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Nutrition and Osteoarthritis in Dogs: Does It Help?

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Osteoarthritis (OA) is a common syndrome having multiple causes and characterized by pathologic change of the synovial or diarthrodial joint accompanied by clinical signs of pain and disability. Confusion about the definition of OA has arisen over the years; recently, the American Academy of Orthopaedic Surgeons proposed the following consensus definition: osteoarthritic diseases are a result of mechanical and biologic events that destabilize the normal coupling of degradation and synthesis of articular cartilage chondrocytes, extracellular matrix (primarily collagen and aggrecan), and subchondral bone. Although they may be initiated by multiple factors, including genetic, developmental, metabolic, and traumatic factors, osteoarthritic diseases involve all the tissues of the diarthrodial joint. Ultimately, osteoarthritic diseases are manifested by morphologic, biochemical, molecular, and biomechanical changes of cells and matrix that lead to softening, fibrillation, ulceration, articular cartilage loss, sclerosis and subchondral bone eburnation, and osteophyte production. When clinically evident, osteoarthritic diseases are characterized by joint pain, tenderness, limitation of movement, crepitus, occasional effusion, and variable degrees of inflammation without systemic effects [1]. OA has been estimated to affect as many as 20% of dogs older than 1 year of age [2]. For years, the discussion of OA and nutrition in small animal medicine has centered around nutrition and developmental orthopedic disease or the association between obesity and OA. The enormous public interest in the relation between diet supplements and OA has recently taken over center stage when discussing OA and nutrition, however. Physicians and veterinarians are constantly asked about these well-advertised supplements. Purely speculative information on nutritionally based therapies to treat OA has permeated every form of media available to the public. Unfortunately, few well-designed scientific studies have been initiated to explore these treatments in clinical

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patients. Thus, this article focuses solely on the evidence for dietary modification, including nutraceuticals formulated into diets, in patients with chronic OA.

Our initial discussion focuses on the use of evidence-based medicine. Evidence is defined as "the data on which a judgment or conclusion may be based, or by which proof or probability may be established" [3]. Evidence-based medicine is the integration of best research evidence with clinical expertise and patient values [4]. There are many ways in which to analyze and integrate evidence into the practice of veterinary medicine and several schemes by which to rank the strength of evidence. In this article, we review results of randomized placebo-controlled studies, and, where none exist, clinical trials or controlled experimental studies. Searches were performed on PubMed, setting the search limits to include only "clinical trial" and "randomized controlled trial." These searches were limited to "dogs" or "humans." The final search using "dog AND (arthritis OR osteoarthritis OR degenerative joint disease) AND (diet OR nutrition OR nutrient OR nutraceutical OR supplement)," supplemented with a search of bibliographies of articles that discussed the management of canine OA, yielded seven articles, of which five were randomized controlled studies. These studies varied in quality and type of design, limiting the strength of evidence they can provide to the clinician. The studies are briefly abstracted to give the reader some idea of the different studies done and their limitations. The most striking limitation shown here is the sheer lack of the number of studies and the number of dogs involved.

STUDY RESULTS

Study by Bui and Bierer

Bui and Bierer [5] evaluated the efficacy of green-lipped mussel (GLM; *Perna canaliculus*), added to a complete dry diet, for alleviating clinical signs of arthritis in dogs. A blind, randomized, longitudinal study design was used, with 31 dogs exhibiting varying degrees of arthritis. Each dog was evaluated by a veterinarian, and joints were individually scored for degree of pain, swelling, crepitus, and reduction in range of movement. Summation of all scores for an individual dog comprised its total score. Both groups were fed the same base dry diet, to which 0.3% GLM powder was added in the test group. The change in total score, by the end of 6 weeks, showed a significant improvement ($P < .05$) in the test group versus the control group. Significant improvements were also observed in joint pain and swelling scores in the test group. Changes in joint crepitus and range of joint movement were not significantly different between the test and control groups.

Study by Dobenecker and colleagues

The objective of the study by Dobenecker and colleagues [6] was to compare dog owners' perceptions of the effects of chondroitin sulfate (CS) or New Zealand GLM extract with a placebo in a double-blind field study in dogs with a chronic degenerative joint disease. Seventy dogs of different breeds, ages,

and genders were included in the study. Patients were randomized into three groups: the first group was given CS, the second group received mussel extract (GLM powder), and the third group was fed a placebo. The supplements were mixed into the normal diet of the patients. Changes in clinical symptoms during the 12-week oral application period were verified separately by dog owners and the attending veterinarians using standardized questionnaires at the beginning and end of the study. Fifty-eight dogs (83%) finished the trial. An important result of this study is that none of the tested substances led to a distinct improvement in the recorded symptoms or even to total recovery in general. The evaluation of the questionnaires of the attending veterinarians revealed good correspondence between the judgment of owners and experts. Both groups reported a slight improvement of the symptoms regarding the means of all three treatment groups, including that fed a placebo.

Study by Innes and colleagues

P54FP is an extract of Indian and Javanese turmeric, *Curcuma domestica* and *Curcuma xanthorrhiza*, respectively, that contains a mixture of active ingredients, including curcuminoids and essential oils. Innes and colleagues [7] conducted a randomized, blind, placebo-controlled, parallel-group clinical trial of P54FP as a treatment for OA of the canine elbow or hip. Sixty-one client-owned dogs with OA were recruited for the study at a single center. After a 2-week wash-out period, they were randomly allocated to receive P54FP or a placebo orally twice daily for 8 weeks and were re-examined after 4, 6, and 8 weeks of treatment. The effectiveness of the treatment was assessed in terms of the peak vertical force (PVz) and vertical impulse of the affected limbs, as measured with a force platform, by clinical assessments of lameness and joint pain by the investigators and overall assessment of the response to treatment by the investigators and owners. The results from 25 P54FP-treated dogs and 29 placebo-treated dogs showed that there was no statistically significant difference between the groups in terms of the PVz of the affected limb. The investigators' overall assessment showed a statistically significant treatment effect in favor of P54FP ($P = .012$), but the owners' assessment failed to reach statistical significance ($P = .063$). No serious adverse effects were recorded, but 2 P54FP-treated dogs and 4 placebo-treated dogs were withdrawn from the study because their condition deteriorated.

Study by Reichling and colleagues

Reichling and colleagues [8] conducted an open multicenter clinical trial comparing conditions before and after treatment with a natural resin extract of *Boswellia serrata*. Twenty-nine dogs with manifestations of chronic joint and spinal disease were enrolled. OA and degenerative conditions were confirmed radiologically in 25 of 29 cases. The resin extract (BSB108; Bogar AG, Wallisellen, Switzerland) was administered with the regular food at a dose of 400 mg per 10 kg of body weight once daily for 6 weeks. A statistically significant reduction of severity and resolution of typical clinical signs in individual animals, such as intermittent lameness, local pain, and stiff gait, were reported after 6 weeks. In

5 dogs, reversible brief episodes of diarrhea and flatulence occurred, but only once was a relation to the study preparation suspected.

Study by Gingerich and Strobel

Gingerich and colleagues [9] designed a questionnaire method for dog owners to monitor the orthopedic disabilities of their pets for evaluation of a nutraceutical with joint health claims. Fifty large-breed dogs presented with signs of OA were randomly allocated to placebo and active treatment groups. Degree of disability was assessed by physical examination, a standard questionnaire on daily activities, and a case-specific questionnaire that monitored specific impairments of each dog. The test product was a special milk protein concentrate (SMPC; Microlactin, Stolle Milk Biologics, Cincinnati, Ohio). Only 35 of the dogs completed the study. Overall improvement was noted in 68% and 35% of the SMPC and placebo groups, respectively. A significant ($P < .05$) improvement in mean standardized and patient-specific questionnaire scores and in owner global assessments was detected in the SMPC group but not in the placebo group. Compared with the placebo group, the treatment response was significantly better in the SMPC group with regard to case-specific scores ($P < .001$) and owner global assessments ($P = .004$).

Study by Moreau and colleagues

The efficacy, tolerance, and ease of administration of a nutraceutic agent, carprofen, or meloxicam were evaluated in a prospective double-blind study by Moreau and colleagues [10] in 71 dogs with OA. The client-owned dogs were randomly assigned to one of the three treatments or to a placebo control group. The influence of OA on the dogs' gait was described by comparing the ground reaction forces of the arthritic dogs and 10 normal dogs. Additionally, subjective assessments were made by the owners and by the orthopedic surgeons. Changes in the ground reaction forces were specific to the arthritic joint and were significantly improved by carprofen and meloxicam but not by the nutraceutic agent; the values returned to normal only with meloxicam. The orthopedic surgeons assessed that there had been an improvement with carprofen and meloxicam, but the owners considered that there had been an improvement only with meloxicam. The treatments were well tolerated, except for a case of hepatopathy in a dog treated with carprofen.

Study by Impellizeri and colleagues

Impellizeri and colleagues [11] conducted a study on the effect of weight reduction on clinical signs of lameness among overweight dogs with clinical and radiographic signs of hip OA. This was a nonblind prospective clinical trial. Nine client-owned dogs with radiographic signs of hip OA that weighed 11% to 12% greater than their ideal body weight and were examined because of hind limb lameness were included in the study. Baseline body condition, hind limb lameness, and hip function scores were assigned. Severity of lameness was scored using a numeric rating scale and a visual analog scale. Dogs were fed a restricted-calorie diet, with the amount of diet fed calculated to provide 60% of

the calories needed to maintain the dogs' current weight. Evaluations were repeated midway through and at the end of the weight loss period. Dogs lost between 11% and 18% of their initial body weight. Body weight, body condition score, and severity of hind limb lameness were all significantly decreased at the end of the weight loss period.

OA is the most common form of arthritis recognized in dogs [12]. Hip dysplasia, cruciate instability, and osteochondritis dissecans are common causes of canine OA (degenerative joint disease). As previously described, degenerative OA is characterized as a slowly progressive condition in which two primary pathologic processes occur: articular cartilage degeneration and subchondral bone changes. A low-grade synovitis often occurs. Inflammation is present in these joints, and steroidal or nonsteroidal anti-inflammatory drugs may modulate this inflammation. Although nutritional imbalances may result in developmental skeletal disease (see the article by Lauten elsewhere in this issue), which, in turn, may lead to degenerative joint disease, the role of nutrition in the management of degenerative joint disease is less clear. Nutrition may aid in treatment of degenerative joint disease through optimizing body condition and body weight (managing obesity), by modifying degenerative or inflammatory processes (specific nutrient effects), and by influencing pharmacologic therapy (drug-nutrient interaction).

OBESITY

Obesity can be defined as accumulation of body fat in excess of what is necessary to maintain optimum condition and health. This may be obvious in a grossly obese individual, particularly when obesity-related disease is present; however, it is less obvious in a patient that is overweight and otherwise clinically healthy but is at risk for obesity-related disease, such as degenerative OA. Quantitatively, obesity in dogs is generally defined as exceeding ideal body weight by 15% to 20% or more. One technique that is useful in the management of patients is a body condition score. The advantage of assigning a body condition score is that it uses information additional to body weight. It is a measure of the appearance of the animal, of fat stores that are identified, of muscle mass and tone, and of general health.

Obesity may result in OA as a result of excess forces placed on joints and articular cartilage, which may lead to inactivity and further development of obesity; thus, a vicious cycle ensues. Additionally, adipose tissue is recognized as being metabolically active and proinflammatory; therefore, obesity may contribute to inflammation [13–15].

Several studies have demonstrated a relation between obesity and OA [16]; however, a cause and effect mechanism has not been found [17,18]. A long-term study was performed in 48 Labrador Retrievers from seven litters divided into two dietary groups: one group was fed an adult maintenance dog food at 0.27 kJ of metabolizable energy per kilogram of body weight per day, and the second group was fed the same diet at 75% of the amount (0.2025 kJ of metabolizable energy per kilogram of body weight per day) [19,20]. Restricted fed

dogs lived, on average, 2 years longer, weighed less, had better body condition scores, and had longer delay to treatment of chronic disease, including OA [21]. Therefore, maintaining an optimal or slightly lean body condition may be associated with lower risk of development of OA, development of less severe OA, and delay of onset of clinical signs of OA in dogs.

Weight reduction from an obese state is beneficial in the management of OA in human beings [22–24]. In addition to improvement in mobility, weight reduction was associated with better quality-of-life scores in human beings with knee OA [25]. Two uncontrolled clinical studies of obese dogs with OA demonstrated improvement in mobility [11,26]. In one study of 9 dogs with a body condition score of 5 of 5 and coxofemoral OA, obesity management resulted in loss of 11% to 18% of body weight, a decrease in body condition to optimal condition, and improvement in the severity of subjective hind limb lameness scores [11]. In a second study of 16 dogs with coxofemoral OA, weight loss of 13% to 29% of body weight and decrease of body condition to optimal resulted in improvement of ground reactive force as well as improvement in subjective mobility and clinical signs of OA [26]. Although these are uncontrolled clinical trials in a small number of dogs, results suggest that weight reduction may be beneficial in dogs with OA.

ω-3 FATTY ACIDS

Degenerative OA involves an inflammatory component; thus, it may be possible to modify the inflammation by nutritional components, specifically ω-3 (n3) fatty acids. Arachidonic acid (an ω-6 [n6] fatty acid) is incorporated into cell membranes; when metabolized, it yields prostaglandins, leukotrienes, and thromboxanes of the 2 and 4 series. Many drugs used to treat degenerative OA inhibit conversion of arachidonic acid to these eicosanoids. These n6-derived eicosanoids have, for the most part, vasoactive and proinflammatory effects. Substituting an n3 fatty acid in the membrane may decrease these responses. Metabolism of n3 fatty acids results in eicosanoids of the 3 and 5 series, which are less vasoactive and less proinflammatory.

Several studies have been published that demonstrate a beneficial response to n3 fatty acid incorporation into diets of human beings with rheumatoid arthritis [27–31], although other studies have not demonstrated a benefit [32]. There is a growing body of data showing positive effects of n3 fatty acids on cartilage and its metabolism in the face of degradative enzymes. Recent work has provided direct evidence that n3 fatty acid supplementation can reduce or abrogate the inflammatory and matrix degradative response elicited by chondrocytes during OA progression [33–36]. Unfortunately, there are no randomized controlled clinical trials published of n3 fatty acids and OA in dogs. An unpublished study has been performed in dogs evaluating n3 fatty acids and experimentally induced stifle arthritis [37]. Eighteen dogs were randomly assigned to one of three isocaloric diet groups containing 21.4% fat (dry matter basis) differing only in their fatty acid composition: a diet with an n6-to-n3 fatty acid ratio of 28.0:1.0 (high-n6 diet), a diet with an n6-to-n3 fatty acid ratio of

8.7:1.0 (control diet), and a diet with an n6-to-n3 fatty acid ratio of 0.7:1.0 (high-n3 diet). Diets were fed for a total of 21 months. Initially, the dogs were started on their assigned diet 3 months before surgical transection of the left cranial cruciate ligament, continued until surgical repair 6 months later, and maintained for an additional 12 months after repair. When compared with the high-n6 and control diets, consumption of the high-n3 diet was associated with lower serum concentrations of cholesterol, triglycerides, and phospholipids; lower synovial concentrations of prostaglandin E2; better ground reaction forces; and fewer radiographic changes of OA. Synovial membrane fatty acid composition mirrored the fatty acid composition of the diets consumed by the dogs. Recently, a randomized study was presented in abstract form, where 38 dogs with naturally occurring OA were placed on a commercially available therapeutic food formulated to contain an n6-to-n3 ratio of 0.7:1.0 (Prescription Diet J/d; Hill's Pet Nutrition, Topeka, Kansas) or a typical dry dog food [38]. Ground reaction forces as well as owner and veterinarian clinical evaluations were collected at days 0, 45, and 90. Ground reaction forces increased and weight bearing increased in the dogs fed the therapeutic diet when compared with the control diet. It should be noted that the two diets differed in more than just the fatty acid composition, but this was the major difference. Finally, one study in dogs reported results of observations of dog owners who perceived improvement in their pet's arthritic symptoms when treated with fatty acids for various dermatologic problems [39].

ANTIOXIDANTS

The formation of free radicals as a consequence of cellular metabolism occurs constantly, but the potential deleterious effects are minimized by antioxidants. The balance between free radicals and antioxidant defenses is a key factor in preventing development of noxious processes at the cellular and tissue levels. Recent evidence supports the theory that excessive production of free radicals or the imbalance between concentrations of free radicals and antioxidant defenses may be related to such processes as aging, cancer, diabetes mellitus, lupus, and arthritis [40]. Progressive hypoxia resulting in the production of reactive oxygen species may play a role in rheumatoid arthritis [41]. Thus, antioxidant therapy may be of benefit in the treatment of OA [42].

Most studies of antioxidant therapy for arthritis in human beings involve rheumatoid arthritis, although several studies of knee OA have been published. An early pilot study of vitamin E (tocopherol) demonstrated improvement in clinical signs and pain scores in 52% of 29 patients with knee OA compared with 4% receiving a placebo [43]. In another placebo-controlled study of human beings with OA of the coxofemoral or knee joint, high-dose tocopherol was as efficacious as diclofenac in reducing pain and improving mobility [44]. This was also found in studies of human beings with rheumatoid arthritis [45,46]. Other studies have not demonstrated a benefit of vitamin E for rheumatoid arthritis or OA [47–49]. Likewise, the efficacy of vitamin C in human beings with OA has been difficult to determine because of contradictory results of studies

[50–53] Selenium was not shown to be beneficial in human beings with rheumatoid arthritis [54]. Methyl-sulfonyl-methane (MSM) is a derivative of dimethyl sulfoxide and has been suggested as an agent for the management of pain and inflammation and as an antioxidant. The rationale for its use lies in the possibility of a dietary sulfur deficiency, with a resultant deficiency of sulfur-containing compounds in the body, such as antioxidants and CS [55]. Currently, there are no randomized controlled clinical trials evaluating MSM in human beings; however, in a recent pilot clinical trial involving a placebo control, MSM reduced the Western Ontario and McMaster University Osteoarthritis Index visual analog scale scores and pain and improved physical function when compared with placebo [56]. There are no controlled studies evaluating or documenting a benefit of vitamin C, MSM, or selenium in dogs with OA, although they may be recommended [57,58]. Dogs do not require exogenous vitamin C because they are capable of synthesizing it endogenously; therefore, its use is not encouraged.

CHONDROMODULATING AGENTS

Chondromodulating agents are purported to slow or alter the progression of OA. These agents are considered to be slow-acting drugs in osteoarthritis (SADOAs) and can be subdivided into symptomatic slow-acting drugs in osteoarthritis (SYSADOAs) and disease-modifying osteoarthritis drugs (DMOADs). Beneficial effects may include a positive effect on cartilage matrix synthesis and hyaluronan synthesis by synovial membrane as well as an inhibitory effect on catabolic enzymes in osteoarthritic joints [59]. Compounds fall into two different categories. One group is agents that are approved by the US Food and Drug Administration and can have label claims of clinical effects, such as polysulfated glycosaminoglycan (Adequan; Luitpold Pharmaceuticals, Shirley, New York). The second group comprises products that are considered to be nutritional supplements, which are not regulated and legally cannot claim any medical benefits. Examples of this group include glucosamine and CS (Glycoflex; Vetri-Science Laboratories, Essex Junction, Vermont and Cosequin; Nutramax Laboratories, Baltimore, Maryland). Although many of these products are administered as a supplement or alternative treatment, some, such as glucosamine and GLM, are incorporated into pet foods.

Glucosamine and Chondroitin Sulfate

Glucosamine is an amino sugar that is a precursor for biochemical synthesis of glycosylated proteins and lipids. D-glucosamine is made naturally in the form of glucosamine-6-phosphate and is the biochemical precursor of all nitrogen-containing sugars [60]. Specifically, glucosamine-6-phosphate is synthesized from fructose-6-phosphate and glutamine [61] as the first step of the hexosamine biosynthesis pathway. The end product of this pathway is uridine diphosphate (UDP)-N-acetylglucosamine, which is then used for making glycosaminoglycans, proteoglycans, and glycolipids. Because glucosamine is a precursor for glycosaminoglycans and glycosaminoglycans are a major

component of joint cartilage, supplemental glucosamine may help to rebuild cartilage, and there are in vitro data to support this claim [62–65]. There are conflicting data on evidence of any clinical effect of glucosamine in veterinary medicine, however [10,66,67]. Commonly used forms of glucosamine include glucosamine sulfate and glucosamine hydrochloride, and it is often combined with CS and MSM. A review of studies of pharmacologic dosages of glucosamine is beyond the scope of this article; however, glucosamine, with CS, is included in dog foods at low concentrations.

When evaluating glucosamine and CS inclusion in a manufactured dog food, two questions might be asked. Are the glucosamine and CS in the food stable and bioavailable? Is the amount of glucosamine and CS in the food enough to provide a beneficial effect? It is difficult to find the amount of glucosamine and CS in pet foods. Many dog foods formulated and marketed for adult dogs, geriatric dogs, and large-breed growth contain glucosamine and CS, but the amounts are not readily available from the manufacturer or from electronic or print information. These compounds are not recognized by the American Association of Feed Control Officials, and thus are not included in dog nutrient profiles. Furthermore, they are not considered as "generally regarded as safe" (GRAS) ingredients.

New Zealand Green-Lipped Mussel

New Zealand GLM is a rich source of glycosaminoglycans, although its proposed benefit is thought to be from the anti-inflammatory effects of tetraenoic acid of the n3 series [68]. In 1986, dried mussel extracts that were stabilized with a preservative became available. The earlier studies that found no beneficial effect of GLM on arthritis all used preparations that had not been stabilized, which is a point that may help to explain some of the discrepancies in the research. A stabilized lipid extract (Lyprinol, Pharmalink International, Lancashire, England) is more effective than a nonstabilized extract at inhibiting inflammation [69]. In an uncontrolled clinical trial, Lyprinol administration resulted in an 80% improvement in human beings with rheumatoid arthritis [70]. In a randomized controlled clinical study of 31 dogs with arthritis, GLM powder (0.3%) was added to the diet during processing of one group of dogs [5]. Compared with the control group, which was fed the same diet without added GLM powder, there was significant improvement in subjective arthritis scores, joint swelling, and joint pain in the treated group. These data must not be overinterpreted, however. In a systematic review of agents used to treat canine OA, the data regarding the benefits of GLM extract in dogs were promising but uncertainties existed relating to the scientific quality of the data, and no definitive relation has been proven between clinical improvements and the therapy [71].

OTHER DIETARY COMPOUNDS

There are many other dietary supplements, including herbs and other nutraceutic agents, that are recommended. Few, if any, have been evaluated in a controlled manner. Because of limitations of space, only a few are discussed.

P54FP

P54FP is an extract of Indian and Javanese turmeric, *C domestica* and *C xanthorrhiza*, respectively, which contains a mixture of active ingredients, including curcuminoids and essential oils [7]. There is evidence that these active ingredients possess anti-inflammatory activity. Specifically, curcumin has been shown to inhibit prostaglandin E2 and cyclooxygenase-2 as well as nuclear factor-κB [72–74]. One randomized blind study in dogs with OA found no difference in objective ground reaction forces but did see some improvements in certain subjective outcome measures [7].

Avocado/Soy

Avocado/soybean unsaponifiables (ASUs) are composed of the unsaponifiable fractions of avocado and soybean oils in a 1:3 to 2:3 proportion, respectively [75,76] In vitro data show that ASUs have antiosteoarthritic properties by inhibiting interleukin-1 and stimulating collagen synthesis in cartilage cultures [77,78] In vivo, there is one report in an ovine meniscectomy model of OA providing some support for disease-modifying capabilities [79]. Human clinical trials have shown some beneficial effects of ASUs on clinical symptoms of symptoms of OA and suggest that ASUs may have some structure modification capabilities. There are, however, some conflicting data, because one study found no long-term benefits [80–83]. ASUs have not yet been evaluated in dogs with OA.

Boron

Boron deficiency in food may be part of the cause of some arthritides [84]. Epidemiologic studies suggest that human beings in countries with low boron intake (less than 1.0 mg/d) have a higher risk of development of arthritis when compared with human beings in countries in which boron intake is higher (3–10 mg/d) [85]. In a double-blind placebo/boron supplementation trial in 20 subjects with OA, a significantly favorable response to a boron supplement at 6 mg/d was found; 50% of subjects receiving supplement improved compared with 10% receiving placebo [85]. Whether boron deficiency occurs in pet dogs is unknown. Furthermore, whether boron supplementation and what dosage of boron would be best are unknown. Until studies are performed, supplementation cannot be recommended.

Boswellia Resin

Boswellia, also known as Boswellin or Indian frankincense, comes from the Indian *Boswellia serrata* tree. Resin from the bark of this tree is purported to have anti-inflammatory properties. Boswellia resin has been shown to improve clinical signs and pain in human beings in controlled studies [86–88]. Boswellia resin has been evaluated in 24 dogs in an open multicenter study [8]. Improvement in clinical signs, lameness, and pain was found in 17 of 24 dogs. In 5 dogs, diarrhea and flatulence occurred. Further controlled clinical trials are needed to validate these findings.

Cat's Claw

Cat's claw, an Amazonian medicinal plant, has anti-inflammatory and antioxidant effects and has been shown to decrease clinical signs of knee arthritis and rheumatoid arthritis in human beings [89,90]. It has not been evaluated in dogs with OA.

Creatine

Creatine is used in muscle for production of ATP, which provides energy for muscle contraction. Creatine is sometimes used by body builders and people who exercise with the intent to increase muscle mass and muscular energy; however, some recommend its use with arthritis, especially rheumatoid arthritis in human beings. In rheumatoid arthritis, skeletal muscle weakness often accompanies the arthropathy. In one study, creatine supplementation in human beings with rheumatoid arthritis increased serum and skeletal muscle creatine content but failed to increase skeletal muscle creatine phosphate concentration or strength [91]. In another study of human beings undergoing total knee replacement, creatine supplementation did not improve body composition or skeletal muscle strength [92]. No randomized controlled studies have been performed in dogs with OA.

Special Milk Protein Concentrate

Milk contains a number of biologically active compounds, including immunoglobulins, cytokines, enzymes, hormones, and growth factors. These compounds impart anti-inflammatory properties that have been recognized in human breast milk [93] and milk from hyperimmunized cows [94,95]. An SMPC prepared from milk of hyperimmunized cows (Microlactin) exerts anti-inflammatory properties [96]. The anti-inflammatory properties do not seem to be caused by inhibition of arachidonic acid metabolism but by suppression of neutrophil migration from the vascular space [97]. A randomized controlled clinical trial has been performed evaluating the SMPC in dogs with naturally occurring OA [9]. In this study, dogs receiving the SMPC had improvement in subjective clinical signs of OA and owner global assessment compared with dogs receiving placebo. Further studies need to be completed to validate these findings.

CURRENTLY AVAILABLE VETERINARY DIETS

Many over-the-counter dog foods contain claims of being "joint friendly" because they contain glucosamine, CS, and perhaps other ingredients theorized to be beneficial for joint health. There are four diets specifically formulated and marketed for dogs with arthritis: CNM Joint Mobility JM (Ralston Purina, St. Louis, Missouri), Prescription Diet J/d (Hill's Pet Nutrition), Mobility Support JS 21 (Royal Canin, St. Charles, Missouri), and Mobility Support JS 21 Large Breed (Royal Canin). Nutritional characteristics are presented in Table 1. Most adult maintenance dog foods have n6-to-n3 ratios of greater than 8.0:1.0; therefore, these diets are higher in n3 fatty acids relative to maintenance adult dog foods.

Table 1
Average nutrient content for CNM Joint Mobility, Prescription Diet J/d, Mobility Support JS 21, and Mobility Support JS 21 Large Breed

Nutrient	Unit	JM dry	J/d dry	J/d canned	JS dry	JS LB dry
Protein	g/100 kcal ME	7.9	5.4	4.7	6.2	6.9
Carbohydrate	g/100 kcal ME	9.9	13.8	12.6	12.7	11.3
Fat	g/100 kcal ME	3.3	3.9	4.6	2.7	3.59
Fiber	g/100 kcal ME	0.35	2.70	0.70	0.81	0.38
Calcium	g/100 kcal ME	0.34	0.18	0.16	0.35	0.21
Phosphorous	g/100 kcal ME	0.25	0.14	0.13	0.24	0.14
Ca/P		1.4:1.0	1.3:1.0	1.2:1.0	1.5:1.0	1.5:1.0
Total n3 fatty acids	g/100 kcal ME	0.25	0.95	1.01		
Total n6 fatty acids	g/100 kcal ME	0.44	0.67	0.68		
n6/n3 fatty acid ratio		1.7:1.0	0.7:1.0	0.7:1.0	4.7:1.0	3.5:1.0
Vitamin E	mg/100 kcal ME	25.4			14.1	15.4
Glucosamine	mg/100 kcal ME	34			100	200
Other ingredients			Carnitine	Carnitine	Green-lipped mussel	Green-lipped mussel

Abbreviations: Ca/P, calcium-to-phosphorous ratio; J/d, Prescription diet J/d canine diet (Hill's Pet Nutrition, Topeka, Kansas); JM, CNM Joint Mobility JM canine diet (Ralston Purina, St. Louis, Missouri); JS, Mobility Support JS 21 canine diet (Royal Canin, St. Charles, Missouri); JS LB, Mobility Support JS 21 Large Breed (Royal Canin); ME, metabolizable energy.

Recent research supports a role of nutrition and nutritional modification in the management of OA in dogs. Furthermore, weight management, including weight reduction and prevention of obesity, has a positive impact on the incidence and clinical signs of OA in dogs. Feeding diets that contain increased n3 fatty acids and GLM has been shown to help dogs with OA. Whether other dietary ingredients provide benefit has yet to be determined.

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