CRITICALLY APPRAISED TOPIC:

Evaluation of glucosamine hydrochloride/chondroitin sulfate nutraceuticals as a treatment to improve symptoms associated with canine and feline joint disease

Despite some evidence that a combination of glucosamine hydrochloride and chondroitin sulfate nutraceuticals improves symptoms associated with joint disease in dogs and cats, strong clinical evidence of efficacy is lacking, and these compounds are understudied.

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CLINICAL QUESTION
Does a combination of glucosamine hydrochloride and chondroitin sulfate nutraceuticals (i.e., chondroprotectants) improve symptoms associated with joint disease in dogs and cats?

CLINICAL BOTTOM LINE
The limited number of high quality clinical trials and the lack of data on objective measures of efficacy preclude recommendations of glucosamine hydrochloride and chondroitin sulfate nutraceuticals as a sole medical treatment for joint disease in dogs and cats.¹-³

In brief, the benefits of using a combination of glucosamine hydrochloride and chondroitin sulfate nutraceuticals to improve symptoms associated with canine and feline joint disease has yet to be determined.

EVIDENCE SUMMARY
PubMed database search details (January 2000 through current):
• Canine: (“glucosamine”[MeSH Terms] OR “glucosamine”[All Fields]) AND (“chondroitin”[MeSH Terms] OR “chondroitin”[All Fields]) AND (“dogs”[MeSH Terms] OR “dogs”[All Fields])
• Animals: (“glucosamine”[MeSH Terms] OR “glucosamine”[All Fields]) AND (“chondroitin”[MeSH Terms] OR “chondroitin”[All Fields]) AND (“animals”[MeSH Terms:noexp] OR animals[All Fields])

MAIN RESULTS
Veterinary clinical trials evaluating the efficacy, the duration of effect and absorption of glucosamine hydrochloride and chondroitin sulfate nutraceuticals are limited and results are conflicting to some extent.¹²⁴⁵

The purity and quality of these compounds vary widely in commercial supplements.²⁴

Assessments of the safety of these products for dogs and cats are scarce, but some evidence shows that there are few side effects associated with either short or long term use.³⁶
COMMENTS

The studies reviewed for this report mainly included dogs as study participants (n=4); one study involved cats as study participants and one systematic review included both. Most efficacy studies involving the combination of the two compounds are extrapolated from these studies. It is recommended to use these compounds in dogs and cats requiring further investigation. A validated owner questionnaire is needed in order to evaluate joint disease associated pain at home.

Currently, dosages are most likely extrapolated from studies involving other species. Further studies are necessary to determine how purity, source and composition affect efficacy of glucosamine hydrochloride and chondroitin sulfate preparations in veterinary patients. Beneficial effect and bioavailability have yet to be established for glucosamine hydrochloride and chondroitin sulfate when included in manufactured pet food.

A few in vitro studies show beneficial effects and support the chondroprotective effect. Some evidence exists that diets supplemented with green-lipped mussel extract, glucosamine hydrochloride and chondroitin sulfate improves mobility in cats with joint disease.

Bioavailability and pharmacokinetic data, although limited, suggest that when combined, the compounds are absorbed in dogs and that there is accumulation after multiple dosing, suggesting a possible residual effect. This is consistent with in vivo studies and the two compounds may therefore be more beneficial when used together.
### Table 1: Evidence Summary

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Participants (n)</th>
<th>Study Design &amp; Measures</th>
<th>Intervention</th>
<th>Findings/Conclusions</th>
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<tbody>
<tr>
<td>Lascelles, et al. 2010</td>
<td>40 cats (20 in each diet group)</td>
<td>10-week, blinded, parallel group, placebo controlled clinical study; owner-completed subjective surveys (activity-related behaviors); objective measures were captured using accelerometry</td>
<td>Cats were stratified based on high/low mobility impairment, then randomized to either a controlled-diet or degenerative joint disease-diet (green-lipped mussel extract and glucosamine/chondroitin sulfate) based on pain rating using a block design; investigators were blinded.</td>
<td>Evaluation of the owner’s assessments revealed there were significant activity changes within groups and between groups, however, author acknowledges that type I error could have resulted. Objective measures revealed increased mobility for the test-diet ($P&lt;0.001$) and a decreased in mobility for the controlled-diet ($P&lt;0.001$)</td>
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<td>Aragon, et al. 2007</td>
<td>Systematic review of 16 studies</td>
<td>Examined a number of clinical trials that evaluated the efficacy of various joint disease treatments and of those, one study was reviewed that examined the efficacy of a mixture of chondroitin sulfate, glucosamine hydrochloride and manganese ascorbate</td>
<td>Quality rated a randomized, controlled trial (study design type I) involving 19 dogs that were given a combination of chondroitin sulfate, glucosamine hydrochloride and manganese ascorbate.</td>
<td>Results of the study indicated no improvement subjectively or objectively compared with dogs receiving placebo, and it was quality rated as insufficient for generalization.</td>
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<tr>
<td>McCarthy et al. 2006</td>
<td>35 dogs</td>
<td>70-day randomized, double-blind, positive-controlled, multicenter clinical trial</td>
<td>Dogs were randomly assigned to two treatment groups: 1) Chondroitin sulfate/glucosamine hydrochloride (Synoquin® SA, Vet Plus Ltd.) or 2) Carprofen (Rimadyl®, Pfizer). Interval subjective assessments were conducted by veterinarians using a clinical scoring system.</td>
<td>Significant improvements ($P&lt;0.001$) in pain, weight-bearing and overall condition scores were found at day 70 when compared to pre-treatment assessment scores</td>
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<td>Neil, et al. 2005</td>
<td>n/a</td>
<td>Review article</td>
<td>Provide veterinary practitioners with information regarding the mechanism of action, pharmacokinetics, clinical efficacy, and safety of glucosamine and chondroitin sulfate</td>
<td>When used in combination in vitro, results support the chondroprotective effect. Orally administered glucosamine and chondroitin sulfate are rapidly absorbed in dogs. For both glucosamine and chondroitin sulfate, safety profiles are good and seem to have few side effects, may be a good alternative to nonsteroidal anti-inflammatory drugs (NSAIDs). Beneficial effects of glucosamine and chondroitin sulfate, alone and in combination, have been established in vitro in several species. Determination of the minimal effective concentration of these compounds and beneficial effects in dogs and cats require further investigation.</td>
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Table 1: Evidence Summary (cont’d)

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<tr>
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| Adebowale, et al. 2001 | 8 Beagle dogs | Characterized the bioavailability and pharmacokinetics of chondroitin sulfate and glucosamine by performing a single dose bioavailability and dose proportionality study and a multiple dose pharmacokinetic study | Study 1) Randomized three-way crossover study with a one-week washout period between treatments  
• Dogs randomly assigned to one of three treatments
1. IV solution of 500 mg glucosamine HCL and 400 mg of low molecular weight chondroitin sulfate
2. Product equivalent to 3 double strength Cosequin®/Cosamin® caps
3. Product equivalent to 4 double strength Cosequin®/Cosamin® caps
• Blood and plasma samples were analyzed  
Study 2) Multiple dose open study  
• Dogs received a supplement equivalent to 3 double strength Cosequin®/Cosamin® caps from days 1 to 7 and then received a supplement equivalent to 6 double strength Cosequin®/Cosamin® caps from days 8 to 14  
• Blood and plasma samples were analyzed | This study revealed that glucosamine and chondroitin sulfate are bioavailable after oral dosing and low molecular weight chondroitin sulfate results in significant accumulation upon multiple dosing. |

REFERENCES

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Ashlee Addleman, MPH, graduated from Portland State University in 2004 with a Bachelor of Science degree in Community Health Studies and received her Master of Public Health degree from Walden University in 2010. Her master’s practicum and dissertation focused on research synthesis, population-based research, and evidence-based medicine and practice. Ashlee joined the Banfield Applied Research & Knowledge team as a research project specialist in 2006 and has been with Banfield, The Pet Hospital, since 2002.