**Current evidence for non-pharmaceutical, non-surgical treatments of canine osteoarthritis**

*Authors*

1. Dr Christine Pye BSc(Hons) BVSc GPCert(SAS) PgC(SAS) MPhil MRCVS\*

Institute of Life Course and Medical Sciences, Faculty of Health and Life Sciences, University of Liverpool, William Henry Duncan Building, 6 West Derby Street, Liverpool L7 8TX. Email: christine.pye@liverpool.ac.uk Telephone: 07894877262

2. Dr Natasha Clark BVMedSci (Hons) BVM BVS MPhil MRCVS

Institute of Life Course and Medical Sciences, Faculty of Health and Life Sciences, University of Liverpool, William Henry Duncan Building, 6 West Derby Street, Liverpool L7 8TX. Email: Natasha.clark@liverpool.ac.uk

3. Miss Natalie Bruniges BSc BVSc Cert AVP(ECC) Dip. ECVAA FHEA MRCVS

University of Liverpool Small Animal Teaching Hospital, University of Liverpool, Leahurst Campus, Chester High Road, Neston, CH64 7TE. Email: nmb@liverpool.ac.uk

4.  aProfessor Mandy Peffers BSc MPhil PhD BVetMed FRCVS

Institute of Life Course and Medical Sciences, Faculty of Health & Life Sciences, University of Liverpool, William Henry Duncan Building, 6 West Derby Street, Liverpool, L7 8TX. Email: peffs@liverpool.ac.uk

1. aProfessor Eithne Comerford MVB PhD CertVR CertSAS PGCertHE DipECVS FHEA FRCVS

Institute of Life Course and Medical Sciences, Faculty of Health and Life Sciences, University of Liverpool, William Henry Duncan Building, 6 West Derby Street, Liverpool L7 8TX. Email: eithne.comerford@liverpool.ac.uk

*a These authors have contributed equally to this publication.*

\**Corresponding author*

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# Abstract

Osteoarthritis is a progressive degenerative disease process that affects a significant proportion of the canine population, impacting these animals’ quality of life. Currently, there is no cure and treatment consists of managing the clinical signs of pain and reduced mobility. There are many treatments for canine osteoarthritis and in this review we discuss the evidence base behind non-pharmaceutical, non-surgical treatments of this disease. These treatments include weight management, nutraceuticals, acupuncture, physiotherapies such as therapeutic exercise, hydrotherapy as well as other therapeutic modalities including photobiomodulation therapy, electromagnetic field therapy, and others.

# Introduction

Osteoarthritis (OA) is a progressive, degenerative disease of synovial joints, and is a significant cause of pain, lameness and morbidity in dogs (Anderson *et al.*, 2018). In the UK, it has been estimated that canine OA has a prevalence of between 2.5% and 6.6% of dogs presenting to primary care practices (Anderson *et al.*, 2018, O. Neill *et al.*, 2014), although the true prevalence is likely to be much higher once discrepancies in the reporting systems and unreported cases are considered (O'Neill *et al.*, 2014).

The evidence base behind pharmaceutical treatments of canine OA have been previously discussed (Pye *et al.*, 2022). In the current review, we examine the evidence base behind non-surgical, non-pharmaceutical treatment of canine OA which includes weight management, environmental modifications, nutraceuticals, physiotherapy, hydrotherapy, acupuncture, and other physiotherapeutic techniques such as photobiomodulation (laser) therapy, therapeutic ultrasound and magnetic field therapy. As these treatments become more available and widespread, veterinary practitioners must be aware of the treatment options and their underlying evidence to adequately advise owners. The current review provides an overview of each treatment modality, enabling a consolidated review of the supporting evidence behind non-pharmaceutical, non-surgical treatment options. We discuss the more commonly used complementary therapies in this review acknowledging that it is not an exhaustive list of all physical therapy modalities for canine OA.

# Weight management

Obesity is increasingly prevalent in both humans and dogs in developed nations (German *et al.*, 2018, Pegram *et al.*, 2021, O’Neill *et al.*, 2021, Haase *et al.*, 2021). Several systematic reviews in people found that obesity is a primary OA risk factor in various joints, including the knee and hand (Blagojevic *et al.*, 2010, Yusuf *et al.*, 2010). Obesity is also a risk factor for canine OA, with a recent systematic review for canine OA risk factors concluding that overweight dogs were significantly more likely to develop stifle OA secondary to cranial cruciate ligament disease (Anderson *et al.*, 2020). Obesity leads to increased compressive forces on load-bearing joints and alters joint kinematics during gait (Brady *et al.*, 2013, Al Khatib *et al.*, 2022). A biochemical as well as biomechanical link between obesity and OA is likely, as adipose tissue is a metabolically active endocrine organ synthesising and secreting hormones such as adipokines (Coelho *et al.*, 2013). As well as acting on the hypothalamus to increase metabolism (Baskin *et al.*, 1999), adipokines (e.g. leptin and adiponectin) stimulate the sympathetic nervous system (Satoh *et al.*, 1999), and induce a state of chronic inflammation by activating inflammatory responses disrupting haematopoiesis and causing dysregulation of immune responses (Abella *et al.*, 2017). Serum leptin has been found to be increased in both obese people (Vuolteenaho *et al.*, 2012) and obese dogs (Park *et al.*, 2014a) compared to their lean counterparts. Both serum and synovial fluid leptin concentrations have been found to be significantly increased in human knee OA (Ku *et al.*, 2009, Kroon *et al.*, 2019). In laboratory experiments, leptin inhibited the growth of cultured chondrocytes, as well as inducing the production of pro-inflammatory cytokines and other enzymes involved in destruction of chondrocytes in OA (Simopoulou *et al.*, 2007, Koskinen *et al.*, 2011). Obesity is also linked to other diseases including cardiovascular disease and diabetes mellitus, and it has been hypothesised that OA progression may be worsened by these co-morbidities (Conaghan *et al.*, 2005, Schett *et al.*, 2013).

Therefore, weight management is an important factor in OA treatment. Weight loss improved outcomes in terms of joint function, reduced pain and improved QOL for overweight or obese people with knee and hip OA (Panunzi *et al.*, 2021, Messier *et al.*, 2018). These improved clinical outcomes were more pronounced in people who lost more than 10% body weight (Messier *et al.*, 2018, Atukorala *et al.*, 2016).

In dogs, four studies investigated outcomes in overweight or obese dogs with OA following a weight loss regime (Table 1). Three of these examined outcomes based on weight loss alone. A study involving weight loss in nine overweight and obese dogs with hip OA found a significant improvement in subjective measurements of lameness after 19 weeks, with the dogs losing between 11 and 18% of their body weight over the study (Impellizeri *et al.*, 2000). Objective outcomes were used by two studies (Burkholder and Hulse, 2000, Marshall *et al.*, 2010). Weight loss led to improved objective measurements of lameness using kinetic gait analysis in 16 dogs with hip OA when body condition score fell from seven or eight out of nine, to four or five out of nine (Burkholder and Hulse, 2000). Marshall *et al.* (2010) found improvements in subjective measurements of lameness, and objective kinetic gait analysis, after a weight loss of 6.1% of body weight and 8.85% body weight respectively in 14 obese dogs with either hip and/or elbow. One published study examined outcomes when physical therapy and weight loss were combined (Mlacnik *et al.*, 2006). the effect of weight reduction and physical therapy (either a home-based physical therapy protocol or intensive program including transcutaneous electrical nerve stimulation) on lameness was assessed, with greater improvements in the group undergoing weight reduction and intensive physical therapy compared to weight loss alone.

These highlighted studies have limitations. Small sample sizes, lack of blinding and lack of control groups limit the level of evidence they provide, although it is difficult to blind owners and assessors to weight loss as it causes a visible change in appearance. However, from the evidence available, it is recommended to maintain a lean body condition in dogs with OA, and pursue a weight loss program in dogs that are overweight or obese.

# Nutraceuticals

## The term “nutraceutical” is defined as “a substance produced in purified or extracted form, which, when administered orally to patients, provides them the necessary elements for their structure and normal function to better their health and well-being” (Boothe, 1997). Many nutraceuticals are marketed towards the prevention or treatment of canine OA; however, they are not subject to any regulation due to the lack of evidentiary efficacy reported (Comblain et al., 2017, Vandeweerd et al., 2012). Two previous systematic reviews of veterinary nutraceuticals concluded that there was evidence for clinical efficacy of omega-3 fatty acids in the treatment of canine OA,(Vandeweerd et al., 2012, Barbeau-Grégoire et al., 2022), and the more recent of these also found a weak efficacy of collagen (Barbeau-Grégoire et al., 2022). Neither found evidence that glucosamine hydrochloride and chondroitin sulphate provided any beneficial effects in the treatment of canine OA. The most commonly used nutraceuticals are discussed and the evidence behind their efficacy is evaluated. Table 2 details published studies for each of these nutraceuticals.

## Green-lipped mussel **(**Perna canaliculus**)**

Green-lipped mussel (GLM) is derived from a mussel native to New Zealand and their extract provides essential amino acids, glycoproteins and omega-3 fatty acids. Hielm-Björkman *et al.* (2009), Soontornvipart *et al.* (2015) and Vijarnsorn *et al.* (2019) all demonstrated improvements in clinical outcomes in canine OA by alleviating inflammation and increasing weight-bearing abilities. Furthermore, there has been reported improvement in limb manipulation with a reduction in pain, swelling, crepitus after treatment with GLM in OA dogs (Servet *et al.*, 2006). Dobenecker *et al.* (2002), however, found no observed effect of adding powdered GLM extract into the animal's diet and GLM was found to be less effective than carprofen (Hielm-Björkman *et al.*, 2009).

Although studies investigating the use of GLM have provided some positive clinical effects in canine OA, there are multiple inconsistencies with respect to the benefits provided. There is currently no recommended dose of GLM, and it is difficult to compare study findings due to different dosages and administration techniques used. Further research is needed to investigate the efficacy of GLM versus non-steroidal anti-inflammatory drugs (NSAIDs) and other pharmaceutical therapies, but also to clarify the optimal dose of GLM to gain improvements in the clinical presentation of OA.

## Polyunsaturated fatty acids (omega-3)

Omega-3 fatty acids modulates the expression and activity of inflammatory biomarkers causing cartilage degradation in OA (Barrouin-Melo *et al.*, 2016, Buddhachat *et al.*, 2017, Adler *et al.*, 2018). Multiple double-blinded randomised studies have found a significant improvement in clinical signs of OA in dogs fed omega-3 supplementation (Fritsch *et al.*, 2010, Roush *et al.*, 2010, Mehler *et al.*, 2016). However, most of these improvements were recorded using subjective methodology, for example, owner questionnaires using non-validated scoring systems. Both Hielm-Björkman *et al.* (2012) and Moreau *et al.* (2013) used objective gait analysis to determine peak vertical force (PVF) and vertical impulse (VI). Moreau *et al.* (2013) found that the omega-3-infused diet improved locomotor and performance abilities, as well as increased PVF, suggesting that the dogs were inclined to load more weight on the arthritic limbs. Hielm-Björkman *et al.* (2012) also found greater PVF values and QOL scores, compared to a significant deterioration in veterinary assessments in the placebo group. The study provided evidence that supplementing omega-3 could be used as part of multimodal analgesia for dogs suffering from OA.

## Collagen

The undenatured form of type II collagen (UC-II) is a nutraceutical derived from the cartilage of chicken sternum (Bagi *et al.*, 2017) and has recently been shown to prevent the increase of pro-inflammatory and cartilage degeneration biomarkers in Labrador retrievers (Varney *et al.*, 2022). Previous research has shown that UC-II has greater efficacy compared to other supplements such as glucosamine-hydrochloride and chondroitin-sulphate (Gupta *et al.*, 2012). A similar study highlighted the beneficial effects of UC-II; Deparle *et al.* (2005) found that daily treatment of arthritic dogs with undenatured type-II collagen reduced OA signs with the greatest physical improvements noted following 90-days treatment. Stabile *et al.* (2019) also noted a clinical improvement in OA dogs treated with UC-II similar to those treated with robenacoxib after 30 days. There are no approved dosages of UC-II, although 440mg of UC-II daily improved clinical signs without adverse effects (D'Altilio *et al.*, 2007).

 UC-II has been found to be non-toxic (Marone *et al.*, 2010) and has no known adverse effects in the liver or kidneys. However, more work is required to identify the objective effectiveness of UC-II as caregiver bias can influence the results of many subjective studies (Conzemius and Evans, 2012).

## Glucosamine hydrochloride and chondroitin sulphate

Glucosamine and chondroitin are aminosaccharides which have anti-inflammatory and anti-catabolic effects *in vitro* (Henrotin and Lambert, 2013). In humans, glucosamine is available in several dosage forms (Bhathal *et al.*, 2017), however, there is variable efficacy due to inconsistent dosages and poor oral bioavailability (Altman, 2009, Sawitzke *et al.*, 2010). There are multiple manufactured glucosamine and chondroitin products, all with varying strengths and formulations. Based on current literature, the beneficial effects of glucosamine and chondroitin in the treatment of canine OA can neither be confirmed or denied as clinical trials have had mixed results. McCarthy *et al.* (2007) found dogs consuming glucosamine/chondroitin had statistically significant improvements in scores for pain, weight-bearing and OA severity by day 70, and was non-inferior to carprofen at day 70. Contrastingly, Scott *et al.* (2017) found that dogs treated with oral glucosamine hydrochloride and chondroitin sulphate for 90 days did not display increased activity levels when compared with a placebo, although owner assessment scores increased, indicating a possible caregiver placebo effect.

Further research (evidence level I or II) is required to determine the efficacy of using glucosamine and chondroitin in improving clinical outcomes in OA as their analgesic efficacy has not been well demonstrated (Moreau *et al.*, 2003).

## Curcuminoids

Curcuminoidsare natural turmeric-derived polyphenols (Henrotin *et al.*, 2010). Many *in vitro* studies have demonstrated the anti-oxidant and anti-inflammatory properties of these compounds (Henrotin *et al.*, 2010, Comblain *et al.*, 2017). However, the bioavailability of naturally occurring curcumin in dogs is uncertain. Innes *et al.* (2003) described a significant effect for dogs treated with Curcuminoid P54FP using objective assessments, although owners failed to notice a difference in their dogs’ mobility. In contrast, Comblain *et al* (2017) found no changes in objective variables (PVF and OA biomarkers). A recent systematic review of 10 human studies demonstrated reduction in pain and improved function in patients with knee OA pain (Paultre *et al.*, 2021).

Curcumin has been shown to be an active iron chelator *in vivo*, although it is unclear how this would affect carnivores such as dogs (Jiao *et al.*, 2009, Badria *et al.*, 2015). There is need for a large-scale clinical trial as most data is relying on experimental, *in vivo* studies. Currently, recommended doses include 50-250mg curcumin three times daily (Fougère and Wynn, 2007), although future trials also need to focus on the bioavailability of the available forms and thus accurate dosages before these can be recommended as a reliable treatment for canine OA.

## Elk velvet antler

Elk velvet antler is a Chinese medicine used to treat various diseases and is derived from the inner antler core in the velvet stage of growth (Zhang *et al.*, 1992). *In vivo* studies have shown anti-inflammatory effects in a rodent model of inflammation (Cheng *et al.*, 2022). Velvet antler also contains chondroitin sulphate (Bhathal *et al.*, 2017, Henrotin and Lambert, 2013, Moreau *et al.*, 2003, Scott *et al.*, 2017). Moreau *et al.* (2004) used quality elk velvet antler in dogs with OA, with the majority of dogs improving in daily activities and their weight-bearing abilities (based on gait analysis). Further research into how elk velvet antler can inhibit the degenerative process of OA would be useful, alongside its efficacy compared to commonly prescribed OA medication (e.g. NSAIDs).

## Vitamin E

Several human studies have shown benefits of Vitamin E on OA clinical signs over a short-term period, primarily by reducing free radicals and synthesis of pro-inflammatory cytokines (Chin and Ima-Nirwana, 2018, Farbstein *et al.*, 2010, Rizvi *et al.*, 2014). In dogs with surgically induced OA, nitric oxide and prostaglandin E2 in synovial fluid were lower following treatment with Vitamin E, and histological OA lesions were reduced in dogs fed a high dose of vitamin E (400IU/day) (Rhouma *et al.*, 2013). Lameness and pain (assessed by visual analogue scales (VAS), numerical rating scales (NRS) and electrodermal activity) were also reduced in the vitamin E treated group (Rhouma *et al.*, 2013). Vitamin E is thought to be well tolerated in dogs with no adverse effects reported (Musco *et al.*, 2019). However, there is requirement for studies in naturally occurring canine OA and a longitudinal study to assess the synergy between Vitamin E and other compounds used to treat canine OA to determine the overall effectiveness.

## Avocado/soybean unsaponifiables

The use of avocado/soybean unsaponifiables (ASU) *in vitro* has shown to reduce interleukin-1 beta, and increase collagen synthesis in chondrocytes (Mauviel *et al.*, 1991). Oral treatment improved subchondral bone structure (Cake *et al.*, 2000) and reduced early OA cartilage and subchondral bone lesions (Boileau *et al.*, 2009). ASU acts by downregulating synthesis by chondrocytes and correcting the imbalance between catabolic and anabolic processes which contribute to the onset and development of cartilage lesions in OA (Henrotin *et al.*, 2003). Some studies have demonstrated that the beneficial effects of ASU can persist after treatment has ended (Blotman *et al.*, 1997, Maheu *et al.*, 1998). One human study found ASU to be a slow-acting drug, with symptomatic efficacy only occurring from the second month (Maheu *et al.*, 1998). Canine studies have a maximum duration of treatment of eight weeks (Boileau *et al.*, 2009). Thus, a longer study is required to identify the use and efficacy of ASU in the management of canine OA when used alone and in conjunction with other medication.

## S-adenosyl L-methionine (SAMe)

S-adenosyl L-methionine (SAMe) is a nutraceutical commonly used to treat canine liver diseases such as chronic hepatitis, hepatic lipidosis and cholangiohepatitis (Center *et al.*, 2005, Wallace *et al.*, 2002). Due to its anti-oxidant properties, some have suggested that SAMe may have a beneficial use in canine OA (McCarty and Russell, 1999, Gutierrez *et al.*, 1997). SAMe has been shown to maintain the biomechanical strength of articular cartilage (Gutierrez *et al.*, 1997) and promote a functional articular matrix (Bradley *et al.*, 1994). One study found that SAMe was not an effective standalone treatment for canine OA as both subjective and objective outcomes did not show improvement in reducing clinical signs within six weeks of treatment (Imhoff *et al.*, 2011). Previous human research has shown that SAMe has a slower onset of action when compared with NSAIDs; patients noticed no difference in pain scores with SAMe and NSAIDs after 2 months (Najm *et al.*, 2004). Imhoff *et al.* (2011) did not assess the equivalence between SAMe and NSAIDs, thus, further research would be interesting for comparison to human medicine. However, from current research, there is no evidence to show the use of SAMe would be beneficial in the treatment of canine OA.

## Nutraceuticals - Conclusion

In reviewing the available evidence, the use of omega-3 could provide some analgesic effect for dogs with OA . However, commonly used products such as chondroitin-glucosamine have not been shown to have an analgesic effect (Paultre *et al.*, 2021). Despite this, it is important to note that OA is a progressive disease and the duration of the trial is a key factor when assessing response to treatment. Other nutraceuticals such as green lipped mussel and elk velvet antler demonstrate promising results, yet evidence is minimal for these products and further clinical studies are required to fully assess their efficacy.

# Acupuncture

Acupuncture originated as a treatment of pain for people in China around 3000 years ago (Hao and Mittelman, 2014). Over the past few decades, a growing yet mixed body of evidence has emerged in human medicine as to its effectiveness in the treatment of human OA (Tian *et al.*, 2022, Manheimer *et al.*, 2018). In dogs, the use of acupuncture as a treatment modality for chronic musculoskeletal pain has gained more acceptance over the past few decades, with a variety of postgraduate courses available.

Acupuncture involves the stimulation of specific anatomical locations, termed acupuncture points, that relate to areas linked with neurovascular structures, such as nerve fibres, mechanoreceptors, small arterioles and venules, as well as lymphatics and mast cells (Dewey and Xie, 2021). These points are mainly located along pathways called “meridians” that are associated with certain internal organs, body systems and major nerve pathways (Wang *et al.*, 2010). Acupuncture points correspond with areas of increased electrical conductance or reduced electrical resistance (Reichmanis *et al.*, 1975, Johng *et al.*, 2002), and have been described in the dog (Yang *et al.*, 2017).

There are various forms of acupuncture, including dry-needle acupuncture, electro-acupuncture, aquapuncture, moxibustion and implantation acupuncture (Hielm-Bjorkman *et al.*, 2001, Jaeger *et al.*, 2006, Kapatkin *et al.*, 2006, Li *et al.*, 2016, Sha *et al.*, 2016).

*Mechanisms of action of acupuncture*

The analgesic effects of acupuncture are multimodal and complex, and are believed to be exerted through local, spinal and supraspinal mechanisms (Carlsson, 2002, Huntingford and Petty, 2022) which are briefly summarised here. Locally, inserting a needle during acupuncture causes a microtrauma, which provides a stimulus that leads to anti-inflammatory and immune responses in the tissue (Carlsson, 2002). These include increased local blood flow, the activation of peripheral sympathetic nerve fibres, the release of neuropeptides and endogenous opioids, and a decrease of pro-inflammatory cytokines (Kimura *et al.*, 2006, Park *et al.*, 2014b, Chen *et al.*, 2020). At the spinal level, acupuncture has been found to reduce chemokines and inflammatory cytokine release, reducing neuronal excitability and having an anti-inflammatory effect (Liang *et al.*, 2016, Wei *et al.*, 2021). At the supraspinal level, within the brain, acupuncture has been found to activate descending inhibitory pain pathways (Zhang *et al.*, 2018, Huang *et al.*, 2021, Lyu *et al.*, 2021).

*Evidence for the use of acupuncture as a treatment for OA*

Designing a rigorous randomised controlled trial to study the effects of acupuncture has particular challenges (Chen *et al.*, 2019). Placebo-controlling an acupuncture clinical trial can be difficult, and therefore many trials use forms of “sham” acupuncture as control. Sham acupuncture often consists of inserting needles into non-acupuncture point areas, or inserting them very superficially, but this action itself may have a physiological effect on subjects (Kim *et al.*, 2022). Other clinical trials use a group that receive no treatment as a control. In dogs, as many outcomes rely on owner assessment, the owner can be blinded to the treatment group if the dogs are removed from their owner while they either receive acupuncture or no treatment (Baker-Meuten *et al.*, 2020).

Several systematic reviews and meta-analyses have examined the efficacy of acupuncture in human participants with OA and have mixed conclusions (Allen *et al.*, 2022, Manheimer *et al.*, 2010, Manyanga *et al.*, 2014, Manheimer *et al.*, 2018, Tian *et al.*, 2022). Current guidelines from the National Institute for Health and Care and Excellence (2022) in the UK advises against offering acupuncture or dry needling to manage OA in people. These guidelines cite a lack of evidence of clinical benefits and cost-effectiveness, although they do conclude that there may be some benefit to electroacupuncture in some people and advise further research is required.

Clinical trials investigating acupuncture as a treatment for canine OA are listed in Table 3. These studies include a mixture of acupuncture techniques, including dry needle acupuncture (Baker-Meuten *et al.*, 2020, Lane and Hill, 2016, Silva *et al.*, 2017, Teixeira *et al.*, 2016), electroacupuncture (Kapatkin *et al.*, 2006, Chomsiriwat and Ma, 2019, Silva *et al.*, 2017) and gold wire or gold bead implants at acupuncture points (Hielm-Bjorkman *et al.*, 2001, Jaeger *et al.*, 2006). The evidence behind the efficacy of acupuncture as a treatment for canine OA in these trials is mixed.

Baker-Meuten *et al.* (2020) investigated the efficacy of acupuncture on the treatment of OA in various joints in 32 client-owned dogs over one year of age and over 10 kilograms in bodyweight. The investigators found no difference between baseline measurements versus placebo and acupuncture treatments for objective gait analysis, accelerometery or subjective orthopaedic examination, but did find a significant improvement with acupuncture versus baseline and placebo in some of the clinical metrology instrument (CMI) scores.Teixeira *et al.* (2016) also found improvements in CMI scores after 4 weeks of acupuncture treatments in dogs with hip dysplasia. Lane and Hill (2016) investigated the effect of a combined acupuncture and manual therapy protocol compared to no treatment in 47 dogs with lameness of various causes, including OA. The study found a short-term improvement in subjective owner assessments after two treatments six days apart. However, no objective outcome measurements were used, and as acupuncture was combined with other physical therapies, it cannot be concluded that the effects were due to acupuncture alone. Silva *et al.* (2017) concluded that the use of acupuncture alone or in combination with analgesics reduced pain and improved QOL in dogs with neurological and musculoskeletal conditions, however the trial was not blinded, used a mixture of acupuncture, electroacupuncture and other alternative therapies and only states the outcomes of dogs with a range of musculoskeletal disorders and not specifically OA.

Studies investigating electroacupuncture in dogs with OA present mixed conclusions. Kapatkin *et al.* (2006) found no significant improvement in nine dogs with elbow OA treated with electro-acupuncture for three weeks in either owner assessment or objective gait analysis. Chomsiriwat and Ma (2019) however, did find a significant improvement in CBPI scores and hip joint range of movement in 31 dogs treated with either electroacupuncture or laser therapy for eight weeks compared to baseline in dogs with hip OA. This study, however, lacked a control group.

Implantation of gold wire or gold beads at acupuncture points was performed on 38 and 78 dogs with hip OA respectively (Hielm-Bjorkman *et al.*, 2001, Jaeger *et al.*, 2006). Hielm-Bjorkman *et al.* (2001) found no significant effect, whereas Jaegar *et al.* (2006) found significanly greater improvements in signs of pain and mobility with subjective outcome measures in the treated group compared to control.

## Acupuncture - conclusions

Currently available research investigating acupuncture for the alleviation of OA-associated pain does not draw firm conclusions regarding its efficacy in either veterinary or human medicine (Tian *et al.*, 2022, Manheimer *et al.*, 2018, Baker-Meuten *et al.*, 2020, Kapatkin *et al.*, 2006) . There are published studies that have reported improvements in outcomes such as CMI scores and subjective outcome measurements for canine OA using different forms of acupuncture (Lane and Hill, 2016, Chomsiriwat and Ma, 2019, Baker-Meuten *et al.*, 2020, Jaeger *et al.*, 2006). Further larger scale randomised controlled trials using acupuncture as a treatment for canine OA in different joints, and comparing acupuncture with and without other therapeutic modalities and pharmacological treatments could improve the evidence base

# Physiotherapy and hydrotherapy

Physiotherapy in the human field is an accepted treatment modality for patients with OA, and multiple studies show its effectiveness at reducing clinical signs of OA (Bannuru *et al.*, 2019, Deyle *et al.*, 2005, Mazzei *et al.*, 2021, McAlindon *et al.*, 2014, Roddy *et al.*, 2004). In veterinary physiotherapy, published randomised controlled trials investigating the efficacy of physiotherapy in dogs with OA are limited (Crook *et al.*, 2007, Mlacnik *et al.*, 2006, Drum *et al.*, 2021, Barale *et al.*, 2022).

The aims of physiotherapy in OA treatment are to improve muscle strength, joint mobility, balance and stability (Dycus *et al.*, 2017, Millis and Levine, 1997). Physiotherapy protocols for the treatment of canine OA can take multiple forms. These protocols include land based therapeutic exercise programmes and manual therapies, hydrotherapy and other physiotherapeutic modalities including the application of different temperatures (e.g. cryotherapy or thermal heat), and different energies such as laser, electric, magnetic or ultrasound (Drum *et al.*, 2021, Langley-Hobbs, 2010, Millis and Levine, 1997)

Recently, the idea of a “physiotherapy pyramid” aimed at considering a systematic approach to canine OA management has been proposed (Mille *et al.*, 2022). This pyramid has four layers, and starts at the bottom with environmental modification, followed by an exercise plan, home exercises specifically designed for dogs with OA, and finally by treatment from a trained physiotherapist. This pyramid idea outlines the importance of considering and implementing cost-effective, practical modifications at home, and gaining owner agreement and compliance to follow exercise plans and home exercises (Mille *et al.*, 2022).

Published studies investigating the efficacy of different physiotherapeutic modalities in the treatment of canine OA are outlined in Table 4.

## Environmental modifications

Making modifications to the home environment can improve the ability of OA dogs to carry out daily functions, which is likely to improve their everyday QOL. Environmental modifications can include the use of non-slip mats or rugs in the house where a slippery flooring (e.g. laminate flooring) exists, supportive bedding to improve comfort, slings to reduce pressure on limbs, raised food and water bowls to reduce the need for affected dogs to bend down, and ramps for vehicular access (Goldberg, 2022). Implementation of these changes is a relatively simple, often cost-effective step that can help to involve owners in their dogs’ care and aid the ease at which dogs can exist within their homes. Despite this, having these discussions with owners may be overlooked by veterinary practitioners (Belshaw *et al.*, 2020).

## Manual therapies

Manual therapies include “hands-on” physiotherapy techniques, such as massage therapy and myofascial release, passive range of movement exercises and stretches (Crook *et al.*, 2007, Hyytiäinen *et al.*, 2013, Riley *et al.*, 2021). Massage therapy for OA is common in the human field, however the exact mechanism of action of massage as a pain-relieving treatment is unknown. Many potential mechanisms exist, including improved local perfusion (Monteiro Rodrigues *et al.*, 2020), improved lymphatic drainage and increased blood lactate clearance (Bakar *et al.*, 2015), reduced inflammation (Waters-Banker *et al.*, 2014), reduced cortisol levels and lowered stress, anxiety and depression in humans (Field *et al.*, 1996). There is some evidence that massage may improve short term outcomes in patients with knee OA, although the quality of clinical trials are limited (Wu *et al.*, 2022). In dogs with musculoskeletal pain, an uncontrolled study examining subjective outcomes after massage therapy sampled 527 dogs treated by over 60 practitioners by means of a survey of their current or retrospective cases (Riley *et al.*, 2021). The vast majority (95.5%) of dogs were reported by the practitioners to have responded to treatment, with significant reductions in pain scores and improvements in QOL reported (Riley *et al.*, 2021).

## Land based therapeutic exercise

Land based therapeutic exercise regimes aim to improve muscle strength, improve balance and reduce stiffness in OA affected patients (Bennell *et al.*, 2008). In humans, therapeutic exercise in patients with OA is considered an important part of non-pharmaceutical treatment. A Cochrane systematic review of the literature found that exercise moderately reduced pain, increased QOL and improved physical function in human patients with knee OA (Fransen *et al.*, 2015).

In dogs, therapeutic exercise can play a key role in the multi-modal management of OA (Drum *et al.*, 2021, Drum *et al.*, 2015). Land-based therapeutic exercises comprise simple exercises such as walking, with a gradual build-up of the duration of each walk depending on the dogs’ comfort (Greene *et al.*, 2013). Using command driven exercises such as sit, lying down and bowing, are strengthening exercises, and can be carried out at home by owners (Drum *et al.*, 2021). Exercising using exercise equipment, such as balance boards and exercise balls can be beneficial to build balance and strength, ideally by a trained canine physiotherapist (Goldberg, 2022). A thorough review of the use of strengthening exercises has been recently published (Drum *et al.*, 2021).

Published studies investigating the efficacy of land-based therapeutic exercise for management of canine OA is limited. Previous studies have examined how different exercises affect the gait of dogs with elbow and hip OA, using kinematic gait analysis, revealing that walking up an incline, down an incline and over low obstacles all alter joint kinematics not just in the OA affected joint but in multiple joints compared to non-OA dogs (Bockstahler *et al.*, 2011, Bockstahler *et al.*, 2012). In a clinical setting, Mlacnik *et al.* (2006) found a significant improvement in lameness of dogs with OA following a weight loss program with either home-based physical therapy or an intensive physical therapy program (including TENS) compared to baseline, with improvements seen more rapidly in the intensive physical therapy group. Further clinical trials are required to improve evidence for physiotherapy exercise protocols in canine OA.

## Hydrotherapy

Hydrotherapy is a form of physiotherapy that takes place within water, either with the use of a pool, an underwater treadmill, or (less commonly in the veterinary field) with a whirlpool or hot-tub (Cartlidge, 2015). Hydrotherapy is commonly used as a complementary therapy in canine patients with OA with a large number of hydrotherapy centres across the UK (Waining *et al.*, 2011).

Exercising in water reduces the degree of weight bearing by limiting the pull of gravity due to the effect of buoyancy (Levine *et al.*, 2010). It has been shown that there is a reduction in vertical ground reaction forces exerted by dogs’ limbs when they are immersed in water, with further decreases in these forces as the water depth increases (Levine *et al.*, 2010, Barnicoat and Wills, 2016). By reducing ground reaction forces, it is proposed that hydrotherapy can improve exercise tolerance, by reducing the impact of exercise on dogs with OA affected limbs (Levine *et al.*, 2010, de Oliveira Reusing *et al.*, 2021). Another potentially therapeutic effect of exercising in water is caused by the effect of hydrostatic pressure, which is the compressive pressure exerted on an object by a body of fluid when immersed in that fluid. Hydrostatic pressure may lead to an improvement in circulation, aiding in the resolution of oedema, lymphoedema, soft tissue and joint swelling, and reducing pain and stiffness in joints (Gibson and Shields, 2015, Kamioka *et al.*, 2010). There is also an increase in resistance when exercising in water due to drag forces, which could lead to increased muscle mass and strength in OA patients (Miyoshi *et al.*, 2004, Barnicoat and Wills, 2016). Improved exercise tolerance with hydrotherapy can also help with weight reduction programs (Chauvet *et al.*, 2011). Weight reduction improved clinical outcomes in OA dogs (see section on weight management above) (Marshall *et al.*, 2010).

Water temperature of the hydrotherapy pool or treadmill could also impact treatment efficacy. A temperature of between 28 and 30 degrees Celsius (°C) has been recommended for canine hydrotherapy (Lindley and Watson, 2010, Prankel, 2008). Alternating between warm and cold water, a process known as contrast hydrotherapy, has been investigated in humans finding potential benefits versus either warm or cold water alone (Abd elFatah *et al.*, 2019, Fokmare and Phansopkar, 2022) , but no studies have been published in dogs.

Altogether, these physical aspects of aquatic exercise are hypothesised to lead to improved exercise tolerance, improved balance and co-ordination during exercise, improved joint mobility and reduced joint stiffness improved muscle strength, reduced swelling around affected joints and an overall reduction in OA related pain (Bartels *et al.*, 2016).

A number of studies have investigated how hydrotherapy, either by underwater treadmill or swimming , affected the gait of healthy dogs (Levine *et al.*, 2010, Barnicoat and Wills, 2016, Bliss *et al.*, 2022) and those with orthopaedic disorders such as elbow dysplasia (Preston and Wills, 2018) and post-operative rehabilitation after cranial cruciate ligament rupture (CCLR) surgery (Marsolais *et al.*, 2003). However, there are limited studies investigating the clinical outcomes such as reduction in lameness and pain in dogs with OA. During and after an eight-week program of hydrotherapy with outdoor pool swimming in a group of 22 dogs with hip OA, subjective clinical assessment scores including pain, lameness and joint mobility significantly improved in the OA dogs (Nganvongpanit *et al.*, 2014). Interestingly, serum biomarkers of OA also significantly changed in the OA affected dogs in this study, with an increase in serum hyaluronan and a decrease in serum chondroitin sulphate epitope WF6 suggesting a reduction in cartilage breakdown in these dogs (Nganvongpanit *et al.*, 2014). Serum hyaluronan also increased in healthy dogs that underwent swimming, but not in healthy dogs that did not swim. One major limitation to this study was the lack of a control group.

A recent study found reductions in pain severity (as measured by the CBPI) and an increase in thigh circumference in dogs with hip OA after twice weekly hydrotherapy sessions in an underwater treadmill either as a sole treatment or with other physical therapy modalities versus no physical therapy (de Oliveira Reusing *et al.*, 2021).

Despite hydrotherapy being more readily available and widely used as a complementary therapy in canine OA (Waining *et al.*, 2011), there is currently a very limited number of clinical studies using this therapy in the literature (Nganvongpanit *et al.*, 2014, Preston and Wills, 2018, de Oliveira Reusing *et al.*, 2021). This is not to say that hydrotherapy is not an effective therapy in OA, as there is evidence in the literature supporting its use in human OA (Bartels *et al.*, 2016), and many anecdotal reports of its benefits in canine OA (Prankel, 2008), but the lack of studies into its use in canine OA highlights a gap in the evidence base to gain a better understanding of its effectiveness in reducing pain and clinical signs in dogs with OA.

# Other therapeutic modalities.

Other therapeutic modalities implemented in physiotherapeutic regimes for canine OA include photobiomodulation therapy (laser therapy), magnetic field therapy, electrotherapy (including transcutaneous electrical nerve stimulation), extracorporeal shockwave therapy, and therapeutic ultrasound (Mueller *et al.*, 2007, Gaynor *et al.*, 2018, Barale *et al.*, 2022, Boström *et al.*, 2022). These therapies are based upon the application of different energies to an affected area. Due to the limited scope of this review, an overview of these techniques and their evidence is given here. Details of clinical trials using these modalities is given in Table 4.

## Photobiomodulation therapy (Laser therapy)

Photobiomodulation therapy (PBMT) has been increasing in popularity in recent years as a therapy for canine OA. The term PBMT encompasses an array of light and laser therapies, and is defined as a “A form of light therapy that utilizes non-ionizing forms of light sources, including lasers, LEDs, and broadband light, in the visible and infrared spectrum” (Anders *et al.*, 2015). The mechanisms behind PBMT and its effect on OA are still being investigated *in vitro* and *in vivo* (Oliveira *et al.*, 2021). In laboratory studies, the enzyme cytochrome *c* oxidase in mitochondria has been found to be a photo-acceptor which is activated by PBMT (Karu *et al.*, 2005) leading to an increased production of molecules involved in cell signalling pathways related to cell proliferation, protein synthesis and anti-inflammatory effects (Karu, 2008).

In the human field, the evidence behind the use of PBMT in the treatment of OA is mixed, and a lack of consistency between study protocols and methods makes it difficult to draw firm conclusions (Bridges *et al.*, 2020). Recent systematic reviews of published randomised controlled investigating the effect of PBMT on pain and disability in humans with OA concluded that there was some evidence that PBMT provided significant improvements in pain, function and QOL in patients with knee OA and in aged patients with OA, although further research was advised (Stausholm *et al.*, 2019, Bridges *et al.*, 2020).

To date, four studies have investigated the efficacy of PBMT in dogs with OA (Table 4). These include three prospective studies (Looney *et al.*, 2018, de Oliveira Reusing *et al.*, 2021, Barale *et al.*, 2022), and one retrospective study (Barale *et al.*, 2020). Looney *et al.* (2018) investigated the effect of a six-week course of low-level laser therapy (LLLT) in 20 dogs with elbow OA, compared to sham light therapy in a multicentre, randomised, blinded, controlled trial. An improvement in subjective lameness score as well as the Helsinki Chronic Pain Index CMI was found in the treated group (Looney *et al.* 2018). A significant increase in the daily step count and number of daily activities recorded by accelerometery was found after a six-week course of LLLT in 23 dogs with either hip or stifle OA (Barale *et al.* 2022). Prior to this publication, the same investigators published the results of a retrospective study on 17 dogs describing the reduction in CBPI and VAS in these dogs with weekly LLLT treatments (Barale *et al.*, 2020).

## Electromagnetic field therapy

Electromagnetic field therapy involves the application of a magnetic field (either low frequency, high frequency or pulsed) to an area to promote a therapeutic benefit. Pulsed electromagnetic field therapy (PEMT) is most commonly used in veterinary medicine (Gaynor *et al.*, 2018).

Two randomised controlled trials investigated the efficacy of PEMT in dogs with OA (Sullivan *et al.*, 2013, Pinna *et al.*, 2013). Sullivan *et al.,* (2013) compared treatment with PEMT for one hour on nine consecutive days in 35 dogs with an untreated control group of 24 dogs. The PEMT group had lower CBPI scores at assessment timepoints of 11 and 42 days. Another clinical trial examining the effects of PEMT in 40 OA affected dogs also found evidence of a clinical improvement similar to a firocoxib treated control (Pinna *et al.*, 2013).

## Extra-corporeal shockwave treatment

Extra-corporeal shockwave therapy (ECSWT) involves the application of shockwaves (which are nonlinear, high pressure, high-velocity sound waves of short duration) to a treatment site, in order to transmit mechanical energy to the tissues (Alvarez, 2022, Durant and Millis, 2014). This mechanical energy transmitted by the shockwave acts directly and indirectly on the tissue to generate an anti-inflammatory response, by the production of free radicals, anti-inflammatory cytokines, and growth factors within tissues that can reduce inflammation and promote healing (Durant and Millis, 2014). The mechanisms behind the analgesic effect of shockwaves are less well understood (McClure *et al.*, 2005, Abed *et al.*, 2007). A few small randomised controlled trials have investigated the efficacy of ECSWT in OA dogs. Souza *et al.* (2016) found improvements in objective force plate gait analysis in dogs with hip dysplasia for up to 90 days. However, Mueller *et al.* (2007) found no significant improvements in gait analysis in dogs with hip OA treated with ECSWT. Millis *et al.* (2011) found significant improvements in objective gait analysis in dogs with elbow OA treated by ECSWT, although the sample size in this trial was small at 15 dogs.

## Therapeutic ultrasound

Therapeutic ultrasound is the application of either continuous or pulsed ultrasound waves, at either low or high frequencies, to tissues to gain a therapeutic effect (Boström *et al.*, 2022). The therapeutic effects may be elicited via both thermal and non-thermal effects. Thermal effects on tissue by the application of ultrasound waves increase blood flow, and non-thermal mechanical energy affects cell membranes, leading to release of growth factors (Tezel and Mitragotri, 2003, Tsai *et al.*, 2006).

A recent meta-analysis including eight studies found some evidence that pulsed ultrasound therapy led to improvement in function and pain relief compared to placebo in human knee OA (Zeng *et al.*, 2014).

In dogs, one study of eight dogs with stifle OA receiving therapeutic ultrasound found improvements in joint mobility and reduced subjective pain scores after 10 daily sessions. However, this study did not include a control group, and gave little information on whether the OA was post traumatic (e.g. after CCLR), whether it was chronic or acute, and if other medications were given concurrently (Muste *et al.*, 2015).

## Transcutaneous electrical nerve stimulations

Transcutaneous electrical nerve stimulation (TENS) is a form of electrotherapy, where a mild electrical current is applied via a device with patches applied to the skin, to stimulate nerves in the tissue to achieve an analgesic effect (Chen *et al.*, 2016). These effects are believed to be exerted through over-riding nociceptive signals, and by triggering release of endorphins centrally (Han *et al.*, 1991, Radhakrishnan and Sluka, 2005). In human OA , there are mixed conclusions as to the effectiveness of TENS. One systematic review and metanalysis of 18 randomised-controlled trials concluded that that TENS reduced pain in knee OA (Chen *et al.*, 2016), whereas another found the evidence was inconclusive (Rutjes *et al.*, 2009). In dogs, no clinical trials have examined the use of TENS alone as a therapy for canine OA. One study examined the use of TENS along with other physical therapies and weight reduction programs compared to home-based exercise in obese dogs with OA, but conclusions as to whether TENS or weight loss or the other exercises led to an improvement in clinical signs cannot be drawn as all of these modalities were implemented simultaneously in the treated group (Mlacnik *et al.*, 2006).

***Summary***

Osteoarthritis (OA) is a progressive, degenerative disease which can cause inflammation within the joints and poses a risk to canine health and welfare (Summers *et al.*, 2019). There is no cure for OA, but there are now many management options aimed at reducing pain and improving mobility in affected dogs. A multi-modal approach to the treatment of canine OA, including both pharmaceutical and non-pharmaceutical therapies has been proposed to be most effective in treating this disease (Fox, 2016, Pye *et al.*, 2022). With more complementary therapies becoming available to veterinary practitioners, this review has aimed to address commonly used non-surgical, non-pharmaceutical treatment options for canine OA and highlight current evidence gaps.

Weight management has shown to be beneficial in the management of OA but can take time to see results (Burkholder and Hulse, 2000; Marshall *et al.*, 2010; Mlacnik *et al.*, 2006). Therefore, it is important that owners are kept engaged with regular visits for weight checks and pursue an appropriate weight loss program for their dogs. There is evidence for the use of certain nutraceuticals such as omega-3 fatty acids. Acupuncture, PBMT and ECSWT may also play a role in reducing the clinical signs of OA, although further research is needed to gain a greater understanding of their efficacy (de Oliveira Reusing *et al.*, 2021, Boileau *et al.*, 2009, Moreau *et al.*, 2003, Souza *et al.*, 2016). There is a lack of randomised controlled trials investigating the efficacy of different physiotherapy programs, both land-based and aquatic, which would aid the development of best practice guidelines for canine OA treatment.

For many of the management options outlined in this review, there is a need for larger scale clinical trials to inform veterinary professionals on the best practice for treating canine OA. Objective measurements such as force-plate gait analysis should be used where possible to reduce caregiver bias (Conzemius and Evans, 2012) and assessment of the above therapies compared to pharmaceutical therapies alone would be useful to determine their efficacy in reducing clinical signs of canine OA. Assessing the use of different complementary therapies as part of a multi-modal treatment regime in dogs with differing OA severity would allow greater evidence for best-practice in the treatment of this chronic disease.

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Table 1. Studies investigating weight loss as a treatment for canine osteoarthritis

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Study type** | **Groups** | **Sample size** | **Study length** | **Outcome measures** | **Conclusions** | **Evidence level****(Aragon and Budsberg, 2005)** |
| Impellizeri *et al*. (2000) | Non-blinded prospective clinical trial | Weight loss program | 9 | 19 weeks | Subjective: NRS, VAS. | Dogs lost between 11 and 18% of their bodyweight over 10-19 weeks. All measures of lameness were significantly lower at the end of the study compared to baseline. | III |
| Burkholder and Hulse (2000) † | Non-blinded prospective clinical trial | Weight loss program | 16 | Not given | Objective: kinetic gait analysis | Significant improvement in objective measurements with weight loss to optimal body condition.  | III |
| Mlacnik *et al*. (2006) | Non-blinded prospective randomised clinical trial | Caloric restriction and intensive physical therapy including TENS Caloric restriction and home-based physical therapy | 29 | 6 months | Subjective: subjective lameness and pain scores (0-4)Objective: kinetic gait analysis | Mean weight loss after 6 months was 13.6% in group 1 (Caloric restriction and intensive physical therapy) and 9.3% in group 2 (Caloric restriction and home-based physical therapy).Significant improvement in kinetic gait analysis in both groups at end of study, but more rapid change was evident in dogs receiving intensive physical therapy. | III |
| Marshall *et al*. (2010)  | Non-blinded prospective clinical trial | Weight loss program | 14 | 16 weeks | Subjective: NRS, VAS.Objective: Kinetic gait analysis | Dogs lost an average of 8.6% of initial bodyweight. Significant decrease in subjective measures of lameness from weight loss of 6.1% of bodyweight onwards. Significant reduction in objective measurements of lameness from 8.85% onwards.   | III |

Abbreviations: NRS=numerical rating scale; VAS= visual analogue scale; TENS=transcutaneous electrical nerve stimulation

†=abstract from conference proceedings

Table 2. Studies investigating nutraceuticals as a treatment for canine osteoarthritis

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Nutraceutical category investigated** | **Nutraceutical compound investigated** | **Author** | **Study type** | **Groups** | **Sample size** | **Study length** | **Outcome measures** | **Conclusions** | **Evidence level (Aragon and Budsberg, 2005)** |
| **Omega-3-based nutraceuticals** | Green-lipped mussel (Perna canaliculus)  | Bierer and Bui (2002) | Double-blind, randomised, non-placebo-controlled study  | Green-lipped mussel powder Green-lipped mussel incorporated into a treat  Green-lipped mussel incorporated into a main meal  | 96 dogs   | 6 weeks   | Subjective: veterinary assessment, NRS    | Total OA scores and scores for joint pain and joint swelling were significantly reduced following 6wk of green-lipped mussel supplementation in all three forms  | III  |
| Dobenecker *et al.* (2002) | Double-blind, randomised, placebo-controlled study   | Chondroitin sulphate Mussel extract Placebo   | 70 dogs   | 12 weeks   | Subjective: owner-reported questionnaire, veterinary assessment  | None of the tested substances led to a distinct improvement of the recorded symptoms or even to a total recovery in general  | II  |
| Pollard *et al.* (2006) | Double-blind, randomised, placebo-controlled study  | Green-lipped mussel  Placebo   | 81 dogs   | 56 days  | Subjective: owner-reported questionnaire, veterinary assessment  | Green-lipped mussel had a beneficial effect on the clinical signs of dogs presumptively diagnosed with mild-to-moderate DJD  | II  |
| Hielm-Björkman *et al.*, (2009)  | Double-blind, randomised, placebo-controlled study   | Green-lipped mussel Carprofen Placebo (isotonic sodium-chloride solution)   | 45 dogs   | 8 weeks  | Subjective: veterinary-assessed mobility index and owner-evaluated chronic pain index via VAS  Objective: Force plate analysis (PVF)  | Freeze-dried green-lipped mussel is more effective than the placebo in treating chronic pain due to moderate to severe. Although green-lipped mussel was not as effective as carprofen  | II  |
| Soontornvipart *et al.*, (2015)  | Double-blind, randomised, non-placebo-controlled study  | Green-lipped mussel  Omega-3 fatty acids in fish oil  | 66 dogs   | 24 weeks  | Subjective: veterinary assessment, weight-bearing scores   Objective: Serum OA biomarkers (WF6), force plate analysis (PVF), range of motion (ROM) via goniometer  | Green-lipped mussel administration led to good clinical outcomes. The fish oil did not show any positive effects in the canine OA treatment.  | III  |
| Vijarnsorn *et al.*, (2019)  | Randomised, double-blinded study  | Firocoxib Green-lipped mussel  Combination of firocoxib and Green-lipped mussel    | 79 dogs   | 4 weeks  | Subjective: veterinary assessment (OAS (orthopaedic assessment score)  CMI: CBPI   Objective: PVF, serum prostaglandin E2 concentration  | A combination of both green-lipped mussel and firocoxib is most effective in alleviation of inflammation and improvement of weight bearing ability.   | II  |
| Fish oil (Omega-3)   | Hielm-Björkman *et al.*, (2012)  | Double-blind, randomised, placebo-controlled study  | Deep sea fish oil  Corn oil (placebo)   | 77 dogs   | 16 weeks  | Subjective: locomotion assessment via VAS, QoL VAS, comparative questionnaire, veterinary assessment, owner assessment of outcome.   CMI: HCPI  Objective: PVF and VI, use of rescue NSAIDs  | There was no statistically significant benefit in using deep sea fish oil as an analgesic. However, owners indicated an improvement in mobility at the end of the study with the HCPI CMI  | II  |
| Mehler *et al.*, (2016)  | Double-blind, randomised, placebo-controlled, cross-over designed study  | Triglyceride n-3 oil  Placebo oil   | 78  | 84 days  | Subjective: veterinary assessment using multiple VAS    | Daily supplementation of a dog’s diet with omega-3 correlates to reduced pain and lameness in OA dogs. | II  |
| Moreau *et al.*, (2012)  | Double-blind, randomised, placebo-controlled study  | Veterinary therapeutic diet rich in omega-3 fatty acids (omega-3) from fish origin Regular diet used as control  | 30 dogs   | 13 weeks  | Subjective: veterinary assessment  CMI: CSOM  Objective: Force plate analysis (PVF)  | High levels of omega-3 from fish origin improved both CSOM and PVF scores | II  |
| **Collagen-based nutraceuticals** | Collagen  | Deparle *et al.*, (2005)  | Double-blind, randomised, placebo-controlled study  | No undenatured type-II collagen (placebo)  Undenatured type-II collagen at 1mg/day  Undenatured type-II collagen at 10mg/day  | 15 dogs   | 90 days followed by a 30-day withdrawal period  | Subjective: veterinary assessment using VAS and observational questionnaire.   Objective: Biochemical assay (creatinine, blood urea nitrogen, alanine aminotransferase and aspartate aminotransferase)   | Daily treatment of arthritic dogs with undenatured type-II collagen reduces signs and symptoms associated with OA. The greatest physical improvements were noted after a treatment period of 90 days.   | II  |
| Stabile *et al.*, (2019)  | Blinded, randomised, prospective, controlled study  | Undenatured type-II collagen (1 tablet/day) Robenacoxib (1 mg/kg/day)  | 60   | 30 days  | Subjective: veterinary assessment  CMI: LOAD questionnaire  Objective: Radiography   | The results of this study showed that undenatured type-II collagen and robenacoxib were able to similarly improve mobility of dogs affected by OA  | II  |
| Collagen, glucosamine hydrochloride and chondroitin sulphate  | Gupta *et al.*, (2011)  | Double-blind, randomised, placebo-controlled study  | Placebo  10mg active undenatured type-II collagen  2000mg glucosamine hydrochloride and 1600mg chondroitin sulphate 10mg active undenatured type-II collagen, 2000mg glucosamine hydrochloride and 1600mg chondroitin sulphate  | 7-10 dogs per group  | 150 days  | Subjective: veterinary assessment by multiple VAS and visual gait analysis   Objective: Force plate analysis (PVF and VI) and biochemical assay (creatinine, blood urea nitrogen, alanine aminotransferase and aspartate aminotransferase)   | Dogs treated daily with undenatured type-II collagen (10 mg) showed a marked reduction in OA pain with maximum improvement seen on day 150.   Efficacy of undenatured type-II collagen is significantly greater than glucosamine hydrochloride and chondroitin sulphate   | II  |
| D’Altilio *et al.*, (2007)  | Double-blind, randomised,  prospective, controlled study  | Placebo  10mg active undenatured type-II collagen, 2000mg glucosamine hydrochloride and 1600mg chondroitin sulphate  2000mg glucosamine hydrochloride and 1600mg chondroitin sulphate 10mg active undenatured type-II collagen   | 20 dogs  | 120 days followed by a 30-day withdrawal period   | Subjective: veterinary assessment by multiple VAS   Objective: Body weight, Biochemical assay (creatinine, blood urea nitrogen, alanine aminotransferase and aspartate aminotransferase)   | Supplementing glucosamine hydrochloride, chondroitin sulphate with undenatured type-II collagen reduced overall pain, pain upon limb manipulation, and exercise induced lameness to a significant extent. Although this benefit was also lost following the 30-day treatment withdrawal period  | II  |
| **Nutraceuticals with chondroitin-glucosamine** | Chondroitin sulphate  | Dobenecker *et al.* (2002) | See study details above under Omega-3-based nutraceuticals section |   |
| Glucosamine hydrochloride and chondroitin sulphate  | Gupta *et al.*, (2011) and D’Altilio *et al.*, (2007)  | See study details above under Collagen-based nutraceuticals section  |   |
| McCarthy *et al.*, (2007)  | Multi-centred double-blind, randomised prospective controlled study  | 475mg/g glucosamine hydrochloride, 350mg/g, chondroitin sulphate, 50mg/g N-acetyl-D-glucosamine, 50mg/g ascorbic acid and 30 mg/g of zinc sulphate  Carprofen (2mg/kg BID for 7 days followed by 2mg/kg SID for 63 days)   | 42 dogs  | 70 days  | Subjective: Veterinary assessment via VAS  | Dogs treated with glucosamine hydrochloride and chondroitin sulphate+ showed statistically significant improvements in scores for pain, weight-bearing and severity of the condition by day 70. Slower onset of clinical response than for carprofen-treated dogs.   | II  |
| Scott, Evans and Conzemius, (2017)  | Double-blind, randomised placebo-controlled study  | Glucosamine hydrochloride and chondroitin sulphate Placebo   | 60 dogs  | 97 days  | Subjective: Veterinary assessment  CMI: Canine brief pain inventory (CBPI)  | Treatment with oral glucosamine hydrochloride and chondroitin sulphate for a 90-day treatment period when compared to placebo treatment did not result in a significant increase in activity counts in dogs with clinical OA.  | II  |
| **Others** | Curcumoids  | Innes *et al.*, (2003)  | Double-blind randomised placebo-controlled parallel group clinical study  | P54FP  placebo   | 61 dogs  | 8 weeks   | Subjective: Veterinary assessment, owner-reported assessment   Objective: Force plate analysis (PVF and VI)     | Results showed statistically significant treatment effect in favour of P54FP (P>0.05), but the owners' assessment just failed to reach statistical significance.  | II  |
| Elk velvet antler  | Moreau *et al.*, (2004)  | Double-blind, randomised placebo-controlled study  | Quality elk velvet antler for 60 days (n=25 dogs)  Placebo for 30 days and then quality elk velvet antler for 30 days (n= 13 dogs)    | 38 dogs  | 60 days   | Subjective: Veterinary assessment, owner interpretation   Objective: Force plate analysis (GRF), radiography  | Performances in daily life activities, and vitality were significantly improved on quality elk velvet antler,  exceeding those observed when placebo was administered. Thirteen dogs did not show significant improvement  | II  |
| Vitamin E  | Rhouma *et al.*, (2013)   | Double-blind, randomised placebo-controlled study  | Placebo (n=8)  Vitamin E group receiving 400 IU/animal per day   | 15 dogs   | 55 days  | Subjective: VAS and NRS  Objective: electrodermal activity (EDA), structural assessment of stifle joints at day 56  | Supplement with a high dose of vitamin E showed a reduction in inflammation joint markers and histological expression, as well as a trend to improving signs of pain  | II  |
| Avocado and soybean unsaponifiables  | Boileau *et al.*, (2009)  | Double-blind, randomised placebo-controlled pilot study  | Placebo  Avocado/soybean unsaponifiables (10 mg/kg per day)  | 16 dogs   | 8 weeks   | Objective: Macroscopic and histomorphological analyses of cartilage and subchondral bone of the femoral condyles and/or tibial plateaus, and immunohistochemical  | 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  | II  |
| S-adenosyl L-methionine (SAMe)  | Imhoff *et al.*, (2011)  | Double-blind, randomised placebo-controlled study  | Placebo  SAMe   | 33 dogs  | 6 weeks  | Subjective: veterinary assessment and CBPI  Objective: Force plate analysis (PVF and VI), goniometry   | Data do not support the use of SAMe as an effective standalone treatment for reducing clinical signs of OA  | II  |

Abbreviations: NRS=numerical rating scale; VAS= visual analogue scale; PVF= Peak vertical force, VI= Vertical impulse, CMI= clinical metrology instrument, LOAD= Liverpool Osteoarthritis in Dogs questionnaire, CBPI=Canine Brief Pain Inventory, HCPI*=* Helsinki chronic pain index, OA= osteoarthritis, CSOM*=* client*-*specific outcome measure

Table 3. Studies investigating acupuncture as a treatment for canine osteoarthritis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Type of acupuncture investigated** | **Author** | **Study type** | **Groups** | **Sample size** | **Study length** | **Outcome measures** | **Conclusions** | **Evidence level****(Aragon and Budsberg 2006)** |
| **Dry needle acupuncture** | Teixeira *et al.* (2016) | Randomised, blinded controlled clinical trial | AcupunctureCarprofenPlacebo capsules | 54 HD affected dogs16 healthy dogs | 8 weeks | Subjective: owner evaluation, VASCMI: CBPIObjective: Kinetics | Acupuncture or carprofen groups did not differ significantly from placebo.CBPI and VAS pain intensity assessment decreased in acupuncture group from baseline at week 4 and 6. | II |
| Baker-Meuten *et al.* (2020) | Randomised, blinded, controlled clinical trial | PlaceboAcupuncture | 32 | 4 weeks | Subjective: SOS, Objective: GRF, AC.CMI: CSOM, CBPI | No difference between baseline and acupuncture and placebo for GRF, AC, SOS. Improvement in some CMI scores with baseline vs acupuncture and placebo vs acupuncture. | II |
| **Mixed acupuncture and other physical therapies** | Lane and Hill (2016) | Randomised, blinded, crossover clinical trial | Exercise restriction followed by combined acupuncture and manual therapy (CAMT) | 47 | 42 days | Subjective: owner questionnaire VAS | No significant improvement with exercise restriction alone. Significant improvement in some measures after CAMT appointments. | III |
| Silva *et al.* (2017) | Prospective study | Acupuncture and other alternative therapies (ALG)Acupuncture and pharmaceutical analgesic (AAG) | 145 dogs with neurological disease36 (n=8 ALG, n=28 AAG) dogs with musculoskeletal disease (including OA). | 24 weeks | Subjective: VASCMI: HCPI, QLA | VAS and HCPI reduced in both groups over course of trial, but more so in musculoskeletal group.  | III |
| **Electroacupuncture** | Kapatkin *et al.* (2006) | Randomised, controlled crossover trial | ControlElectroacupuncture Sham | 9 | 3 weeks | Subjective: Owner questionnaire(VAS)Objective: GRF | No significant improvement with EAP | II |
| Chomsiriwat and Ma (2019) | Randomised clinical trial | Electro-acupunctureLaser acupuncture | 31 | 8 weeks | Subjective: veterinary assessmentCMI: CBPI | Improved CBPI scores and hip joint ROM with both treatments.EAP led to significantly greater improvements in pain score and QOL assessment than LAP. | III |
| **Gold bead or wire implantation acupuncture** | Hielm-Bjorkman *et al.* (2001) | Randomised, double blinded, controlled clinical trial | Sham acupunctureGold wire implants at acupuncture points | 38 | 6 months | Subjective: veterinary and owner assessment Radiographs | No statistically significant differences between treated and control groups.  | II |
| Jaeger *et al.* (2006) | Randomised, double blinded, controlled, clinical trial | Gold bead implantation at acupuncture pointsPlacebo (sham) | 78 dogs with hip OA | 6 months | Subjective: Owner questionnaire, veterinary examination | Significantly greater improvements in mobility and reduced pain signs in treated group.  | II |

Abbreviations: QLA= health-related quality of life scale for dogs with signs of pain secondary to cancer, HCPI= Helsinki Chronic Pain Index, VAS= Visual analogue scale; EAP= Electroacupuncture; HD=hip dysplasia; CMI=clinical metrology instrument; CBPI=canine brief pain index; EAP=electroacupuncture; LAP=laser acupuncture; GRF=ground reaction forces; AC=accelerometery; SOS=subjective orthopaedic scoring; CSOM=client specific outcome measures.; OA=osteoarthritis.

Table 4. Studies investigating physiotherapy, hydrotherapy and different physiotherapeutic modalities for treating canine osteoarthritis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Type of therapeutic modality investigated** | **Author and year** | **Study type** | **Groups** | **Sample size** | **Study length** | **Outcome measures** | **Conclusions** | **Evidence level****(Aragon and Budsberg 2005)** |
| **Massage therapy** | Riley *et al.*, (2021) | Cross sectional study of current and retrospective cases | -dogs with various musculoskeletal disorders | 527 | -- | Subjective measurements of pain and QOL | Improvements in clinical outcomes in majority of dogs after massage therapy. Non-controlled and un-blinded study. | IV |
| **Aquatic exercise (outdoor pool swimming)** | Nganvongpanit *et al.*, (2014) | Randomised prospective blinded clinical trial | -OA with swimming-non-OA with swimmingNon-OA without swimming | 45 | 8 weeks | Subjective clinical scoring.Radiographs.Serum biomarker analysis (hyaluronan and chondroitin sulfate WF6 epitope. | Reduced pain and lameness scores in OA dogs after swimming. Reduced serum CS-WF6 in OA dogs after swimming. | III |
| **Hydrotherapy (underwater treadmill), physiotherapy and photobiomodulation therapy** | de Oliveira Reusing *et al.* (2021) | Randomised, prospective blinded clinical trial | Dogs with hip dysplasia-control -laser therapy +physiotherapy-hydrotherapy +physiotherapy-both laser therapy, hydrotherapy and physiotherapy | 32 | 2 months | CMI: CBPIObjective: muscle depth on ultrasound, goniometry, thigh circumference | Improved QOL scores in dogs receiving all treatment modalities compared to those receiving none or one. Thigh circumference increased in dogs receiving all treatments and decreased in those receiving none. Hip extension improved in dogs receiving hydrotherapy.  | II |
| **Photobiomodulation therapy**  | Looney *et al.* (2018) | Multicentre, randomised, blinded, placebo controlled clinical trial | Dogs with elbow OA receiving either:-PBMT(LLLT)-Sham light therapy | 20 | 6 weeks | Subjective: Lameness scoreCMI: HCPI | Improved lameness and pain outcomes in PBMT group compared to sham group. | II |
| Barale *et al.* (2020) | Retrospective report | Dogs with OA undergoing LLLT | 17 | 6 weeks | Subjective: VASCMI: CBPI, CSCPS | CBPI and VAS significantly reduced over treatment period compared to pre-treatment levels.  | IV |
| Barale *et al.* (2022) | Prospective clinical study | Dogs with stifle or knee OA undergoing LLLT | 23 | 6 weeks | CMIs: LOAD, CBPIObjective: Accelerometery | Significant improvement in daily step count and number of daily activities with LLLT | III |
| **Pulsed electromagnetic field therapy** | Sullivan *et al.* (2013) | Randomised, blinded, controlled clinical trial | Dogs with OA in differing joints-control group (rested)-PEMT group | 59 | 42 days | CMI: CBPIObjective: goniometry, force-plate gait analysis | PEMT group had lower CBPI scores than the control group at assessment timepoints at 11 and 42 days | II |
| Pinna *et al.* (2013) | Randomised, blinded, controlled trial | Dogs with OA in differing joints-firocoxib-PEMT | 40 | Up to 12 months | Subjective: veterinary examinations, owner questionnaire.  | Outcomes with the PEMF group were not less than the control group | II |
| **Extracorporeal shockwave therapy** | Dahlberg *et al.* (2005) | Randomised controlled trial | Dogs with stifle OA-control (no treatment)-ESWT | 12 | 16 weeks | Subjective: owner questionnaireObjective: force-plate gait analysis, goniometry | 4/7 treated dogs had improved PVF compared to 1/5 control dogsTrend towards increased ROM in stifle joints of treated dogs. No differences in owner assessments.  | II |
| Mueller *et al.* (2007) | Randomised controlled trial | Dogs with hip OA-ESWT-untreated control | 24 | 3 months | Objective: force-place gait analysis | Improved PVF and PI in treated group, but not significantly different to control | II |
| Millis *et al.* (2011) † | Randomised control trial | Dogs with elbow OA-ESWT-untreated control | 15 | 28 days | Subjective: veterinary assessmentObjective: kinetic gait analysis | ESWT led to significant improvements compared to control in all outcomes | II |
| Souza *et al.* (2016) | Randomised blinded controlled trial | Dogs with HD-ESWT -untreated control | 30 | 90 days | Subjective: veterinary assessment VAS, owner questionnaireObjective: force-plate gait analysis | Improved outcomes in all outcome measures in treated compared to non-treated limbs.  | II |
| **Therapeutic ultrasound** | Muste *et al.* (2015) | Prospective clinical study | Dogs with stifle OA | 8 | 3 months | Subjective: veterinary assessmentObjective: goniometry | Improvement in subjective outcomes with therapeutic ultrasound. Low sample size.  | III |
| **Physiotherapy including transcutaneous electrical nerve stimulation** | Mlacnik *et al.* (2006) | Non-blinded prospective randomised clinical trial | Dogs with OA in various joints-Caloric restriction and intensive physical therapy including TENS -Caloric restriction and home-based physical therapy | 29 | 6 months | Subjective: subjective lameness and pain scores (0-4)Objective: kinetic gait analysis | Significant improvement in kinetic gait analysis in both groups at end of study, but changes happened more quickly in dogs receiving intensive physical therapy and TENS. | III |

Abbreviations: QLA= health-related quality of life scale for dogs with signs of pain secondary to cancer, HCPI= Helsinki Chronic Pain Index, VAS= Visual analogue scale; HD=hip dysplasia; CMI=clinical metrology instrument; CBPI=canine brief pain index; GRF=ground reaction forces; AC=accelerometery; SOS=subjective orthopaedic scoring; CSOM=client specific outcome measures; PVF=peak vertical force; PI=peak impulse; TENS=transcutaneous electrical nerve stimulation. †=published abstract