CPD article

Nutraceutical use in osteoarthritic canines: a review

Osteoarthritis is prevalent in the UK canine population and has a clear impact on animal welfare. Treatment of osteoarthritis is advised to be multimodal, with nutraceuticals becoming a popular part of this approach. However, veterinary nutraceuticals are not subject to any regulation and systematic reviews are still uncommon in the veterinary field, which makes evaluating these products difficult. This article looks at the most commonly used veterinary supplements and how to critically evaluate the evidence of their efficacy. Evidence is promising for omega-3 fatty acids but is limited for other common ingredients. There are limited numbers of rigorous, randomised controlled trials and veterinary studies are often hampered by small sample sizes. Standardisation of reporting, as performed in human medicine, is needed to allow more robust systematic reviews of nutraceuticals to subsequently enable vets to make more informed decisions.

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Osteoarthritis is a condition that every first opinion vet will have frequently encountered. Prevalence rates in published papers have varied wildly, with most reporting between 20 and 30% of the canine population aged over 1 year displaying some radiographic degree of osteoarthritis (Paster et al, 2005; Aragon et al, 2007; Comblain et al, 2016) and up to 40% of all cats being affected clinically, increasing to 90% of cats over 12 years of age (Lascelles, 2010).

The largest study of osteoarthritis in dogs under veterinary care was conducted recently by VetCompass, covering 455 557 dogs. The results showed a lower prevalence of 2.5% of dogs being recorded with clinical and or radiographic signs of osteoarthritis in 2013 (Anderson et al, 2018). However, this still equates to 200 000 affected dogs in the UK annually. By looking at the frequency, duration and severity of clinical signs all together, osteoarthritis was found to be one of three conditions that had the highest welfare impact overall on dogs. Obesity was one of the other top three conditions affecting animal welfare and it is worth noting that overweight dogs had 2.3 times the risk of developing osteoarthritis.

Take the example of Barney, the 9-year-old overweight chocolate Labrador Retriever, presenting with a right thoracic limb lameness. On clinical examination, pain is detected on elbow extension and there is a decreased range of motion in both hip joints. Radiography of the hips and elbows finds peri-articular new bone formation affecting these joints, consistent with osteoarthritis. Most importantly, Barney needs to lose some weight, but what else can we do to help? Although osteoarthritis is commonly initiated in early life, secondary to developmental disease (such as hip dysplasia), the condition is multifactorial in its progression, with diet, genetics, environment, age and obesity all playing a role (Sanderson, 2012; Innes et al, 2018). In the VetCompass study, 75% of cases were recommended pain relief (Anderson et al, 2018) and there are no shortage of peer-reviewed studies demonstrating the efficacy of non-steroidal anti-inflammatories (NSAIDs) for the treatment of canine and feline osteoarthritis (Vasseur et al, 1995; Innes et al, 2010). However, Barney's owner takes glucosamine for her arthritis and has read some amazing things on the internet about cannabinoids for the treatment of osteoarthritis, subsequently she asks whether nutraceuticals or dietary supplements really work? This article looks at the most common veterinary supplements and how to critically evaluate the evidence of their efficacy.

What is a nutraceutical?

The term nutraceutical is derived from the combination of the word nutrition and pharmaceutical and is often used in the literature. However, its definition lies in a grey area between food, food supplement and pharmaceutical. Stephen DeFelice coined the term and described it as 'a food (or part of a food) that provides medical or health benefits, including the prevention and/or treatment of a disease' (DeFelice, 1995). The term is

not recognised by the US Food and Drug Administration and European Food Safety Authority, who instead prefer the term 'dietary or food supplement' (Halsted, 2003; Santini et al, 2018). Regulatory differences exist between medicines and nutraceuticals, particularly in that no evidence of efficacy has to be demonstrated in order to market nutraceuticals. In contrast to humans, veterinary dietary supplements are not subject to any regulation (Vandeweerd et al, 2012; Comblain et al, 2016).

Osteoarthritis has a clear impact on animal welfare and so it is important to understand the efficacy of nutraceuticals that are used in veterinary medicine in order to ensure animal welfare is not compromised. Systematic reviews, such as those standardised in human medicine (Glasziou et al, 2001), are still uncommon in the veterinary field, which makes evaluating these products difficult. Much of the veterinary literature uses clinical signs for the evaluation of treatments, which can be biased by the caregiver placebo effect and natural fluctuations in arthritic signs, which can artificially inflate the perceived effect of the treatment (Conzemius and Evans, 2012). The caregiver placebo effect for dogs with osteoarthritis was documented to be approximately 57% for owners and 40–45% for veterinarians, which must be kept in mind when evaluating owner responses, clinical research reports and clinical trials that do not contain a control group.

Tips for evaluating an osteoarthritis paper

- Randomised, double-blind, controlled trials are the gold standard (level one studies) and are the most scientifically rigorous method of hypothesis testing available (Akobeng, 2005).
- Force plate data or objective clinical metrology instruments, such as the Liverpool Osteoarthritis in Dogs questionnaire (Walton et al, 2013), are key. While the placebo effect is unlikely in animals themselves, it may become a factor when owners and/or veterinary surgeons are providing subjective outcome data (Cockcroft and Holmes, 2008). In a double-blind randomised study, the lack of correlation between owner assessment and force plate data suggests owners focus on behaviours other than lameness when making efficacy evaluations in their dogs (Brown et al, 2013).
- Is there adequate follow up? Studies must be long enough for any realistic outcome to become evident. In veterinary practice, a small drop-out or 'attrition' rate might reasonably be expected, but any study where a high level of dropout is reported should be reviewed with caution (Cockcroft and Holmes, 2008).

There are now many veterinary nutraceuticals that are targeted for the management of osteoarthritis, but evaluating which one is the most effective, if any at all, is challenging. As such, it can be difficult to know how best to advise a client as to what they can use as part of a multimodal approach to osteoarthritis. It is important to note that nutraceuticals are not a replacement for NSAIDs and bodyweight optimisation; no studies have proven that a dietary supplement can outperform an NSAID (Alves et al, 2017). Vets need to examine the recent data for the most commonly included nutraceutical ingredients, so they can educate and provide their clients with evidence-based medicinal options for them to choose from.

Curcumin

Curcumin is the major component of the spice turmeric and is certainly not a new supplement, as its use originated from traditional Chinese medicine (Henrotin et al, 2010). There seems to have been a surge in popularity for this yellow spice, derived from the roots of the *Curcuma longa* plant, with many owners asking about its efficacy and new companion animal turmeric supplements, such as TurmOil by the Golden Paste Company, being released in 2020.

Many in vitro studies document the anti-oxidant properties of curcumin and the anti-inflammatory effects on different cell culture models (Henrotin et al, 2010; Comblain et al, 2016). One of the main concerns is the uncertain bioavailability of natural curcumin in the dog and lack of clinical data regarding its efficacy. Two randomised, blinded, placebo-controlled studies demonstrated no statistical differences in ground reaction forces between dogs receiving dogs receiving curcuminoid extract and a placebo group (Innes et al, 2003; Comblain et al, 2017).

Green lipped mussel

Green lipped or Greenshell mussels are endemic to the coastal waters of New Zealand and have been extensively studied in medical trials, including in dogs suffering with osteoarthritis. In several studies, green lipped mussel has been shown to improve mobility and movement and decrease pain in dogs, compared with a placebo group (Vandeweerd et al, 2012; Comblain et al, 2016). Two studies used objective measures of assessment with force plate data to demonstrate a beneficial effect (Hielm-Björkman et al, 2009; Rialland et al, 2013). A single-blind, placebo-controlled study did find contradictory results, reporting that green lipped mussel made no distinct improvement to recorded symptoms (Dobenecker et al, 2002). It is always challenging to directly compare studies because of differences in study design, with differences in dosages and administration methods making meta-analysis impossible.

Overall, no adverse effects of using green lipped mussel were reported and there is moderately strong evidence that animals demonstrate beneficial effects with doses between 4-49mg/kg/day, depending on the formulation of the extract (Eason et al, 2018). Beneficial activity has been linked to key active ingredients including omega-3 polyunsaturated fatty acids.

Polyunsaturated fatty acids (omega-3)

Polyunsaturated fatty acids can be classified as omega-3, omega-6 and omega-9. Omega-3 fatty acids are present in fish oils, flaxseeds and walnuts and are most commonly studied in regard to canine osteoarthritis. Omega-3 fatty acids, particularly eicosapentaenoic acid and docosahexaenoic acid, modulate the expression and activity of inflammatory factors that cause cartilage destruction during arthritis, such as proteoglycan degrading enzymes (aggrecanases) and cytokines (cyclooxygenase-2 and interleukin-1α) (Curtis et al, 2000).

Four randomised controlled studies demonstrated a significant effect on clinical signs of osteoarthritis in dogs fed commercial diets with a high ratio of omega-3 to omega-6 fatty acids. These studies were of high quality and found a significant effect on clinical signs

of osteoarthritis. They reported reductions in carprofen dosage needed and improvements in mean peak vertical force in the group of dogs fed commercial diets with a high ratio of omega-3 (Fritsch et al, 2010a, 2010b; Roush et al, 2010a, 2010b). However, in addition to the force plate data, some of the conclusions were drawn from owner questionnaires using subjective scores and no validated objective scoring system. These trials were funded by a dog food manufacturer, while this does not draw the data into question, the authors of this paper do not know if there were any data from these trials that was not published.

Recent studies examining dogs postoperatively, following tibial plateau levelling osteotomy, concluded that dogs fed omega-3 fatty acid and protein enriched diets demonstrated greater peak vertical force and had lower synovial fluid prostaglandin concentrations than dogs in a control group (Baltzer et al, 2018; Verpaalen et al, 2018).

Hielm-Björkman et al (2012) also found greater peak vertical force values and quality of life score, using a validated owner questionnaire, in dogs fed a deep sea fish oil supplement, with a reduction of NSAID consumption, but no significant or beneficial impact on pain relief compared with placebo.

In human literature, a large meta-analysis found a benefit of fish oil supplementation in rheumatoid arthritis (Calder and Zurier, 2001). Overall, there is moderate-to-good strength evidence that diets or supplements rich in polyunsaturated fatty acids, particularly omega-3, will be beneficial in dogs with osteoarthritis.

Glucosamine and chondroitin

Glucosamine and chondroitin are aminosaccharides that are commonly recommended as nutraceuticals. They exert anti-inflammatory and anti-catabolic effects in vitro and these effects have led to hypotheses regarding potential mechanisms of symptom control and cartilage structure modification in animals with osteoarthritis (Henrotin and Lambert, 2013). It should be noted that human and veterinary products differ and that the majority of veterinary products contain glucosamine hydrochloride I, which is known to have poorer bioavailability and clinical effects in humans (Beale, 2004). This is likely because the hydrochloride salt is cheaper to produce and provides a greater amount of glucosamine per gram, despite the lower oral bioavailability.

Studies differ in their findings in dogs with osteoarthritis, with one study finding no changes in ground reaction force in dogs given the glucosamine nutraceutical but significant improvement in dogs given carprofen and meloxicam (Moreau et al, 2003). Another study concluded that dogs treated with glucosamine/chondroitin showed statistical improvements in pain scores by veterinarians (McCarthy et al, 2007). This paper did not use force plate data as an objective outcome measure and the scoring system was subjective and unvalidated.

A recent systematic review of glucosamine and chondroitin concluded that the potential benefits in osteoarthritic dogs could neither be confirmed or denied, as there were mixed results in clinical trials. Several trial shortcomings, such as the absence of standardisation and the risk of funding bias, led to questionable validity (Bhathal et al, 2017). The review went on to propose a future study design for a veterinary randomised clinical trial.

In human literature, data supporting the efficacy of glucosamine and chondroitin is similarly lacking. A large meta-analysis concluded that there was no effect on joint pain compared with placebo and discouraged prescriptions containing glucosamine or chondroitin (Wandel et al, 2010), while another found that there was a very small benefit compared with placebo of chondroitin alone, but that the studies claiming this were mostly of a lower quality (Singh et al, 2015).

Cannabinoids

The endocannabinoid receptor system has been known to play a role in pain modulation and attenuation of inflammation for some time (Maione et al, 2011). The two active cannabinoids with the most compelling evidence for their use as analgesia are tetrahydrocannabinol (THC) and cannabidiol (CBD). However, THC also has psychoactive effects and is derived from cannabis, which is illegal in the UK, so most studies in companion animals look at CBD oil derived from hemp.

CBD oil has not been approved by the Veterinary Medicines Directorate or Food Standards Agency and as of September 2018, CBD products have been classified as a veterinary medicine, therefore cannot be administered without a veterinary prescription. Vets are only able to prescribe human CBD oil products under the veterinary cascade.

Conclusive scientific evidence that CBD oil is beneficial to dogs with osteoarthritis is limited. One study used a 2 mg/kg dose in an oil-based product and found a significant change in baseline score of the Canine Brief Pain Inventory score, indicating a decrease in pain and an increase in activity. However, there was no significant difference in subjective veterinary lameness score and weight-bearing capacity throughout the study (Gamble et al, 2018).

A recent study found no difference in owner or veterinary assessment of pain when dogs were administered 20 mg/day of naked CBD, but found statistically significant reductions in pain symptomology, using the validated Helsinki Chronic Pain Index assessment, when naked CBD was administered at a 50 mg/day dose in a double-blind, placebo-controlled trial (Verrico et al, 2020). The same improvement was seen in a low dose liposomally encapsulated CBD, indicating formulation and dose are both important factors to consider. This study did not examine forceplate data and some variability was demonstrated between veterinary clinical assessment and owner assessment. The sample size was also very low, with only 20 dogs examined.

Conclusions

The veterinary nutraceutical industry is a large, unregulated industry, with new supplements entering the market yearly. There are some promising results relating to the benefits of omega-3 fatty acids and potentially green lipped mussel in dogs with osteoarthritis. However, there are limited numbers of rigorous, randomised controlled trials and veterinary studies are often hampered by small sample sizes. Standardisation of reporting is needed to allow for more robust systematic reviews, enabling vets to make more informed decisions.

KEY POINTS

- Osteoarthritis is prevalent in the UK canine population and has a high impact on the welfare of dogs.
- Veterinary nutraceuticals are not subject to any regulation and no evidence of efficacy has to be demonstrated in order to market nutraceuticals.
- Nutraceuticals are not a replacement for non-steroidal anti-inflammatory drugs and bodyweight optimisation, but can be used as part of a multimodal approach to osteoarthritis and vets should examine the evidence of their efficacy in order to best advise clients.
- Polyunsaturated fatty acids, particularly omega-3, has the most compelling evidence for its efficacy.
- There are limited numbers of rigorous, veterinary randomised controlled trials; standardisation of reporting is needed to allow for more robust systematic reviews and enable vets to make more informed decisions.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

Akobeng AK. Understanding randomised controlled trials. Arch Dis Childhood. 2005;90(8):840–844. https://doi.org/10.1136/adc.2004.058222

Alves JC, Santos AM, Jorge PI. Effect of an oral joint supplement when compared to Carprofen in the Management of hip Osteoarthritis in working dogs. Topics Companion Anim Med. 2017;32(4):126–129. https://doi.org/10.1053/j.tcam.2017.10.003

Anderson KL, O'Neill DG, Brodbelt DC et al. Prevalence, duration and risk factors for appendicular osteoarthritis in a UK dog population under primary veterinary care. Sci Rep. 2018;8(1):1–12. https://doi.org/10.1038/s41598-018-23940-z

Aragon CL, Hofmeister EH, Budsberg SC. Systematic review of clinical trials of treatments for osteoarthritis in dogs. J Amer Vet Med Assoc. 2007;230(4):514–521. https://doi.org/10.2460/javma.230.4.514

Baltzer WI, Smith-Ostrin S, Warnock JJ, Ruaux CG. Evaluation of the clinical effects of diet and physical rehabilitation in dogs following tibial plateau leveling osteotomy. J Amer Vet Med Assoc. 2018;252(6):686–700. https://doi.org/10.2460/javma.252.6.686

Beale BS. Use of nutraceuticals and chondroprotectants in osteoarthritic dogs and cats. Vet Clin North Amer. Small Anim Pract. 2004;34(1):271–289. https://doi.org/10.1016/j.cvsm.2003.09.008

Bhathal A, Spryszak M, Louizos C, Frankel G. Glucosamine and chondroitin use in canines for osteoarthritis: a review. Open Vet J. 2017;7(1):36–49. https://doi.org/10.4314/ovj.v7i1.6

Brown D, Boston R, Farrar J. Comparison of force plate gait analysis and owner assessment of pain using the canine brief pain inventory in dogs with osteoarthritis. J Vet Intern Med. 2013;27(1):22–30. https://doi.org/10.1111/jvim.12004

Calder PC, Zurier RB. Polyunsaturated fatty acids and rheumatoid arthritis. Curr Opin Clin Nutr Metab Care. 2001;4(2):115–121. https://doi.org/10.1097/00075197-200103000-00006

Cockcroft P, Holmes M. Handbook of evidence-based veterinary medicine. Hoboken (NJ), John Wiley and Sons; 2008

Comblain F, Serisier S, Barthelemy N, Balligand M, Henrotin Y. Review of dietary supplements for the management of osteoarthritis in dogs in studies from 2004 to 2014. J Vet Pharmacol Therap. 2016;39(1):1–15. https://doi.org/10.1111/jvp.12251

Comblain F, Barthélémy N, Lefèbvre M et al. A randomized, double-blind, prospective, placebo-controlled study of the efficacy of a diet supplemented with curcuminoids extract, hydrolyzed collagen and green tea extract in owner's dogs with osteoarthritis. BMC Vet Res. 2017;13(1):395. https://doi.org/10.1186/s12917-017-1317-8

Conzemius MG, Evans RB. Caregiver placebo effect for dogs with lameness from osteoarthritis. J Amer Vet Med Assoc. 2012;241(10):1314–1319. https://doi.org/10.2460/javma.241.10.1314

Curtis CL, Hughes CE, Flannery CR et al. n-3 fatty acids specifically modulate catabolic factors involved in articular cartilage degradation. J Biol Chem. 2000;275(2):721–724. https://doi.org/10.1074/jbc.275.2.721

DeFelice SL. The nutraceutical revolution: its impact on food industry R&D. Trends Food Sci Technol. 1995;6(2):59–61. https://doi.org/10.1016/S0924-2244(00)88944-X

Dobenecker B, Beetz Y, Kienzle E. A placebo-controlled double-blind study on the effect of nutraceuticals (chondroitin sulfate and mussel extract) in dogs with joint diseases as perceived by their owners. J Nutr. 2002;132(6):1690S–1691S. https://doi.org/10.1093/jn/132.6.1690S

Eason CT, Adams SL, Puddick J et al. Greenshell™ mussels: a review of veterinary trials and future research directions. Vet Sci. 2018;5(2):36. https://doi.org/10.3390/vetsci5020036

Fritsch D, Allen T, Dodd C et al. Dose-titration effects of fish oil in osteoarthritic dogs. J Vet Inter Med. 2010a;24(5):1020–1026. https://doi.org/10.1111/j.1939-1676.2010.0572.x

Fritsch DA, Allen TA, Dodd CE et al. A multicenter study of the effect of dietary supplementation with fish oil omega-3 fatty acids on carprofen dosage in dogs with osteoarthritis. J Amer Vet Med Assoc. 2010b;236(5):535–539. https://doi.org/10.2460/javma.236.5.535

Gamble L-J, Boesch JM, Frye CW et al. Pharmacokinetics, safety, and clinical efficacy of cannabidiol treatment in osteoarthritic dogs. Front Vet Sci. 2018;5:165. https://doi.org/10.3389/fvets.2018.00165

Glasziou P, Irwig L, Bain C, Colditz G. Systematic reviews in health care: a practical guide. Cambridge, Cambridge University Press; 2001

Halsted CH. Dietary supplements and functional foods: 2 sides of a coin? Amer J Clin Nutr. 2003;77(4):1001S–1007S. https://doi.org/10.1093/ajcn/77.4.1001S

Henrotin Y, Clutterbuck A, Allaway D et al. Biological actions of curcumin on articular chondrocytes. Osteoarthritis Cartilage. 2010;18(2):141–149. https://doi.org/10.1016/j.joca.2009.10.002

Henrotin Y, Lambert C. Chondroitin and glucosamine in the management of osteoarthritis: an update. Curr Rheumatol Rep. 2013;15(10):361. https://doi.org/10.1007/s11926-013-0361-z

Hielm-Björkman A, Tulamo R-M, Salonen H, Raekallio M. Evaluating complementary therapies for canine osteoarthritis part I: green-lipped mussel (Perna canaliculus). Evid-Based Compl Alternative Med. 2009;6(3):365–373. https://doi.org/10.1093/ecam/nem136

Hielm-Björkman A, Roine J, Elo K et al. An un-commissioned randomized, placebo-controlled double-blind study to test the effect of deep sea fish oil as a pain reliever for dogs suffering from canine OA. BMC Vet Res. 2012;8(1):157. https://doi.org/10.1186/1746-6148-8-157

Innes J, Fuller C, Grover E, Kelly A, Burn J. Randomised, double-blind, placebocontrolled parallel group study of P54FP for the treatment of dogs with osteoarthritis. Vet Rec. 2003;152(15):457–460. https://doi.org/10.1136/vr.152.15.457

Innes JF, Clayton J, Lascelles BDX. Review of the safety and efficacy of long-term NSAID use in the treatment of canine osteoarthritis. Vet Rec. 2010;166(8):226–230. https://doi.org/10.1136/vr.c97

Innes J, Tobias K, Johnston S. Veterinary surgery: small animal. St. Louis, MO: Elsevier Saunders; 2018:1265–1299

Lascelles BDX. Feline degenerative joint disease. Vet Surg. 2010;39(1):2–13. https://doi.org/10.1111/j.1532-950X.2009.00597.x

Maione S, Piscitelli F, Gatta L et al. Non-psychoactive cannabinoids modulate the descending pathway of antinociception in anaesthetized rats through several mechanisms of action. Br J Pharmacol. 2011;162(3):584–596. https://doi.org/10.1111/j.1476-5381.2010.01063.x

McCarthy G, O'Donovan J, Jones B et al. Randomised double-blind, positive-controlled trial to assess the efficacy of glucosamine/chondroitin sulfate for the treatment of dogs with osteoarthritis. Vet J. 2007;174(1):54–61. https://doi.org/10.1016/j.tvjl.2006.02.015

Moreau M, Dupuis J, Bonneau N, Desnoyers M. Clinical evaluation of a nutraceutical, carprofen and meloxicam for the treatment of dogs with osteoarthritis. Vet Rec. 2003;152(11):323–329. https://doi.org/10.1136/vr.152.11.323

Paster ER, Lafond E, Biery DN et al. Estimates of prevalence of hip dysplasia in Golden Retrievers and Rottweilers and the influence of bias on published prevalence figures. J Amer Vet Med Assoc. 2005;226(3):387–392. https://doi.org/10.2460/javma.2005.226.387

Rialland P, Bichot S, Lussier B et al. Effect of a diet enriched with green-lipped mussel on pain behavior and functioning in dogs with clinical osteoarthritis. Can J Vet Res. 2013;77:66–74

Roush JK, Cross AR, Renberg WC et al. Evaluation of the effects of dietary supplementation with fish oil omega-3 fatty acids on weight bearing in dogs with osteoarthritis. J Amer Vet Med Assoc. 2010a;236(1):67–73. https://doi.org/10.2460/javma.236.1.67

Roush JK, Dodd CE, Fritsch DA et al. Multicenter veterinary practice assessment of the effects of omega-3 fatty acids on osteoarthritis in dogs. J Amer Vet Med Assoc. 2010b;236(1):59–66. https://doi.org/10.2460/javma.236.1.59

Sanderson S. The epidemic of canine obesity and its role in osteoarthritis. Israel J Vet Med. 2012;67:195–202

Santini A, Cammarata SM, Capone G et al. Nutraceuticals: opening the debate for a regulatory framework. Br J Clin Pharmacol. 2018;84(4):659–672. https://doi.org/10.1111/bcp.13496

Singh JA, Noorbaloochi S, Macdonald R, Maxwell LJ. Chondroitin for osteoarthritis. Cochrane Database Syst Rev. 2015;28(1):CD005614. https://doi.org/10.1002/14651858.cd005614.pub2

Vandeweerd JM, Coisnon C, Clegg P et al. Systematic review of efficacy of nutraceuticals to alleviate clinical signs of osteoarthritis. J Vet Intern Med. 2012;26(3):448–456. https://doi.org/10.1111/j.1939-1676.2012.00901.x

Vasseur PB, Johnson A, Budsberg S et al. Randomized, controlled trial of the efficacy of carprofen, a nonsteroidal anti-inflammatory drug, in the treatment of osteoarthritis in dogs. J Amer Vet Med Assoc. 1995;206(6):807–811

Verpaalen VD, Baltzer WI, Smith-Ostrin S et al. Assessment of the effects of diet and physical rehabilitation on radiographic findings and markers of synovial inflammation in dogs following tibial plateau leveling osteotomy. J Amer Vet Med Assoc. 2018;252(6):701–709. https://doi.org/10.2460/javma.252.6.701

Verrico CD, Wesson S, Konduri V et al. A randomized, double-blind, placebo-controlled study of daily cannabidiol for the treatment of canine osteoarthritis pain. Pain. 2020;161(9):2191–2202. https://doi.org/10.1097/j.pain.0000000000001896

Walton MB, Cowderoy E, Lascelles D, Innes JF. Evaluation of construct and criterion validity for the 'Liverpool Osteoarthritis in Dogs'(LOAD) clinical metrology instrument and comparison to two other instruments. PLoS One. 2013;8(3):E58125. https://doi.org/10.1371/journal.pone.0058125

Wandel S, Jüni P, Tendal B et al. Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: network meta-analysis. BMJ. 2010;341(sep16 2):c4675–c4675. https://doi.org/10.1136/bmj.c4675