?

The expert says...

Finding the appropriate nutraceutical is not always easy. Veterinarians have an ethical obligation to know which nutraceuticals are available and to recommend the ones shown to be most effective.

STUDIES IN HUMANS
The most comprehensive study demonstrating the beneficial effects of glucosamine and chondroitin sulfate in humans was the Glucosamine/Chondroitin Arthritis Intervention Trial (GAIT).\(^1\) This study investigated celecoxib as a positive control against glucosamine/chondroitin sulfate and a negative placebo.

For a subset of participants with moderate to severe pain, a combination of glucosamine and chondroitin sulfate provided significant pain relief compared with the placebo. About 79% of people with moderate to severe knee pain had a 20% or greater reduction in pain versus about 54% in the placebo group. Participants in the mild pain subset group did not receive significant pain relief from glucosamine and chondroitin sulfate (administered together or individually).

This information is a good starting point for veterinarians. However, since canine cartilage differs from human cartilage, professionals need to seek out data relevant to small animals species when available.

CONTINUES
chondroitin sulfate and glucosamine hydrochloride were administered to dogs iv or orally. Glucosamine hydrochloride was absorbed quickly (about 1.5 H) and did not accumulate in the blood with continued administration. Low–molecular-weight chondroitin sulfate was also absorbed quickly (about 2 H). However, unlike glucosamine hydrochloride, low–molecular-weight chondroitin sulfate showed significant accumulation in serum with steady state administration. This phenomenon explains the carry-over effect of low–molecular-weight chondroitin sulfate following discontinuation of oral administration. This also supports administration of lower levels of glucosamine and low–molecular-weight chondroitin sulfate for long-term maintenance.

Manganese
While glucosamine and low–molecular-weight chondroitin sulfate can beneficially affect cartilage, the addition of manganese acts as a catalyst to increase biosynthetic activity. The benefit of manganese has been shown both \textit{in vitro} and \textit{in vivo}.\textsuperscript{4}

Avocado Soybean Unsaponifiables
Avocado soybean unsaponifiables (ASU) are a potent compound shown to affect joint function and health. ASU decreases the expression of cyclooxygenase-2 and production of prostaglandin E\textsubscript{2}, which are both mediators of discomfort.\textsuperscript{5,6} ASU also inhibits expression of the destructive cytokines, tumor necrosis factor-\textalpha and interleukin-1\beta.\textsuperscript{7} The beneficial effect of ASU, glucosamine, and low–molecular-weight chondroitin sulfate has been demonstrated across species lines, including canine, feline, equine, and human cells.

Eicosapentanoic Acid & Docosahexanoic Acid
The omega-3 fatty acids, eicosapentanoic acid (EPA) and docosahexanoic acid (DHA), which are found in fish oil, reduce destructive enzymes in the joint and other inflammatory mediators.

**CONCLUSIVE CLINICAL DATA**
Glucosamine, Chondroitin Sulfate, & Manganese
As mentioned previously, the combination of glucosamine, low–molecular-weight chondroitin sulfate, and manganese has been demonstrated \textit{in vitro} and \textit{in vivo} to have beneficial effects.\textsuperscript{4}

\textbf{ARE PRODUCT CONTENTS CERTIFIABLE & EFFECTIVE?}
In 2000, a study investigated products containing glucosamine hydrochloride and chondroitin sulfate.\textsuperscript{2} A permeability analysis simulated absorption of the chondroitin component; in 84\% of the products tested, listed ingredients ranged from 0\% to 115\% of the label claim. In addition, price had no bearing on content: the lowest- and highest-priced products correlated the least with label contents (\textit{Figure}). Finally, it was demonstrated (using an absorption model) that some grades of chondroitin sulfate are not absorbed; low–molecular-weight chondroitin sulfate had the best absorption profile.

**WHAT INGREDIENTS ARE MOST EFFECTIVE?**
Many products have multiple and varied ingredients, but it is not always clear what role they play in helping the patient. The following components are generally considered to be effective in some way.

**Chondroitin Sulfate & Glucosamine**
In a 2002 study, low–molecular-weight chondroitin sulfate and glucosamine hydrochloride were administered to dogs iv or orally. Glucosamine hydrochloride was absorbed quickly (about 1.5 H) and did not accumulate in the blood with continued administration. Low–molecular-weight chondroitin sulfate was also absorbed quickly (about 2 H). However, unlike glucosamine hydrochloride, low–molecular-weight chondroitin sulfate showed significant accumulation in serum with steady state administration. This phenomenon explains the carry-over effect of low–molecular-weight chondroitin sulfate following discontinuation of oral administration. This also supports administration of lower levels of glucosamine and low–molecular-weight chondroitin sulfate for long-term maintenance.

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In Combination With Carprofen. In a small clinical study, 4 dogs diagnosed with villanodular synovitis by histopathology were treated medically with either carprofen or a combination of carprofen and glucosamine/low–molecular-weight chondroitin sulfate/manganese. In 3 of the dogs receiving carprofen/glucosamine/low–molecular-weight chondroitin sulfate/manganese, the synovitis improved significantly, and they returned to normal workload.

As an Adjunct to NSAIDs. In vitro, glucosamine/low–molecular-weight chondroitin sulfate/manganese was shown to be effective in countering etodolac's potentially adverse effects on cartilage and enhancing carprofen's mild cartilage stimulatory effect. Data suggest that there is firm rationale for incorporating glucosamine/low–molecular-weight chondroitin sulfate/manganese as an adjunct to some nonsteroidal antiinflammatory drugs (NSAIDs).

For Joint Injury Recovery. Data has also shown that dogs that received glucosamine/low–molecular-weight chondroitin sulfate/S-adenosylmethionine (SAMe) prior to an acute joint injury recovered more quickly. The treated dogs had significantly less synovitis and lameness.

Omega-3 Fatty Acids

In Diets for Dogs With Osteoarthritis. Ninety days after eating a diet supplemented with a high dose of fish–oil–based omega-3 fatty acids, dogs exhibited multiple beneficial effects, including greater peak vertical force on a limb with osteoarthritis than dogs that ate the control diet. In another study, owners reported clinical improvement at 6, 12, and 24 weeks after starting a diet supplemented with fish–oil–based omega-3 fatty acids.

In Combination With Diet & NSAIDs. Dogs receiving an NSAID concurrently with a diet supplemented with fish–oil–based omega-3 fatty acids averaged a 25% decrease in NSAID requirements over a 12-week period.

PART OF THE MULTIMODAL APPROACH

There are multiple approaches to helping dogs with osteoarthritis. From a pain perspective, a multimodal approach can include oral and injectable medications, weight loss, nutrition, a number of physical modalities, and nutraceuticals in the form of glucosamine, low–molecular-weight chondroitin sulfate, manganese, ASU, and omega-3 fatty acids. For these reasons, veterinarians who recommend nondrug products to owners should include those with these specific combinations in order to get the best possible effects.