Waltham International Symposium:
Pet Nutrition Coming of Age

Improvement of Arthritic Signs in Dogs Fed Green-Lipped Mussel (*Perna canaliculus*)[1,2]

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EXPANDED ABSTRACT

KEY WORDS: • *dog* • *arthritis* • *green-lipped mussel* • *canine*

Arthritis is a significant problem in both humans and animals that may occur at any age but is particularly common in older individuals. In dogs, both degenerative and inflammatory arthropathies may occur but the most common form of joint disease is osteoarthritis (OA[4]), a complex, progressive disease characterized by the degeneration of articular cartilage and by the formation of new bone (osteophytes) at joint margins. Inflammation of the synovial membrane may also be present in many cases of OA, but is a variable feature throughout the course of the disease. Conversely, synovitis is the major pathological feature of the inflammatory joint diseases, such as rheumatoid arthritis.

Degeneration of articular cartilage in OA is usually associated with some predisposing joint abnormality that produces focal areas of increased stress within the joint, resulting in accelerated turnover of cartilage matrix. Although both the synthetic and degradative activities of chondrocytes are increased, the balance is tipped toward matrix depletion with a net loss of cartilage matrix components. Joint enlargement may be evident in some affected dogs and is related to osteophyte production, joint effusion resulting from synovial inflammation and thickening of the joint capsule. Structural damage may exist for some time before clinical signs of OA are apparent, and most cases ultimately present with stiffness or lameness. Lameness, attributed to a combination of joint pain and restricted movement of the joint, may be gradual in onset or may present acutely following minor trauma or excessive exercise. A number of mechanisms are thought to be involved in the pathogenesis of joint pain itself, but one factor is the presence of synovial inflammation.

Dietary factors can potentially modify some of the underlying processes involved in arthritis, including modulation of the inflammatory response, provision of nutrients for cartilage repair and protection against oxidative damage. Where effective, dietary management may help to reduce or eliminate the need for conventional drugs, some of which are associated with adverse secondary effects. Shellfish supplements have been used as a traditional remedy for arthritis in humans and, in recent years, interest has focused on the potential benefits of a nutritional supplement prepared from the New Zealand green-lipped mussel, *Perna canaliculus* (1–3). Although green-lipped mussel (GLM) is known to contain anti-inflammatory components and other nutrients that may benefit joint health, the precise mechanism(s) of its actions are unknown. Heat processing of GLM has been shown to destroy its activity. Therefore, the processing of whole GLM and incorporation of the GLM product into food products requires special care and processing techniques to avoid destroying any efficacy of the final product.

In a series of clinical studies, we evaluated the efficacy of GLM powder in alleviating arthritic signs in dogs. The performance of GLM was investigated as a powdered supplement on top of a standard diet and when incorporated into one of two processed dietary products, a semimoist treat and a dry main meal diet. Both of these products used low-temperature manufacturing processes designed to retain the efficacy of the GLM.

MATERIALS AND METHODS

All studies described were designed as double-blind, randomized, controlled trials using mixed breed/sex dogs (4–13 y old) that had exhibited varying degrees of arthritic signs, living at an animal sanctuary. Any dogs exhibiting arthritic signs for <4 mo or dogs that did not consistently exhibit arthritic signs were excluded from the study. Not all the same dogs were used in each study. Any dogs that did not complete the entire study were dropped from the results and are not included here. All dogs were adapted to the same basic, dry,

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[4] Abbreviations used: COX, cyclo-oxygenase; ETA, eicosatetraenoic acid; GLM, green-lipped mussel; NSAIDS, nonsteroidal anti-inflammatory drugs; OA, osteoarthritis; PUFA, polyunsaturated fatty acid(s); SEM, standard error of the means.

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adult maintenance dog food (WALTHAM FORMULA® Canine Senior Dry Diet) for at least 6 wk before the start of each study. This diet was also used as the Control diet during studies. At the start of each study, dogs were randomly assigned to groups and fed either the Control or Test for 6 wk. All diets were fed in amounts designed to maintain body weight. Water was supplied ad libidum. Freeze-dried, stabilized GLM powder was supplied by McFarlane Laboratories, Australia.

Evaluations of arthritic signs were carried out at wk 0 and wk 6 by a veterinarian. All parameters were scored on a scale of 0 to 4 (0 = no signs; 1 = mild; 2 = moderate; 3 = marked; 4 = severe). Each dog was scored for mobility (average of individual scores for lameness in walking, trotting and climbing stairs) and individual joints (carpus, elbow and shoulder or tarsus, stifle and hip) of each limb were individually scored for degree of pain, swelling, crepitus and reduction in range of movement. Summation of the mobility score and all individual joint scores for each dog comprised their total arthritic score.

Study 1/GLM powder

Thirty-two dogs were randomly assigned to two groups, Control (n = 15) and GLM (n = 17) at baseline. In the GLM Group, GLM powder was added on top of the standard food before feeding (>34 kg = 1000 mg GLM powder/d; 34–25 kg = 750 mg/d; <25 kg = 450 mg/d).

Study 2/GLM incorporated into a treat

Thirty-three dogs were randomly assigned to two groups, Control (n = 16) and GLM Treat (n = 17) at baseline. Semimoist treats (PEDIGREE® JointCare™ Treats for dogs) were produced incorporating GLM using a low-temperature process. Treats were fed based on body weight to deliver the following GLM dosage levels: >34 kg = 1000 mg GLM/d (2 pieces); 34–25 kg = 750 mg GLM/d (1.5 pieces); <25 kg = 450 mg GLM/d (1 piece).

Study 3/GLM incorporated into a main meal

Thirty-one dogs were randomly assigned to two groups, Control (n = 17) and GLM main meal (n = 14) at baseline. The test diet was formulated to the same recipe as the control diet but contained GLM powder incorporated using a low-temperature application process at a final inclusion level of 0.3% (WALTHAM® Veterinary Diet Canine Joint Support). This level of inclusion was designed to deliver a GLM dosage similar to that of the two previous studies.

The change between the baseline and 6-wk measurements were determined for all dogs for all parameters and were analyzed by nonequal Tukey's post hoc test to determine statistical significance between treatments at $P < 0.05$ (level of significance). Data in charts are expressed as group means ± SEM.

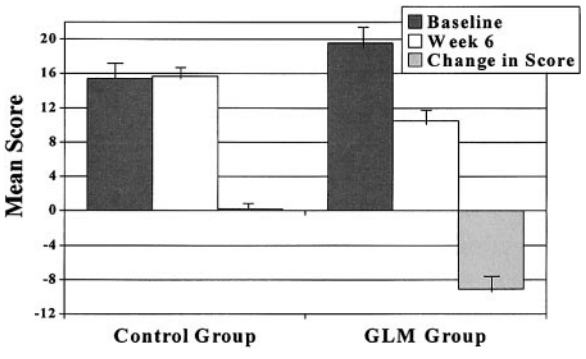

FIGURE 1 Study 1 scores/GLM powder. Mean (± SEM) total arthritic score at baseline and wk 6 and change in score for dogs fed either a standard diet (Control, n = 15) or a diet supplemented with green-lipped mussel powder (n = 17). The change in score was significantly different between the Control and GLM groups ($P < 0.05$).

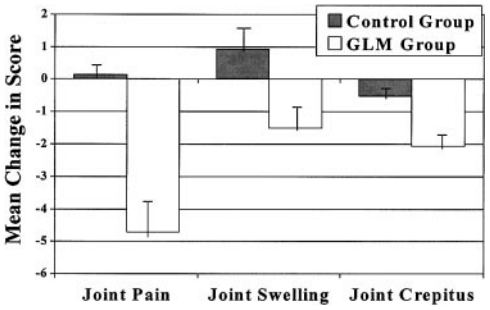

FIGURE 2 Study 1 scores/GLM Powder. Mean (± SEM) changes in joint pain, joint swelling and crepitus scores between baseline and wk 6 for dogs fed either a standard diet (Control, n = 15) or a diet supplemented with green-lipped mussel powder (n = 17). The change in score was significantly different between the Control and GLM groups for all variables ($P < 0.05$).

RESULTS

In the first study, the change in score in the GLM-supplemented group for total arthritic score, joint pain and joint swelling at the end of wk 6 showed significant improvement compared to that of the Control group ($P < 0.05$) (**Figs. 1** and **2**). These same significant differences were also reflected in the other two GLM studies, although only the total arthritic score data are presented in **Figures 3** and **4**. Crepitus scores were also significantly improved in the GLM powder and GLM treat groups compared to those of their respective Control groups.

Study 1/GLM powder

Fourteen of 17 (83%) dogs in the GLM supplemented group demonstrated a 30% or greater reduction in total arthritic scores (indicating an improvement) and of these, six dogs (35%) showed a 50% or greater improvement and three dogs (18%) showed a 70% or greater improvement. However, only 7% (1/15 dogs) of the dogs in the Control group showed a 30% or greater improvement with no dogs showing a 50% or greater improvement in arthritic signs.

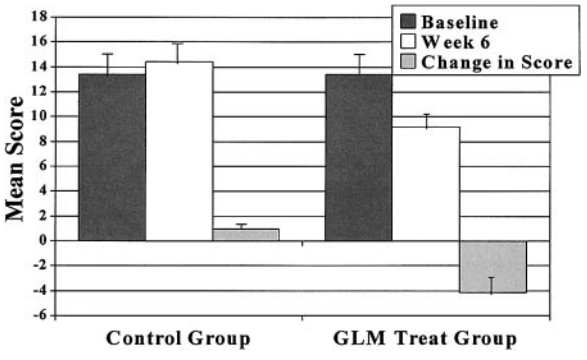

FIGURE 3 Study 2 scores/GLM treat. Mean (± SEM) total arthritic score at baseline and wk 6 and change in score for dogs fed either a standard diet (Control, n = 16) with no treats or the control diet + a treat containing green-lipped mussel powder (n = 17). The change in score was significantly different between the Control and GLM treat groups ($P < 0.05$).

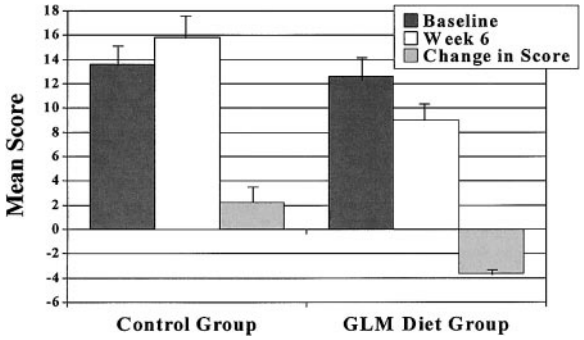

FIGURE 4 Study 3 scores/GLM diet. Mean (± SEM) total arthritic score at baseline and week 6 and change in score for dogs fed either a standard diet (Control, $n = 17$) or a diet containing green-lipped mussel powder ($n = 14$). The change in score was significantly different between the Control and GLM diet groups ($P < 0.05$).

Study 2/GLM incorporated into a treat

Nine of 17 (53%) dogs in the GLM treat group exhibited a 30% or greater reduction in total arthritic scores, of which seven dogs (41%) showed a 40% or greater improvement and two dogs (12%) showed a 50% or greater improvement. However, none of the dogs in the Control group demonstrated a 30% or greater improvement after wk 6 of treatment.

Study 3/GLM incorporated into a main meal

Seven of 14 (50%) dogs in the GLM main meal group demonstrated a 30% or greater reduction in total arthritic scores, including four dogs (29%) that exhibited a 40% or greater improvement and one dog (7%) that showed a 50% or greater improvement after wk 6 of treatment. In the Control group, none of the dogs demonstrated 30% or greater improvement after wk 6 of treatment.

DISCUSSION

These data provide evidence that GLM powder is effective in reducing arthritic signs in dogs when sprinkled directly onto a standard diet or when incorporated into processed treat and main meal products. Total arthritic scores and scores for joint pain and joint swelling were significantly reduced following 6 wk of GLM supplementation in all three forms. Although the mechanism for this is not fully understood, the effect may be the result, in part, of a reduction in the synovial inflammatory response. Anti-inflammatory activity of freeze-dried powdered GLM has been demonstrated in rats (4,5). More recently, a lipid-rich extract of stabilized GLM has been shown to be a potent, but relatively slow-acting, anti-inflammatory agent, with the highest anti-inflammatory activity being found in the polyunsaturated free fatty acid (PUFA) component of the mussel (3,6).

The anti-inflammatory properties of GLM have been attributed to a variety of pharmacologically active components. Most important, GLM has been shown to contain a unique omega-3 fatty acid, eicosatetraenoic acid (ETA), which appears to act as dual inhibitor of arachidonic acid oxygenation by both the cyclooxygenase (COX) and lipoxygenase pathways. Arachidonic acid metabolites play a major role in the inflammatory sequence. Unlike many nonsteroidal anti-inflammatory drugs (NSAIDs), however, GLM is nongastrotoxic and does not affect platelet aggregation, suggesting that ETA may selectively block the pro-inflammatory COX-2 pathway rather than the physiologically important COX-1 pathway (5,7). In fact, studies have suggested that GLM can actually help to reduce gastrointestinal irritation associated with long-term ingestion of some NSAIDs (5,7).

No significant effects were observed with regard to mobility and reduction in range of joint movement with the addition of GLM in any of the studies. Longer study lengths and more sensitive assessment methods may be helpful in detecting any possible effects in these parameters.

Freeze-dried GLM powder contains a variety of nutrients that may have a beneficial effect on joint health, including glycosaminoglycans (chondroitin sulfates), omega-3 fatty acids [ETA; eicosapentaenoic acid (EPA); docosahexaenoic acid (DHA)], amino acids (glutamine, methionine), vitamins (E, C) and minerals (zinc, copper, manganese) (7,8). Glycosaminoglycans are long, unbranched carbohydrates that are major components of cartilage matrix and synovial fluid. Dietary supplementation with glycosaminoglycans, particularly chondroitin sulfate, may help to stimulate cartilage matrix production, inhibit degradative enzyme activity in cartilage and help to prevent thrombus, plaque and fibrin formation in synovial and subchondral blood vessels (9,10). Oral supplementation with a glycosaminoglycan preparation, derived from GLM, was found to reduce lameness and pain in a high proportion of arthritic dogs after an 8-wk treatment (8).

It is possible that the nutrients present in whole freeze-dried GLM powder may act synergistically to reduce inflammation and pain, to limit further cartilage degeneration and, potentially, to support the regeneration of damaged joint cartilage and synovial fluid. The findings of the studies reported here support the conclusion that dietary supplementation with GLM may be of particular benefit in the management of dogs with arthritic signs. Potentially, GLM-supplemented diets may help to reduce an animal's requirement for conventional medical therapy and in some cases the reported gastroprotective action of GLM may provide an additional clinical benefit.

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