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CBD

WHAT? WHY? WHEN? EVER?



**canine arthritis
management**

CBD - WHAT? WHY? WHEN? EVER?

CBD is a trending health care product of the moment in both humans and animals. Having risen in popularity in the last few years, we are seeing a huge amount of discussion on this subject on Holly's Army and questions directed to us at Canine Arthritis Management with owners keen to learn more.

This CAM handout aims to **help you**, the owner, circumnavigate this well marketed industry because many CBD-based supplement products

now offer bold label claims, such as "controls arthritic pain" without the body of evidence in animals to support these claims.

Please note this handout is not suggesting or advising that CBD is suitable for any pet. In the UK there are currently no authorised CBD-based products for animals, and it is an offence to supply it without a prescription from your vet.

CUT TO THE CHASE

At present, our position on the use of CBD-based supplement products is that there are currently too many uncertainties about whether CBD supplements are beneficial for dogs with osteoarthritis, as there is no suitable licensed animal pharmaceutical product on the UK market that has proven efficacy and established safety margins for dosing.

Some companies market human CBD-based supplements. Human supplements containing cannabinoids do not fall under the scope of the VMD or the MHRA (the UK's Medicines and Healthcare products Regulatory Agency) but are regulated by the UK Food Standards Agency (FSA). As food supplements, these products must follow rules on their labelling and that includes not making any specific medical claims. It is illegal to make specific medical claims for these products. Although these products are regulated by a network of organisations, studies tend to show that label claims often do not match contents so without a certificate of analysis we have no way of knowing what these products contain. For example; a recent survey by the Centre for Medical Cannabis of 30 high street products revealed concerning results. One product had zero CBD in it and was retailing at £90. 11 had less than 50% of their stated CBD content. 8 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. As you can see prescribing a human supplement is not easy when there are many rogue products out there and vets are rightly concerned about product quality.

New studies are currently being conducted and in time evidence may present itself. When this occurs CAM will promptly review our stance on these products.

Here is some terminology that can cause confusion when discussing CBD products:

CANNABIS – refers to the plant itself. Cannabis sativa is one of three plants and the plant from which many products are harvested for both therapeutic, nutritional and pleasure reasons. The Cannabis plant contains hundreds of compounds of medicinal interest, of which over 100 are known as cannabinoids. Of these hundreds of cannabinoid compounds, the two of greatest current interest are cannabidiol or CBD, and tetrahydrocannabinol or THC.

MARIJUANA – refers to the Cannabis plant that has high levels of THC. THC comes with psychotropic/intoxicating effects (the get you high effects) and should be avoided. Cannabis leaves, buds, and seeds – it is important to understand that different parts of the cannabis plant contain different amounts of cannabinoids. The buds/ flowers of the plant contain the most cannabinoids both, i.e. the most CBD and THC. The leaves and seeds contain little cannabinoids but are still promoted as having medicinal benefits. Hemp (industrial) plant – is the Cannabis plant, which has low THC levels (<0.2% in the UK). These plants used to also contain less CBD, in recent years they have been grown and selected for higher/ therapeutic levels of CBD and are now a staple source for many CBD based products.

HEMP – is a fibrous product that is from the industrial Hemp plant (non-flowering and thus low in cannabinoids). It is used to make rope, paper, beauty products, and a vast array of other products. The name “Hemp” could lead to purchase in pursuit of medicinal benefit when it does not have any benefit.

PHYTOCANNABINOIDS – are the chemical compounds found in cannabis that act upon cannabinoid receptors within the body. THC (Tetrahydrocannabinol) and CBD (Cannabidiol) are just 2 of the hundreds of phytocannabinoids within the Cannabis plant.

CBD – Cannabidiol has gained support for its use as a medical treatment as research has shown it may treat pain, inflammation, and anxiety without the intoxicating effects.

THC – Tetrahydrocannabinol is the most well-known because of its intoxicating effects called the “high.” THC is known to have additional health benefits, but we also know dogs are much more sensitive to THC than we are and can suffer toxicity from high amounts.

TERPENES – the distinctive smell of Cannabis is due to the terpenes contained within.

FLAVONOIDS – are a group of molecules from the plant that provide various flavour profiles and are also believed to possess health benefits.



CBD AND HOW IT WORKS

CBD and other cannabinoids from the plant Cannabis are classified as phytocannabinoids, meaning they are from plants (phyto- meaning plant) and work on the endocannabinoid system (ECS). This 'system', that all vertebrates have, is a relatively new discovery. What we know is that there are substances naturally produced in the body that are similar to cannabinoids and these interact with receptors on cells called cannabinoid receptors; therefore, when plant cannabinoids are taken/given and absorbed into the circulation, they interact with natural cannabinoid receptors. We currently don't know a huge amount about the role of endocannabinoids in the body. Research into this continues, but a general overview is that it acts to bring about a state of homeostasis. It is involved in coordinating movement, pain modulation, memory, sleep, appetite, and the immune system. There are some thoughts that it is the system connected with the placebo effect.

Relatively recent research is highlighting the ECS is involved in many disease processes such as cancer, pain, inflammatory disease, neurological disease and the list goes on.

There are two endocannabinoid receptors CB1 and CB2. CB1 receptors are predominantly located in the central nervous system, and this is the receptor targeted by THC, and explains the psychotropic effects we see. Whereas, CB2 receptors, are located throughout the rest of the body and are closely linked with the immune system. These receptors can increase in expression during disease. For example, CB1 and CB2 receptors increase in the locality of damaged nerves or tissues, which explains CBD's pain-relieving effects.

WHY IS CBD NOT PRESCRIBED MORE OFTEN BY UK VETERINARIANS?

Currently, it is difficult for your veterinarian to advise you regarding incorporating CBD into your treatment plan, as the Veterinary Medicines Directorate (VMD) has reclassified CBD as a medicinal product. This means that it is an offence to supply it without a prescription from your vet. However, a suitable animal CBD-based product which fulfils essential prescription requirements (i.e. has a marketing authorisation, has demonstrated clinical efficacy through extensive clinical trials, has safety data, and an understanding of potential drug interactions and adverse effects) is not currently available as a licensed animal medication in the UK.

Your veterinarian would need to abide by strict rules and follow the prescription cascade, which adds significant complexity to their discussion with you.

The restrictions your vet must respect are not matched in the consumers market. CBD sales are regulated by a patchwork of rules and regulations from different authorities which can lead to inconsistencies and it is a growing and lucrative market.

This is such a big area of confusion so we write again.

- **In the UK, veterinary products containing Cannabidiol (CBD) are veterinary medicines and should be regulated as such.**
- **The veterinary medicines regulator (the Veterinary Medicines Directorate [VMD]) made this clear on 14 September 2018 and has since written to UK CBD suppliers and manufacturers informing them of the position (Vet Record 6 October 2018).**
- **This means that without a marketing authorisation it is illegal to sell, supply or advertise CBD products for pets, with or without specific treatment claims.**
- **There are currently no authorised CBD-based products for animals in the UK.**

VETERINARY PRESCRIPTION AND ADVICE REGARDING CBD PRODUCTS

Vets must follow the prescribing cascade set out by the VMD, which would allow them to prescribe a human medical equivalent. Human product equivalents do exist, Epidyolex (a pure CBD product with a market authorisation for a specific form of childhood epilepsy), Sativex (a THC and CBD product with marketing authorisations for muscle spasticity in Multiple sclerosis sufferers), and Nabilone (a synthetic THC product with marketing authorisation for managing chemotherapy induced nausea). However, these are simply not readily available to animals and cost-prohibitive to prescribe.

The next step in the legally binding prescribing cascade is to prescribe a human focused supplement with independent laboratory testing to prove the reliability and safety of the content.

For a vet 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 veterinary specialist manufacturer and products that are regulated by GMP (Good Manufacturing Practice) and GDP (Good Distribution Practice) guidelines.

Finally, for a vet to comfortably prescribe CBD other recognised evidence-based avenues of treatment/ intervention have to have been tried without success. For example, having been presented with a dog with musculoskeletal pain, it is good practice to initially prescribe a non-steroidal anti-inflammatory (NSAID) as these have a lot of evidence regarding effectiveness and safety in comparison to CBD.



CBD CONTAINING PRODUCTS AVAILABLE FOR PUBLIC PURCHASE

Google search shows 150 million plus “hits” on CBD; this is a booming industry with some unscrupulous marketing strategies. CBD containing products are varied, but most are CBD containing oils and tinctures (a product dissolved in an alcohol base). However, an owner may be exposed to CBD supplement (hemp) containing chews, treats, foods, creams etc. that are not UK based and

should not be marketed to the pet industry in the UK.

At present in the UK, no CBD containing products should be marketed for use in animals. If you find products that are openly marketing to the pet owning public, please be aware that is an offence created for the safety of your pet.

TERMINOLOGY USEFUL WHEN LOOKING AT LABELS

FULL SPECTRUM PRODUCT – Cannabis plants contain other compounds in addition to cannabinoids such as terpenoids and flavonoids which might contribute medicinally.

“Full-spectrum” is a plant-based cannabis product containing the full complement of the medicinal compounds (cannabinoids, terpenes, flavonoids). But note, Cannabis sativa has many variations within this one species, and each variation will have a unique array of active/ medicinal compounds (i.e. cannabinoids, flavonoids and terpenoids) and thus a unique medicinal profile—these “varieties” are called chemovars (from “chemo”, chemical and “var” variety). This profile is further influenced by how and where the plant is grown, as well as the extraction process to harvest the sold product. **A certificate of analysis (CoA)** is essential to know what medicinal components are in the product that you are purchasing. Ideally by an independent laboratory.

Be wary of products labelled as “full spectrum” without an accompanying CoA. Many of today’s Cannabis companies are utilizing this term for products that actually contain only one or very few components.

CBD-RICH PRODUCT – This is a plant variant or product that contains either an equal or greater ratio of CBD to THC.

BUT note. This gives no information regarding what else is in this product, such as other cannabinoids, terpenes or flavonoids. It suggests the THC is lower than CBD concentrations but both, or either, could be unsuitably high. A CoA must still be referred to for greater detail about actual concentrations

CBD-DOMINANT PRODUCT – similar to CBD- rich product this has a higher ratio of CBD to THC, but also has lower levels of THC in total. However, it offers no details of the actual content of the product and a CoA is essential.

HEMP SEED OIL – this is made from Cannabis plant seeds and offers no medicinal benefit but high concentrations of plant-based omega 3 fatty acids. (These have not been associated with suitable anti-inflammatory action within a joint and should not be confused with marine based omega 3 fatty acids that have a substantial evidence base.)

ISOLATE PRODUCT – a single compound product BUT it must explain from where the compound was derived (i.e. hemp, Marijuana etc.), and how much is in it. So, again, a CoA is needed.

AMBIGUOUS PRODUCT DEFINITIONS THAT ARE OFTEN USED:

BROAD SPECTRUM PRODUCT – or “full spectrum product” are commonly used on products with only the THC removed, so will have other cannabinoids, flavonoids and terpenes within it. BUT you still need to see a CoA in order to know what is actually in it.

EXTENDED SPECTRUM PRODUCT – will contain all cannabinoids, flavonoids and terpenes but will have additional cannabinoids and terpenes added. AGAIN there should be a CoA as this does not tell you what is actually in the product.

CBD OIL – this doesn't tell you much about the product and requires a CoA for clarity of content.

PCR (PHYTO-CANNABINOID RICH) PRODUCT – this simply means a plant derived product that contains cannabinoids. AGAIN, this requires a CoA to clarify content.

CBD PRODUCT – this doesn't tell you much about the product and requires a CoA for clarity of content.



CERTIFICATE OF ANALYSIS

- Look into the certificate of analysis, as they may contain high levels of THC which could be dangerous and illegal. A product claiming to have no THC should show they have less than 0.01% on the CoA.
- Read the CoA to understand what cannabinoids are present and discuss with your veterinarian.
- Check that the CoA includes a residual solvent analysis, levels of herbicides, fungicides, insecticides, heavy metals, mycotoxins, microbial contaminants that may be in the product. Please remember that Cannabis plants are very hardy and will grow in poor soil, absorbing lots of unwanted soil-based pollutants. Often the hemp from which the CBD is harvested is intensively grown requiring fungicides and herbicides which may be in the end product. And finally, that the extraction techniques can leave potentially dangerous trace chemicals. Carbon dioxide extraction is generally seen as safe and leaves no dangerous residue behind in the concentrated product, but other extraction methods are also approved for use in botanical pharmaceutical and food products.
- Check for other ingredients in the product that may be dangerous for pets, such as xylitol.



PROMOTED BENEFITS OF CBD v EVIDENCED BENEFITS OF CBD

CBD has received a lot of press regarding its potential benefits; however, a lot of these claims have not been fully proven, especially in animals. There are clinical trials occurring globally, and academic papers being released weekly, so hopefully, over time we will have more evidence to support these exciting claims. At present a lot of what you read will be theoretical from laboratory studies, extrapolated and anecdotal, especially in the pet sector. A lot of what is published regarding CBD is extrapolated from human data, which may not be reliable in a different species.

At present only 5 clinical efficacy trials exist in dogs. One performed at the University of Cornell by Gamble et al (2018). Each dog was treated for 4 weeks with CBD (2mg/kg BID by mouth) and compared to a placebo. This was a well-constructed study with respected methods of assessing improvement or deterioration and indicated CBD oil had efficacy treating dogs with osteoarthritis (OA) related pain, although the study did have a few limitations due to small study number and short duration, so further work in this area is required.

A more recent small (20 dogs) randomised placebo controlled study in 2020 has suggested CBD has a statistically significant influence on symptoms of pain. The short (4 weeks) but well constructed trial used 'blinded' veterinarian and owner assessments and concluded that dose and delivery are important. The higher dose CBD and the liposomal CBD (a novel delivery agent) were shown to be effective whereas placebo and low dose CBD were not, which highlights the importance of collecting a lot more data to find the optimal dose range for dogs.

During this short trial no adverse events were noted which certainly adds to the intrigue regarding CBD as a recognised arthritis intervention in the future. It also demonstrated that the formulation of the CBD product can be crucial. Limited oral bioavailability, due to poor aqueous solubility and extensive first-pass metabolism, was seen, which was not seen in the liposomal encapsulated product. This presentation in humans resulted in a 17-fold increase in bioavailable circulating CBD after oral administration compared to the "naked" product.

CBD is certainly an exciting prospect, but at present, we still require further investigation and good-quality, longer term studies to fully understand its potential medicinal use in dogs and its potential side effects and drug interactions.



CONCERNS REGARDING THE USE OF CBD CONTAINING PRODUCTS

There are many concerns regarding the sudden popularity in CBD containing products.

- The safety of the product itself as it is an inconsistently regulated market.
- Optimal dosage is not currently known
- The potential side effects of its use with other medications. Many owners seek further interventions when their pet is already on medication for the health complaint. More knowledge is required regarding how CBD and other cannabinoids interact with different medications. For example, co-administration of excessively high doses of CBD with therapeutic doses of paracetamol causes liver disease in mice. CBD products have also been shown to significantly enhance the effects of benzodiazepines (Valium and Xanax), gabapentin and tramadol. And it is known that CBD inhibits hepatic cytochrome P450, which may alter the efficacy of other drugs; either enhancing or inhibiting, their metabolism. This means CBD may increase the activity of some drugs or some may inhibit the desired activity of others.
- We know little about the effects of long term (12 months +) administration of CBD in pets and as the biggest market for CBD is a chronic disease (i.e. arthritis, dementia, epilepsy), these pets will likely be on long term courses.
- The availability and claims being made regarding CBD will prevent pets from getting the veterinary care they require. This is of great concern to the veterinary community as we are already seeing cases too late because of freely available non-professional advice online. An “all singing, all dancing” supplement, that can treat all ailments, will certainly add to our fears.
- That an owner will refuse to use products that have evidence of benefit for their dog's condition over the use of a CBD-based supplement product with little evidence and the added complication of potentially unreliable inconsistent content.
- That an owner will designate their definitive funds on a product that we know little about, leaving little funds for a respected investigation and appropriate management.



TIME TO EFFECT

Not only does the product concentration play a role in its effectiveness, so does the method of delivery to the body. Studies have shown that tinctures in an oil or solid formulation can be absorbed through the mucous membranes. (Deabold, 2019; Wakshlag (in press). However when swallowed, they are absorbed within the gastrointestinal tract and follow the same path as nutrients – they pass through the liver, are metabolised and then reach the bloodstream.

Pharmacokinetic studies assess how much of the original product can be found in the blood at different time points. This allows us to know how much of it makes it to the bloodstream in its original or active form (i.e. is not metabolised by the liver) and how quickly it is removed from the body. Currently, the only pharmacokinetic studies in dogs and cats showing significant concentrations of CBD in the bloodstream have been done with oral oil based products and have shown that CBD infused oil preparation may be the most effective formulation.

SIDE EFFECTS

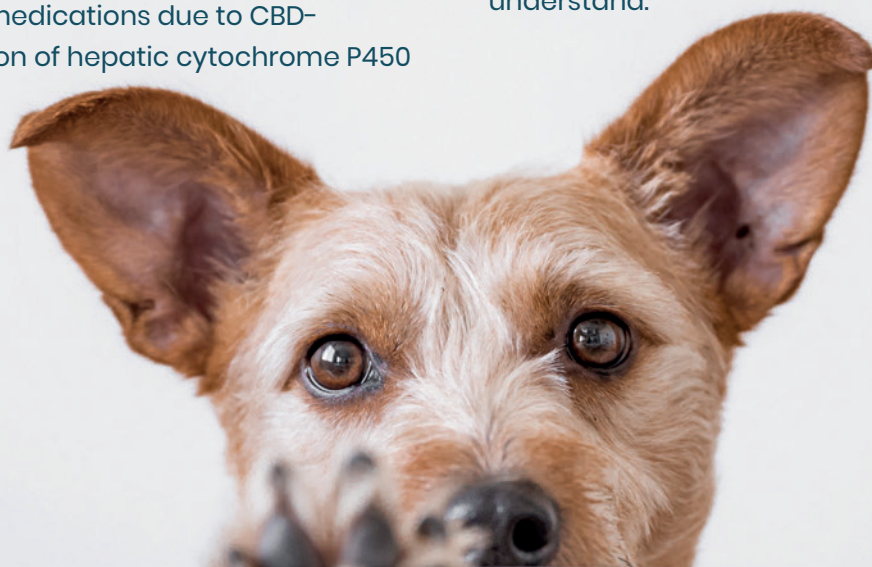
At present CBD only products are seen as low risk regarding side effects which is great, however, we are seeing cases of toxicity, especially in accidentally ingested human products such as concentrated oils used in vapes and products containing illegal levels of THC.

In clinical studies, it has been shown to increase a liver enzyme called alkaline phosphatase (ALP), but what that signifies is not yet known.

There are also concerns regarding its use alongside other medications due to CBD-mediated inhibition of hepatic cytochrome P450

(CYP450) which is essential to either activate or terminate other drugs working in the body. This adds risk to using CBD in animals that are already on other medications.

There is also little known regarding the long-term administration of CBD. At present we do not know if there is a cumulative effect. The potential for a cumulative effect increases with obese animals as CBD can be stored inactively in the fat; this is an area that we do require more information in to understand.



CAM CONCLUSIONS REGARDING PRODUCTS AVAILABLE FOR PETS

- Currently, there are no products specifically for pets with marketing authorisation. This means, there are no products that have the same information regarding efficacy, safety and possible adverse reactions that you would expect from a medication. Any product that has medical claims attached to it or is marketed towards pet owners is flouting UK regulations.
- The CBD containing products currently available to purchase are human food supplements. The regulations applied to these products and monitoring of them is very different from that of medicines. There is concern regarding their safety and whether they meet label content claims and efficacy.
- Please remember that CBD retailers are businesses like any others and use marketing to sell their product.



FURTHER INFORMATION

The BSAVA has published its scientific position on the use of cannabidiol (CBD) in cats and dogs (2020). This reaffirms points already made in the Canine Arthritis Management CBD handout.

KEY POINTS INCLUDE:

There are no cannabidiol (CBD) products with UK veterinary marketing authorisation and so under the provisions of the cascade, a legally obtained human product could be prescribed.

The use of CBD products would be considered 'treatment' of an animal (under the Veterinary Surgeons Act 1966), and therefore, cannabidiol must be prescribed by a veterinary surgeon before being administered by an owner as a treatment.

It is considered a complementary medicine and should not be used instead of medications or treatment with proven efficacy.

The amount of CBD in non-licenced preparations is variable and may not contain the concentration of CBD described on the label and in addition may contain unlabelled components.

There are limited clinical studies on the beneficial effects of CBD in dogs. Studies involve small groups of dogs and results need to be interpreted with caution. Reported side effects of CBD in dogs include ataxia, increases in ALP and development of soft stools and vomiting.

"Information regarding the effects of cannabinoids on animals is predominantly at the stage of pre-clinical testing of individual substances in mice, rats and guinea pigs. There are limited clinical studies looking at the effects of CBD in dogs, and no reported studies in cats."

Furthermore:

Brennen McKenzie (2021) has looked into updated knowledge on the subject of CBD and Arthritis in a new blog: Evidence Update: Discouraging News for CBD & Arthritis in Dogs.

Mejia, S. *et al.* (2021) '[Evaluation of the Effect of Cannabidiol on Naturally Occurring Osteoarthritis-Associated Pain: A Pilot Study in Dogs.](#)', *Journal of the American Animal Hospital Association*. J Am Anim Hosp Assoc. doi: 10.5326/JAAHA-MS-7119.

In this study, 23 dogs were randomly assigned to begin treatment with 2.5 mg/kg twice daily of hemp oil with CBD or hemp oil without CBD, and then were crossed over to the other treatment after 6 weeks. Any effects were assessed by activity counts, weight bearing using a pressure mat, and evaluation of gait by a blinded veterinarian.



Blood testing showed that dogs on the placebo had no measurable CBD or THC in their blood while dogs getting the active treatment had both.

Unfortunately, no difference was identified between the treatment and placebo by any of the measures evaluated.

As is common in studies of CBD, a few dogs had elevations of liver enzymes without apparent clinical symptoms on the substance, and a couple experienced vomiting when taking it, one of whom had serious enough symptoms to be removed from the study. A small placebo effect was detected by one measure of effect, but not by the others.

In this review, Brennen McKenzie mentions the **Decline Effect**. This is a phenomenon in science in which early research into a novel idea tends to show strongly positive findings. However, as more studies are done by a greater variety of scientists, the size of the effect tends to decline, sometimes to zero. This likely represents both the influence of bias in early studies caused by enthusiasm of scientists for their own new hypotheses and a gradual improvement in methods and reduction in overall positive bias as the scientific community studies new ideas over a period of time.

[Read the full BSAVA report here](#)

FURTHER RESOURCES & NOTE OF THANKS

CAM interviewed **Siobhan Menzies** and **Stephen Cital** regarding the use of CBD based products.

You can find the series of videos by clicking on the following links.

[SIOBHAN MENZIES](#)

[STEPHEN CITAL](#)

Resources for further information:

[Veterinary Cannabis](#)

[UK Cannabis Clinic](#)

A note of thanks to Andrea Tarr, Fergus Coutts, Robyn Lowe, Siobhan Menzies and Stephen Cital for their support in writing this owner focused CBD handout.

Conflicts of interest: Some professionals working on this piece have affiliations with CBD-based products.

