



Robyn J. Lowe RVN

I am a Registered Veterinary Nurse who qualified with a degree from Myerscough School of Veterinary Nursing in 2016 and have started my RCVS Diploma in Advanced Veterinary Nursing in 2018. I have worked on a volunteer basis with animals since I was four and my passion for this profession has only grown since then. I spent years of my life at the Horse and Pony Protection Association (HAPPA) and later at a local rescue and rehabilitation yard. Here I met a veterinary surgeon who inspired me, and I went for my first work experience in 2008 at the busy mixed practice where they worked. I have also travelled to Thailand to volunteer my knowledge and skills working with elephants, horses, goats, pigs, water buffalo, cats and dogs. One of my interests in practice is arthritis, I love osteoarthritis clinics and using multimodal approaches to managing the condition, it can be extremely rewarding seeing both owners and patients travel this extremely difficult journey together to improve quality of life for their pet. Email: robynbythe@btinternet.com

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Evidence for the use of supplements in canine arthritis management

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ABSTRACT: Supplements are easily accessible to the general public; there are adverts everywhere for them. The main concern is that very often people seem to have a misconception that they are appropriate as a replacement for conventional analgesic medication when a diagnosis of arthritis is found, but at the present time there does not appear to be enough evidence to suggest this. This article aims to examine the evidence for the use of supplements in canine arthritis management

Keywords: Supplements; caregiver placebo; arthritis

Supplements are easily accessible to the general public; there are adverts everywhere for them. They are available in pet shops, online, on forums and in our practices. The main concern is that very often people seem to have a misconception that they are appropriate as a replacement for conventional analgesic medication when a diagnosis of arthritis is found, but at present time there does not appear to be enough evidence to suggest this.

Supplementation/nutraceuticals

Some supplements or combinations of supplements may certainly be beneficial as one part of the multimodal approach to arthritis management. However they may not be appropriate as a sole intervention. Although some owners seem to have developed a fear of traditional medication, especially when considering it on a long term basis, I think it is important to remember that life should be measured by quality and it is important to educate owners on issues such as central sensitisation which can lead to exacerbated pain response if pain is not adequately controlled.

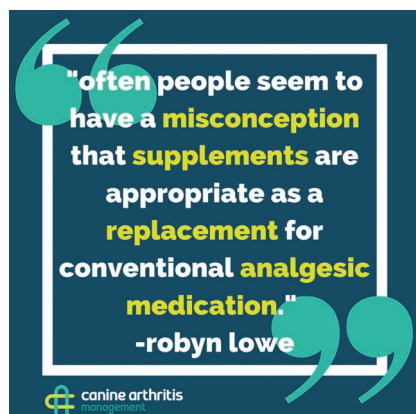
Registered Veterinary Nurses (RVNs) are in a position as part of canine arthritis clinics to discuss supplements, and help direct owner to products with more evidence should they wish to use supplements as part of their multi-modal approach. RVNs are also able to educate about bogus claims/products, and explain issues such as the placebo effect and why the placebo effect

could contribute to some of the anecdotal evidence seen in some cases. This will allow the RVN to educate the owner on the use of objective pain indicators so the owners are in a better position to assess the usefulness and effectiveness of a supplement.

Placebo effect

Caregiver placebo is a phenomenon where a client/owner or 'caregiver' believes they are seeing a marked improvement of health and welfare due to the fact they are giving a treatment, when in fact there is no marked change in the health of the animal. This means that the animal is no better, but the owner believes they are. This could seriously impact the animal's welfare and delay the use of treatments that will actually benefit the dog's health and welfare. We already know that caregiver placebo is extremely prevalent amongst our clients (and veterinary professionals). In one study a caregiver placebo effect was seen at 39.7% of the time for owners evaluating their dog's lameness (Conzemius & Evans, 2012). This highlights the need to warn clients of this issue and educate them to allow them to assess their dog from an independent and objective view point.

There are a huge amount of supplements on the market, below will focus on some commonly discussed, however there are many more not mentioned in this article. The author would encourage veterinary staff to take the time to help research these if a client asks so they can guide to more evidence based options if appropriate.



Omega-3 fatty acids

Nutraceuticals may be considered to aid in further support should the owner be keen to try. Perry (2019) suggests that omega-3 fatty acids have been highlighted as the only nutraceutical with a sound evidence base supporting its use in companion animals. Supplementation has been shown to have an ameliorative effect on OA in pet dogs, resulting in improved weight bearing. The theory is that by supplementing with increased levels of omega-3 encourages the replacement of omega-6 in cell walls. Thus there are less omega-6 fatty acids available for creating increased inflammation in and around the joint. The omega-3 fatty acids found to be effective in this role are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) which are from marine-based sources such as a fish oil.

There is substantial scientific evidence to support their use and recent studies have shown statistically significant mild improvement in owner perception of comfort and mobility.

In a study of 127 dogs with osteoarthritis, dogs fed a high omega-3 diets had improved ability to rise from a resting position and play, over a period of six months, compared to dogs fed a control diet (Roush et al., 2010a). It is important here to highlight the length of this study and that many of these supplement actions do not occur quickly or instantly. For this reason they are not appropriate substitute for medication for dogs experiencing pain. Secondly a further study on dogs fed a diet containing 3.5% omega-3 fatty acids for 90 days showed they had improved peak vertical force values (PVF) and subjective improvement in lameness and weight-bearing when compared with dogs on a control diet (Roush et al., 2010b). This could suggest that supplementing an arthritic dogs diet with omega-3, or feeding a high omega-3 diet could be an

appropriate intervention for an arthritic dog. Furthermore a clinical trial was performed where dogs with stable chronic arthritis who were already treated with Carprofen were fed a diet supplemented with omega-3. This found that they could take a significantly decreased dosage of Carprofen (Fritsch et al., 2010).

Green lipped mussel

Pascale et al, (2013) states that by analysis green lipped mussel (GLM) powder has been shown to contain glycosaminoglycans (chondroitin sulfate), amino acid (glutamine), omega-3 fatty acids including DHA and EPA (as demonstrated in the study as proof of absorption) and eicosatetraenoic acid, minerals (zinc, copper, manganese), and vitamins E and C. The results of this study showed that values of PVF improved significantly in parallel with increased concentrations of plasma DHA and EPA when dogs with OA were fed the GLM-enriched diet. Pascal et al, (2013) suggested that the findings highlighted the OA-modifying activity of a GLM-enriched diet. It was suspected that these components and others included in the diet, such as glucosamine, provided chondroprotective, antioxidant, and anti-inflammatory beneficial effects. They concluded that the study provides strong clinical evidence to support feeding osteoarthritic dogs a GLM-enriched diet. However, they did believe that the study failed to establish a positive effect of a GLM diet on client-specific outcome measure and motor activity values. Surprisingly, PVF, Client specific outcome measures (CSOM) and MA improved throughout the study, from D0 to D90, which suggests a cumulative positive effect of both the standardised control and the therapeutic diets on the assessments of pain and function.

Hjelm-Björkman et al., (2009) concluded that their results suggest that the modern stabilised and freeze-dried GLM is more effective than the placebo in treating chronic pain due to moderate to severe OA and that it has no side-effects. This could suggest that supplementation with a good quality GLM supplement may be beneficial as part of a multimodal arthritis management intervention.

Glucosamine

This is an extremely popular household name of an arthritis supplement for both humans and animals. It has been shown to potentially help repair joints as it is a building block of articular cartilage. However, there is still much debate as to what concentration will actually reach the joint and therefore if it will be any use.

There is a GAIT study in 2006 that suggested that glucosamine alone or with chondroitin sulphate did not perform better than placebo. This has now also been a long term study of 2 year and has also concluded 'over 2 years, no treatment achieved a clinically important difference in WOMAC pain or function as compared with placebo' (Sawitzke et al., 2010). However the Mayo Clinic (2017) suggests that 'oral use of glucosamine sulfate might provide some pain relief for people with osteoarthritis of the knee, hip or spine'. The NHS will no longer prescribe it following a study that looked at evidence in a number of clinical trials (CAM 2019).

In a recent review on glucosamine and chondroitin together it was concluded that 'although glucosamine and chondroitin have benign adverse effect profiles, the clinical benefit of using these agents remains questionable. The available evidence is difficult to interpret due to the use of different manufacturers, salt forms, compositions, sources, strengths, regimens, therapy durations, and combinations of active ingredients.' (Bhathal et al., 2017) meaning no harmful effects. This review discussed based on the available literature the potential benefits of glucosamine and chondroitin use in osteoarthritic canines can neither be confirmed nor denied. It is concluded that further clinical studies using improved methodology are required. The review believed that clinical trials conducted to date have yielded mixed results and this could have been down to shortcomings in the clinical trials. Skeldon (2018) concluded that should the owner wish to add in further supplementation, one small subjectively assessed study showed a positive clinical effect in the treatment of dogs with OA that had received glucosamine/chondroitin supplements so these could be considered.

Chondroitin sulphate

Chondroitin sulphate is extracted from mammalian cartilage. In a similar way to glucosamine it is believed to provide structural components for helping to repair the articular cartilage.

There appears to be only weak evidence of its effectiveness both structurally and in improving clinical condition of arthritis in dogs. It is often paired with glucosamine and or green lipped mussel. One review stated that a few in vitro studies have shown beneficial effects and support the chondroprotective effect. They stated that some in-vivo evidence exists that diets supplemented with glucosamine hydrochloride and chondroitin sulphate together

improves mobility in cats with joint disease. Furthermore it states that bioavailability and pharmacokinetic data is limited but suggests that when combined, the compounds are absorbed in dogs and that there is accumulation after multiple dosing, suggesting a possible residual effect. This is also confirmed by Musco et al. (2019) who stated 'there is evidence supporting that both these compounds (glucosamine and chondroitin) reach and retain a certain concentration in plasma and in joint fluid and cartilage. This statement is consistent with in vitro studies and therefore the two compounds may be more beneficial when used together. However as most evidence is in vitro despite the initial suggestions of their benefit, after looking at the data, they concluded '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' (Addleman, 2010).

Tumeric

Turmeric has been used throughout history as a natural anti-inflammatory. There have been in vitro studies on this claim; these studies suggest antioxidant and anti-inflammatory activity for curcumin and other constituents of turmeric. However it must be highlighted that in vitro studies can never fully prove a clinical benefit for patients. The National Center for Complementary and Alternative Medicine (NCCAM) stated, 'There is little reliable evidence to support the use of turmeric for any health condition because few clinical trials have been conducted' (Skeptvet 2013). A lot of focus is on one of its active ingredients called curcumin. However, there are other ingredients and there is some evidence that these possess anti-inflammatory properties. The most studied in terms of medical applications however, are the curcuminoids. Many of the studies that have been done in humans have focused on curcumin and have found that it is poorly absorbed when taken orally, for example stating that poor bioavailability reported by some investigators are a major limitation to the therapeutic utility of curcumin (Gupta et al., 2013). In one controlled study in dogs there was no objective difference but there was improvement in subjective indicators. There may be more studies emerging in the future to provide a more substantial evidence base.

Boswelia

Boswelia is extracted from the bark and resin of the Indian Boswelia tree. Interestingly

Boswelia resin has been evaluated in 24 dogs in an open multi-center study. Improvement in clinical signs, lameness, and pain was found in 17 of 24 dogs. This suggests that more research is necessary in order to confirm that Boswelia would be a truly beneficial addition to a regime (Reichling et al., 2004).

Devil's claw and cats claw

Musco et al., (2019) discusses that 'the anti-inflammatory activity of the Devil's claw may be critical in the symptomatic treatment of osteoarthritis'. However it is concluded in a review by Ameye & Chee (2006) that there is 'limited evidence found for... plant extracts from *Harpagophytum procumbens*' otherwise known as Devil's Claw. Furthermore Brian et al., (2006) concluded that 'the methodological quality of the existing clinical trials is generally poor... the clinical evidence to date cannot provide a definitive answer to the two questions posed: (1) Does it work? and (2) is it safe?' Therefore, it would be suggested that further evidence is warranted before suggesting Devil's Claw as evidence based intervention. The author cannot find evidence that Devil's Claw has been trailed successfully in dogs.

Looking at cat's claw the author was unsuccessful at finding any evidence for its use in dogs, in humans it has been concluded that there have been very few high quality clinical trials of cat's claw, and that there's no conclusive scientific evidence based on studies in people that supports using cat's claw for any health purpose (NCCIH, 2016).

Avocado and soybean unsaponifiables (ASUs)

CAM (2019) states that ASUs are relatively new supplements made from a specific part of the oil of avocados and from soybeans. It is believed to promote cartilage repair and reduce inflammation within the joint. It has been shown to reduce pain in human osteoarthritis, and improve joint health in horses. However, there are no clinical trials looking at it in dogs with established naturally occurring arthritis. It has been suggested that its role could be to manage articular cartilage management while relying on other forms of pain relief.

One human study concludes that at a clinical level, ASUs reduce pain and stiffness while improving joint function. It states that they address acute pain and actively prevent progression of OA symptoms. It does state however that further studies are required

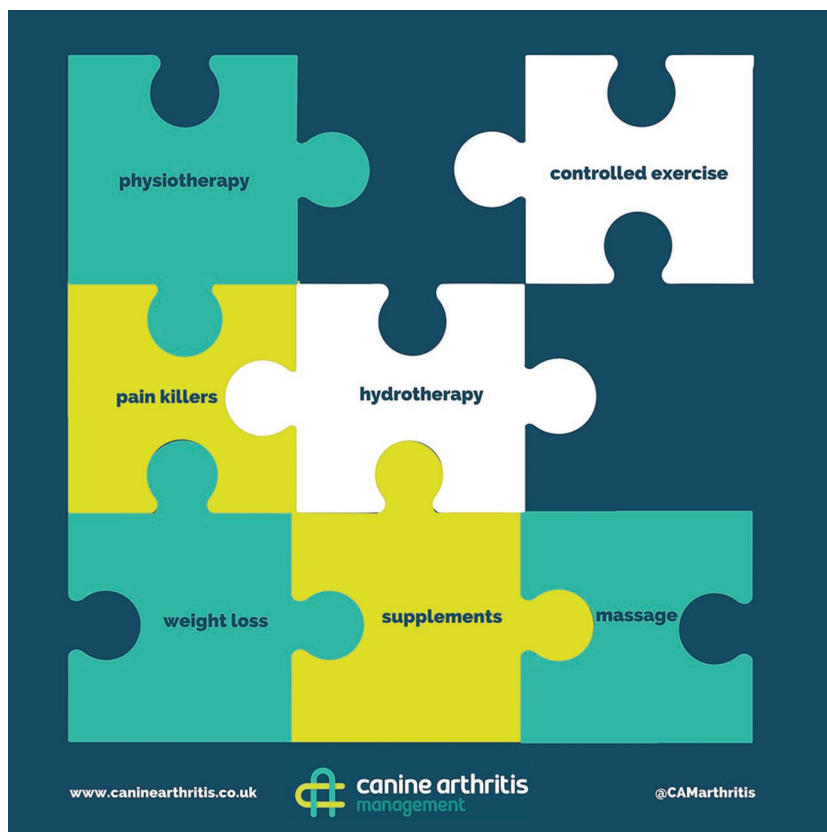
to determine the specific mechanisms and target molecules of ASU function on OA at the cellular and metabolic level. Trials in dogs are limited however, one study demonstrated that treatment with avocado/soybean unsaponifiables can reduce the development of early osteoarthritic cartilage and subchondral bone lesions in the anterior cruciate ligament dog model of osteoarthritis (Boileau et al., 2009). Another small study of artificially stimulated arthritis concluded morphometric analysis of cartilage tissue revealed more immature repair tissue with greater collagen and chondral tissue content in the regenerated tissue in the ASU-treated dogs as compared to the untreated dogs Altinel et al., (2011). As we have limited data in dogs it could be suggested that more substantial evidence is needed in naturally occurring arthritis before the extent of its use in canine arthritis management can be fully understood.

Supplements concluded

Clients must be made aware that the use of all these should only be used in conjunction with other multimodal strategies and can only be assessed fully following a substantial trail period of at least 2–3 months (CAM 2019). Many of these supplements have conflicting evidence to their effectiveness so should not be used as the only modality of treatment in these cases. Clients should also be made aware of the placebo effect, to allow them to objectively measure their dog's pain.

Additional medication or supplements being used without veterinary prescription or guidance affecting owner compliance in administering prescribed medications

It is also important to ask and consider if any other medications or nutraceuticals are being administered that veterinary staff are not aware of that could be impairing the management or causing poor compliance. It is important for owners to understand and appreciate joint supplements as aforementioned are not a replacement for pain relief and anti-inflammatory drugs. Hutchinson (2018) believe this is a common misconception that can be detrimental to the pet's well-being. If supplements or nutraceuticals are used, they should always be adjunctive to prescribed pain medication not instead of.



A product that is currently being discussed is cannabidiol (CBD). It is important to question regarding the use of CBD in pets, as many people are looking into alternatives and may be giving other medications that they have obtained without the knowledge of the prescribing VS causing compliance issues. Although a recent clinical study in OA dogs (Gamble et al., 2018) suggested that 2 mg/kg of CBD twice daily can help increase comfort and activity in dogs with OA, it is important to remember that the VDS currently state that 'as there are currently no CBD products authorised in the UK for veterinary use, a veterinary surgeon may prescribe a legally obtained human CBD product under the provisions of the prescribing cascade. Administration of an unauthorised product containing CBD without a veterinary prescription is an offence under Regulation 8 of the VMR. Companies supplying CBD products for human use in line with the requirements of the Medicines and Healthcare products Regulatory Agency must not indicate or recommend their products for use on animals (VMD, 2018)'. Tarr (2018) sums this up by stating that optimum dose is yet unknown and very little is known about the side effects, except that in the small published clinical trial liver enzymes were raised in more than half of the dogs while on CBD, this finding was also seen in a few other studies. In humans, CBD is metabolised by liver enzymes and so there is a potential for drug interactions, but whether the same

applies to dogs is not known as yet. Tarr (2018) concludes that there are currently too many uncertainties about whether CBD is fully beneficial for dogs with OA. A recent survey by the Centre of Medical Cannabis of 30 high street products revealed concerning results regarding the quality of these easily accessible products. One product had zero CBD in it and was retailing at £90. 11 had less than 50% of their stated CBD content. eight products had solvent and heavy metal contamination. One product had a dangerous level of ethanol in it, and 13 had illegal levels of THC in them. For a vs to prescribe a product, it would need to have independent laboratory testing, a traceable batch number and an independent certificate of analysis (CoA). The safest way to prescribe is using a pharmacy grade product as these are regulated by GMP (Good manufacturing Practice) and GDP (Good Distribution Practice) guidelines after following the cascade system. It is also important to be aware that as the VDS class as an animal medication it should not be given without a prescription. This is something that an RVN may need to address in a consult, explaining why this would be an inappropriate intervention, without the guidance and prescription from a VS.

Conclusion

Clearly there is still have a huge amount to learn about the uses of supplements in

canine arthritis management. There are interesting prospects and literature emerging that will guide decisions on how owners are educated and guide owners to making informed choices about which products are supported by substantial evidence and which are not. Hopefully in the coming years more evidence will emerge that will give us a clearer picture on these products. In the mean time owners should be guided to make good financial decisions, to direct finances to interventions with good evidence, and support them to implement a multi-modal protocol that will hopefully greatly benefit the nation's arthritic pets.

Disclosure statement

No potential conflict of interest was reported by the author.

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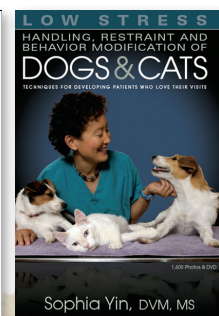
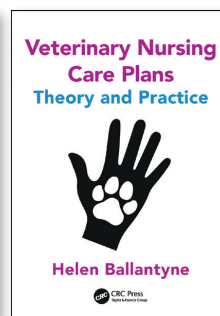
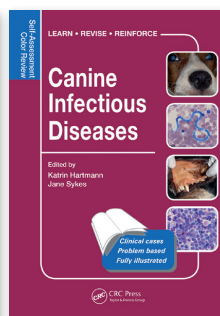
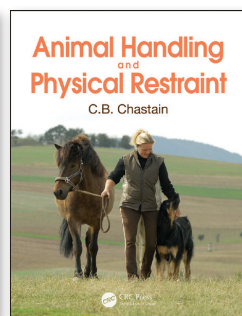
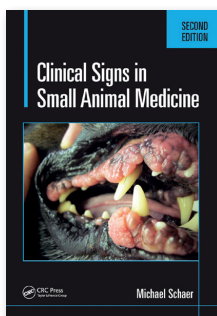
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