Glucosamine and chondroitin are widely promoted and sold as food supplements for cats, dogs, horses and rabbits. They are claimed to help cartilage production and maintain healthy joints, and are used in veterinary medicine to treat animals with osteoarthritis. But are they safe, effective and worth the cost? What evidence is there that they can help the symptoms of osteoarthritis in animals?
**Background**

Osteoarthritis is a slowly progressive, degenerative and, sometimes, incapacitating disease, in which the rate of synthesis of joint cartilage is reduced and cartilage degeneration increased. There is no known curative treatment. Management options in animals include prescribing nonsteroidal anti-inflammatory drugs (NSAIDs), and advising rest, weight loss, physiotherapy, hydrotherapy and the use of food supplements (such as glucosamine and chondroitin).

Glucosamine ($\text{C}_6\text{H}_{13}\text{NO}_5$) is an amino monosaccharide, which is synthesised in the body from glucose and glutamine. It is a building block for glycosaminoglycans, which make up the extracellular matrix of joint cartilage. Chondroitin is a polymer of repeating disaccharide units (galactosamine sulphate and glucuronic acid). It is the predominant component of joint cartilage and is a natural constituent of several other body tissues including tendons, bones and vertebral discs.

**The rationale**

In vitro studies have shown that glucosamine stimulates glycosaminoglycan, proteoglycan and collagen production thereby modulating cartilage metabolism, improving cartilage integrity and increasing cartilage matrix synthesis.\(^1\)–\(^4\) Chondroitin competitively inhibits enzymes that degrade proteoglycans in cartilage and synovium.\(^4\) It increases the viscosity, concentration and hydrodynamic size of hyaluronate (a glycosaminoglycan). There is some evidence that glucosamine and chondroitin have synergistic effects, and the combination has been shown to protect against chemically-induced synovitis in an experimental model in dogs.\(^5\) However, the exact mechanism of action of glucosamine and chondroitin as supplements is not understood. Both glucosamine and chondroitin are absorbed after oral dosing.\(^6\) Glucosamine diffuses into all body tissues and concentrates in liver, kidneys and articular cartilage.\(^7\) Glucosamine is excreted mainly in expired air as CO$_2$, and in the urine both in unchanged form and as metabolites.\(^7\)

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**Nutraceuticals, not medicines**

Oral glucosamine and chondroitin are marketed in the UK as ‘nutraceuticals’, a term (with no official definition) often applied to food supplements used with the aim of preventing or treating disease. In Europe, no specific indications can be legally recognised for nutraceuticals because no official evidence of efficacy or safety is required to market them. In the UK, several glucosamine preparations are authorised as medicinal products for use in humans for the relief of symptoms in mild to moderate osteoarthritis of the knee, but no glucosamine/chondroitin preparations are licensed as medicines for use in animals. Glucosamine is part of the structure of the polysaccharides chitosan and chitin, which make up the exoskeletons of crustaceans and other arthropods. It is produced commercially by the hydrolysis of crustacean exoskeletons or, less commonly, by fermentation of a grain such as corn or wheat.

Commonly sold forms of glucosamine include glucosamine sulphate, glucosamine hydrochloride and N-acetylglucosamine. Chondroitin in supplement preparations is generally made from animal (bovine, shark, poultry) cartilage. Glucosamine is commonly sold in combination with chondroitin, but it is sometimes combined with other substances, including curcumin (natural antioxidants), vitamins E and C, fish oil, methylsulphonylmethane (MSM), manganese and purified type II collagen. Such preparations are available in the form of capsules, tablets, powders and feed additives. As unlicensed products, their content is not standardised. A study of glucosamine supplements on sale in Canada found great variation (42%–108%) between the amounts of glucosamine contained in the products compared with that described on the labels.

**What should we expect of efficacy trials**

There is a large caregiver placebo effect in osteoarthritis therapy and so it is important to include objective measures of treatment effect. Subjective outcome measures are also useful because they measure different aspects of treatment, but it is important to include a control group to help mitigate the caregiver placebo effect in subjective measures. Any beneficial effects of glucosamine/chondroitin would be expected to take several weeks to appear therefore efficacy trials should last at least 4 weeks. In a clinical trial (assessing a different active treatment in osteoarthritis), a sample size of 25 dogs per group was calculated as needed to detect a 10% difference in peak vertical force (an objective measure of gait measured with a force plate) between an active treatment and placebo with a power of 80%.

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Clinical trials in dogs

In one double-blind trial, 71 dogs with moderate–severe osteoarthritis were randomised to treatment for 60 days with capsules containing glucosamine hydrochloride 500mg + chondroitin sulphate 400mg + manganese 75mg (CS-G-M) (Cosequin-GS), or a NSAID (meloxicam 0.2mg/kg on day 1 then 0.1mg/kg daily, or carprofen 2.2mg/kg twice daily) or placebo.12 Ground reaction forces measured with a force plate were compared before treatment and at 30 and 60 days. These were significantly improved by carprofen and meloxicam but not by CS-G-M. There were no significant changes in biochemical and haematological parameters with either CS-G-M or meloxicam; one dog on carprofen developed toxic hepatitis, which the researchers considered was due to the treatment. This trial is of high quality with regard to reporting of the methodology, such as inclusion and exclusion criteria and description of the outcomes of interest. The study was sponsored by Boehringer Ingelheim, which markets meloxicam. Another randomised, double-blind trial lasting 70 days included 42 dogs with osteoarthritis of the hips or elbows.13 The study was designed to compare the efficacy of a combination of oral glucosamine hydrochloride + chondroitin sulphate (the brand Synoquin SA) with the NSAID carprofen (at a loading dose of 2mg/kg twice daily for 7 days, then 2mg/kg once daily). Dogs were re-examined on days 14, 42, and 70 after the start of treatment. Medication was then withdrawn and the dogs re-assessed on day 98. Response to treatment was based on subjective evaluation of five parameters (lameness, joint mobility, pain on palpation, weight-bearing and overall score) by veterinarians using a score of 1–5 for each parameter. By day 70, with glucosamine + chondroitin, the clinical scores for lameness and joint mobility improved by a median of 0.5, while those for pain, weight bearing and overall condition improved by 1.0. For carprofen, the scores for all five parameters improved by a median of 1.0. The difference in the change in scores between the two treatments was not statistically significant. The study was sponsored by VetPlus Ltd, which markets Synoquin SA. There are several limitations with the report of this trial which raise questions about its quality. Inclusion and exclusion criteria were vague with no stated exclusion of dogs that had been treated surgically, or that had received previous medication; there were no defined age or weight limits and the primary outcome of interest was not clearly defined.

Trials in other species

There are many published randomised controlled trials of glucosamine and chondroitin in the treatment of osteoarthritis in humans. Overall, these show no significant clinical benefit for the supplements in osteoarthritis.14,15 There are few published reports of trials of glucosamine and chondroitin in other species. In a published review of trials on the use of glucosamine in horses with osteoarthritis, only three out of 15 studies were considered of good quality. The review’s authors concluded that the lack of quality studies in horses prohibits meaningful interpretation of the results.16 There appear to be no published trials assessing the effects of glucosamine or chondroitin alone or in combination in cats and rabbits.
Adverse effects

The most commonly reported adverse effects with glucosamine/chondroitin supplements are gastrointestinal. Glucosamine and chondroitin caused minor but not clinically important haematologic and haemostatic changes when given to young healthy beagle dogs for 30 days. Since glucosamine is an amino monosaccharide, in theory it could interfere with glucose metabolism or the management of diabetes. Studies have shown that parenteral administration of glucosamine can induce insulin resistance in skeletal muscle in normal rats. However in a short term study (21 days) evaluating the effects of oral glucosamine and chondroitin in healthy dogs, there were no significant changes in serum fructosamine.

Conclusion

The two published clinical trials of glucosamine + chondroitin in dogs with osteoarthritis have produced contradictory results, with the better quality trial (which was larger, with more objective assessment) finding no beneficial effect. In cats, horses and rabbits there is insufficient evidence to judge the efficacy of these supplements. Although there appears to be no risk of serious adverse effects from using glucosamine and chondroitin, the limited evidence on efficacy makes it difficult to recommend their routine use as a treatment to alleviate the clinical signs of osteoarthritis in animals.

What to say to clients

There is no known curative treatment for osteoarthritis. Weight loss, exercise moderation and NSAIDs can help. Although there is some scientific rationale supporting the use of the supplements in joint disease, there is insufficient evidence to show that they have any beneficial effect in animals with osteoarthritis. There is also no evidence that their use causes any significant harm. If clients want to try the supplements for their animals, they should not expect to see any improvement for several weeks. If there is no improvement after, say 2–3 months, they should consider whether it is worth continuing to use the supplements. Money spent on these could instead be used to help pay for other treatments, such as reduced energy density foods which can help to achieve weight loss in dogs and cats, urine and blood tests to increase safety in using NSAIDs, hydrotherapy, omega-3 fatty acid supplements (for which there is some evidence of efficacy in osteoarthritis), or to fund surgery in suitable cases.
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