

# Oral Joint Supplements

## in Agility Dogs

By David Dycus, DVM, MS, Diplomate, American College of Veterinary Surgeons and Debra Canapp, DVM, CCRT, CVA, Diplomate, American College of Veterinary Sports Medicine and Rehabilitation

Osteoarthritis (OA) is a debilitating progressive disease that causes cartilage destruction and ultimately failure of a joint, leading to pain and disuse. OA is the most common form of arthritis with an estimated 20% of middle-aged dogs and up to 90% of older aged dogs affected<sup>1</sup>. Preventing, along with minimizing and slowing the progression of OA, should be a top priority with any dog, but more importantly with agility dogs. Performance dogs tend to have more “wear and tear” as well as placing high repetitive loads on their joints. For this reason oral joint supplements may not only help in the prevention of OA but slowing and minimizing the progression once OA has developed.

Traditionally, OA has been managed with non-steroidal anti-inflammatories (NSAIDs) as the first line of treatment and during flare ups. While NSAIDs do a good job in minimizing pain, their long-term use is not recommended due to side effects. Furthermore, it is now known that inflammation is not the only key factor in the disease process of OA, but oxidative stress is as well<sup>1</sup>. In dealing with the management of OA a multimodal approach should be taken. One such tool in the arsenal of multimodal management is the use of oral joint supplements.

### Commonly Used Oral Joint Supplements

The most common oral joint supplements used in canine OA are glucosamine, low molecular weight chondroitin sulfate, and essential fatty acids.

Oral glucosamine sulfate is 90% absorbed and is the pro-drug of glucosamine, which has the ability to diffuse into the articular cartilage<sup>2, 3</sup>. There is data to suggest that glucosamine can influence chondrocyte (the cells responsible for cartilage production) metabolism. Specifically, glucosamine is able to stimulate the production of certain molecules that act as the backbone to the molecular makeup of cartilage (it stimulates the production of proteoglycan aggregates)<sup>4</sup>. Furthermore, glucosamine can up-regulate the production of the aggrecan protein, hyaluronic acid. Glucosamine is also thought to increase the production of glycosaminoglycans (GAGs) such as chondroitin sulfate. The anti-inflammatory and analgesic (pain relief) effects have been studied. Unfortunately, most of this data is in human medicine and rats while veterinary studies are lacking.

Chondroitin sulfate has approximately 5% bioavailability after a single dose; however, there is evidence of distribution to the joints in dogs<sup>5, 6</sup>. Chondroitin sulfate has a stimulatory role to chondrocytes, and also has been showed to have anti-inflammatory effects<sup>7, 8</sup>. Furthermore, when glucosamine and chondroitin sulfate are used together there is a synergistic effect to aid in cartilage production and inhibit cartilage breakdown versus when each product is used alone.

Newer research has shown promise in the use of essential fatty acids, such as Welactin from Nutramax Laboratories, for the management of OA. Essential fatty acids are a group of polyunsaturated fatty acids that contain both the omega-6 fatty acid; Arachidonic and the omega-3 fatty acids; Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA). These fatty acids are components of the cell membrane. Omega-6 fatty acids such as Arachidonic acid are involved with beginning of the inflammatory pathway. However, omega-3



fatty acids (EPA and DHA) derived from dietary linoleic acid and linolenic acid have anti-inflammatory properties and therapeutic effects to the synovium and cartilage. The omega-3 fatty acids are able to compete with and replace omega-6 fatty acids thus reducing the inflammatory response.

Omega-3 fatty acids derived from fish oils have been shown in dogs to decrease the enzymes responsible for the breakdown of certain components to the cartilage<sup>9</sup>. A large study using peak vertical force has shown that dogs with osteoarthritis that are fed a diet rich in omega-3 fatty acids have improved weight-bearing compared to dogs that were fed a control diet with no omega-3 fatty acids<sup>10</sup>. The same authors also revealed that according to owners, dogs that were fed the diet rich in omega-3 fatty acids had significantly improved ability to rise from resting and play after 6 weeks on the diet; furthermore, after 12 and 24 weeks on the diet there was improved ability to walk when compared to the dogs fed the control diet<sup>11</sup>.

Outside of the omega-3 fatty acids, additional fatty acids known as Esterified Fatty Acid Complex or Cetylated Fatty Acids are currently available for both joint health and periodontal disease prevention. The most commonly used product of these fatty acids is 1-TDC (1-TetraDecanol Complex). This product is available to both humans (Elite Science) and animals (Advanced Canine Rehabilitation Center). Essentially 1-TDC is a cellular lubricant that helps promote increased flexibility and healthy joint function. In a human study with patients suffering knee OA, improved range of motion and overall function was found with those patients taking a Cetylated Fatty Acid<sup>12</sup>. Unfortunately, there are currently no studies looking at the efficacy of 1-TDC

on the management of OA in canines; there is some evidence on the efficacy on the use with periodontal inflammation. The product is reported to have lipoxins (which stimulate the neutrophil to stop secreting pro-inflammatory cytokines), resolvins (which stops neutrophil recruitment and infiltration), protectins and docosatrienes (both are pro-resolving lipid mediators that stabilize the inflammatory response) (Managing Periodontal Inflammation, Dr. James Anthony, Elite Science Product Publication, 2015). Because 1-TDC does not contain therapeutic levels of omega-3 fatty acids, the current recommendation would be to use 1-TDC in conjunction with an omega-3 fatty acid.



## Other Joint Supplements



Outside the three most commonly used joint supplements, there are literally hundreds of other supplements that can be added. For example, Dasuquin by Nutramax Laboratories has avocado/soybean unsaponifiables (ASU), methylsulfonylmethane (MSM), and green tea extract along with glucosamine and chondroitin sulfate. ASU has shown to be protective of the cartilage, decrease the expression of inflammatory mediators, as well as improve joint comfort. Interestingly, the combination of ASU, glucosamine, and chondroitin sulfate has been shown to work better than the combination of glucosamine and chondroitin sulfate alone. MSM is another

supplement that is an organic source of sulfur. MSM is considered by some to be the primary metabolite of dimethyl sulfide (DMSO) which is thought to have both anti-inflammatory and antioxidant effects. Green tea extract has been shown to have a positive effect on cartilage health through its antioxidant properties.

With the newer knowledge base that oxidative stress and inflammation play a large role in the disease process of OA<sup>1</sup>, Nutramax Laboratories just recently released Dasuquin Advanced. Research has shown that the same mediators that cause inflammation cause an oxidative stress response and visa versa<sup>1</sup>. What this means is that certain antioxidants may have anti-inflammatory properties, while certain anti-inflammatories have antioxidant properties. This new formulation has the same ingredients as the original Dasuquin but also has added alpha-lipoic acid, Boswellia serrata extract, Curcumin Longa extract, and Manganese Ascorbate.

Alpha-lipoic acid is a biologic antioxidant mainly found in red meat, vegetables, and yeast. Not only does it have antioxidant properties to combat oxidative stress, but also when combined with ASU it has the ability to decrease the expression of an inflammatory mediator (Prostaglandin E-2) 20% greater than compared to ASU alone<sup>13</sup>. Boswellia serrata extract (a.k.a. frankincense) is an extract found in specific trees in India. The extract contains a selective mix of boswellic acids that have the ability to decrease the inflammatory response. When Boswellia is added to the combination of ASU, glucosamine, and chondroitin sulfate an even greater reduction in inflammatory mediators is found when compared to glucosamine and chondroitin sulfate alone. Curcumin is an antioxidant from the spice turmeric

commonly found in curry powder. Not only does it serve as an antioxidant but it can also act as an anti-inflammatory. Unfortunately, curcumin is poorly absorbed. However, the unique curcumin found in Dasuquin Advanced has been shown to have seven times the overall absorption rate, and three times higher plasma concentrations than typical curcumin extract<sup>14</sup>. Manganese Ascorbate is one of the enzymes used for the production of cartilage. It has also been shown to decrease certain inflammatory mediators<sup>15</sup>.



Other joint supplements worth mentioning, due to their popularity within the canine sport world, are oral hyaluronic acid (HA) supplements, L-carnitine, phycocyanin (Phycox), special milk protein concentrate (Duralactin), natural egg membrane, green lipped mussel (Glyco-Flex), and elk antler.

There has been a long history of usage and discussion on efficacy of oral HA. We currently have many studies showing the efficacy and importance of supplementing HA directly into joint.<sup>16, 17</sup> We know that by injecting HA into joints we stimulate the resident cells to increase HA synthesis, therefore reducing inflammation and protecting cartilage cells.<sup>18</sup> Unfortunately, many studies continue to show that oral HA is not readily absorbed and, in fact, depending on the products' source, less than 5% of the oral dose actually reaches the joints.<sup>19</sup> Recently a research study published in the *Journal of Veterinary Science* showed a positive response, with reduction of clinical signs, to an

oral HA product.<sup>20</sup> Unfortunately this product also contained other supplements, including glucosamine and chondroitin sulfate; therefore, clouding the results as to which product was responsible for the positive outcome. In addition, there is no known distributor of this particular product in the USA. At this time, there is not enough research to support the usage of oral HA products with the canine athlete at this time.

L-carnitine has been shown to promote weight loss, increase lean muscle mass, and reduce fat tissue in canines.<sup>21</sup> This supplement can help keep our weight-challenged canine athletes lean through facilitating metabolism of fatty acids. Daily dosage of an over-the-counter, trusted L-carnitine supplement is 500-2000mg orally per day.

Phycocyanin (Phycox), another common nutraceutical, is an extract of blue-green algae. It acts as an antioxidant and helps block the inflammatory cascade allowing pain relief for arthritic joints. This supplement is often combined with glucosamine and chondroitin sulfate. Unfortunately, there are very limited studies performed only on rats and mice. Currently there is no solid research data that suggests its efficacy in the canine patient.



Special milk protein concentrate (Duralactin) is popular oral supplement used abroad for many years in the canine before its debut in the USA a few years ago. Its primary active ingredient is a dried milk protein harvested from milk of hyperimmunized cows, or Microlactin. This protein has been shown to help reduce the inflammatory response seen in joints secondary to heavy work or underlying arthritis. There were some nonspecific trials performed on rats in the late 1990s and its success has been mostly based on prior data seen in humans. One canine trial completed in 2003 showed improvement in pain assessment scores completed by owners after supplementing their arthritic dogs for 8 weeks.<sup>22</sup>



Natural egg membrane (NEM) is a supplement that provides a natural source of collagen, glucosamine, chondroitin, and HA. In 2009 a human research trial showed when this supplement was taken there was reduced pain from arthritic joints.<sup>23</sup> Unfortunately, to date, there have not been any clinical trials performed in dogs so efficacy has not been established.



Green-lipped mussel (*perna canaliculus*) or Glyco-flex is a very well-known nutraceutical that combines lyprinols, chondroitin, several different vitamins and minerals in addition to omega-3 fatty acids in one supplement. It is important to know that the source and processing of the mussel is extremely detrimental in the efficacy of the product and other over-the-counter sources may not be as safe or effective as the Glyco-flex product. In recent years there have also been several human and canine trials supporting the effects of pain relief from osteoarthritis with the use of Glyco-flex.<sup>24,25</sup> It is also important to

understand that Glyco-flex does not contain glucosamine so its comparison to other products that contain both glucosamine and chondroitin cannot be made.



Elk antler is one additional oral supplement that has received a lot of press over the past few years. Its reported anti-inflammatory effects have been noted in traditional Chinese medicine for years. It comes from the core of elk antler in the velvet stage of growth. The pilose antler peptide that is derived from this source is shown to contain chondroitin sulfate and therefore supports its anti-arthritic claims. In addition there was a clinical study performed in dogs in 2004 showing positive effects in reduction of osteoarthritic signs.<sup>26</sup>

### When to Begin Oral Joint Supplements?

There has been a long-standing debate about the timing for starting oral joint supplements. Some individuals advocate waiting until there are clinical and/or radiographic signs of OA to begin oral joint supplements. Yet, others recommend beginning oral joint supplements prior to the onset of OA in a more prophylactic manner. Using radio-labeling and scintigraphic imaging Canapp, et al.<sup>27</sup> evaluated glucosamine and chondroitin use prophylactically. Dogs were divided into several groups: a placebo group, a group that got glucosamine and chondroitin prior to OA in the wrist joint, and another group that was given glucosamine and chondroitin after OA was induced in the wrist joint. They were able to confirm that the dogs given glucosamine and chondroitin prior to the onset of OA had less inflammation and lameness in the joint compared to the dogs that received the placebo, and the group of dogs that received glucosamine and chondroitin after the onset of OA.

Having this knowledge allows for a recommendation that dogs, especially performance dogs, should be on oral joint supplements at a young age or when training begins, rather

than waiting till after injury, or even worse after the onset of OA. Given what we know about both glucosamine and chondroitin along with essential fatty acids, it only makes sense to begin performance dogs on both a glucosamine/chondroitin sulfate supplement (such as Dasuquin Advanced) and an omega-3 fatty acid (such as Welactin). Just recently, Nutramax has developed Dasuquin Advanced soft chews, which have both DHA and EPA (essential fatty acids); however, supplementation with Welactin is still recommended.

### Choosing the Right Oral Joint Supplement

It is important to understand that oral joint supplements are considered nutraceuticals, not pharmaceuticals. Because of this there is no federal regulation on the production and manufacturing of nutraceuticals. Furthermore, companies are under no legal obligation to meet the claims made on the label. It is very important before giving a dog any oral joint supplement that there is substantial evidence of the purity and quality of the particular product. It has been stated that up to 93% of companies don't meet the label claims. For this reason using a product from a reputable company such as Nutramax Laboratories is recommended. 🐾

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*Dr. Debra Canapp currently serves as the co-principal and medical director at Veterinary Orthopedic & Sports Medicine Group in Annapolis Junction, Maryland, where she practices sports medicine, acupuncture, diagnostic musculoskeletal ultrasound, and rehabilitation. For the past eight years, Dr. Debra Canapp's exclusive area of interest, clinical work, lecturing, and research has revolved around sports medicine and rehabilitation therapy, specifically canine sports-related injury, sport rehabilitation, and performance. She has completed advanced courses in canine rehabilitation, hydrotherapy, acupuncture, sports medicine, orthopedics, and stem cell therapy. Dr. Canapp is active in teaching rehabilitation medicine, diagnostic musculoskeletal ultrasound, and regenerative medicine to visiting veterinary students, rehabilitation therapy certification candidates, and veterinarians. Dr. Canapp's current primary area of interest and research is small animal diagnostic musculoskeletal ultrasound and defining specific pathology and treatment options. Visit [www.vosm.com](http://www.vosm.com) to learn more about Dr. Canapp and VOSM.*

*Dr. David Dycus currently practices orthopedic surgery and sports medicine at Veterinary Orthopedic & Sports Medicine Group in Annapolis Junction, MD. After earning his DVM from Mississippi State University's College of Veterinary Medicine, Dr. Dycus completed a small animal rotating internship at Auburn University, and then returned to Mississippi State to complete a surgical residency. While Dr. Dycus enjoys all aspects of surgery, he has a strong passion for orthopedics and sports medicine, including osteoarthritis, fracture mechanics, and joint problems. Dr. Dycus has completed advanced training in minimally invasive procedures, regenerative medicine, and multiple repair techniques for CCL injuries. Dr. Dycus also enjoys teaching and lecturing, and regularly speaks on the use of nutraceuticals for the management of osteoarthritis, CCL repair techniques, and other topics. For more information on Dr. Dycus and VOSM, please visit [www.vosm.com](http://www.vosm.com).*

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