

Alphabet Soup: A Q&A about CBD

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Cannabidiol, frequently referred to as “CBD”, is gaining in popularity and interest by pet owners and veterinary professionals alike. At Pet Poison Helpline, we get a lot of questions about the safety of CBD and the number of poison control consults regarding CBD products increases significantly year over year. We wanted to take this opportunity to explain what CBD is, reasons it may be given to a pet, its current regulatory status, and what our experience has been when pets are accidentally overdosed on CBD.

What is CBD? CBD is an extract of the *Cannabis sativa* or *Cannabis indica* plant. It is routinely described as non-psychoactive which means it doesn't result in a “high” like THC (tetrahydrocannabinol). CBD often comes from hemp plants which are cultivars of *Cannabis* that are bred to contain very low amounts of THC (< 0.3% THC on a dry weight basis). Each hemp plant contains a small amount of CBD for extraction and use. The remaining majority of the hemp plant is processed for industrial uses such as fabric, paper, construction material, cosmetics, and more.

Where can you buy CBD? Everywhere! There are retail and online stores selling tinctures, oils, creams, lotions, and gummies for humans while chews, treats, tinctures, and topicals are available for cats and dogs.

Are CBD chews, treats, and tinctures considered supplements? No. Strictly speaking, these products are not considered dietary supplements by FDA and are not regulated as such. There are no FDA-approved CBD products for animals or humans; they are only available as over the counter unregulated products.

What about topical products like lotions and ointments? No again. The answer is the same as above--topical use products are not regulated either.

Why would someone give CBD to their pet? CBD is advertised to alleviate arthritis pain, control seizures, mitigate tumor effects, decrease anxiety, improve appetite, boost immunity, and more. Based on advertising claims CBD seems to be a pet and people “cure all”. Pet owners want what is best for their pets and advertisers know this. Why wouldn't a pet owner be willing to try a cure all? Though usage claims can be outrageous like “CBD cures cancer”, most of these claims have not been substantiated and some are just plain false.

What specific pet research exists? A randomized, placebo-controlled, blinded, cross-over study published in 2018 by Gamble, *et al* demonstrated statistically significant reduction of pain and an increase in activity in a group of 16 pet dogs with concurrent arthritis at Cornell University. The dogs were given 2 mg/kg of CBD oil by mouth twice a day for four weeks. Dogs were also allowed to remain on NSAIDs, fish oil, and/or glucosamine/chondroitin supplements during the study. Laboratory work showed an increase in a liver enzyme (alkaline phosphatase) during CBD treatment.

A randomized, placebo-controlled, blinded study published in 2019 by McGrath, *et al* from Colorado State University's veterinary teaching hospital investigated the effect of oral CBD in addition to conventional antiepileptic treatment on 26 pet dogs with idiopathic epilepsy. The treatment group was given 2.5 mg/kg of CBD oil by mouth twice a day for 12 weeks along with their normally prescribed anti-epileptic drugs. The dogs that received CBD did experience less seizures than the placebo group; however, the number of dogs classified as “responders”—meaning they had at least a 50%

decrease in seizure activity—was similar to the placebo group. As with the arthritis study, laboratory work showed a statistically significant increase in alkaline phosphatase during CBD treatment.

Additional studies have been performed in dogs and cats that have investigated the systemic absorption of differing formulations CBD (eg, oral vs topical), pharmacokinetic parameters such as half-life, the effects and safety of various doses, etc. These studies were not trying to treat any specific disease process but were helping us to develop a greater understanding of how CBD is absorbed and processed by the body. See the suggested readings at the end of this article for a listing of these studies.

This doesn't mean other research is not available, but it is not controlled disease-response testing. Prior research is primarily lab animal based, *in vitro*, or case reports.

What agency regulates over-the-counter CBD-containing products? None of them! Non-prescription CBD products are not regulated so products only as good as a company's commitment to quality and purity. This is a red flag screaming "Buyer beware". FDA is in the process of determining how to regulate these CBD products but this could be months to years down the road.

Don't products have to contain what the label says? Again, the answer is an emphatic NO! It bears repeating that these products are not regulated. Several recent studies tested 'off the shelf' CBD products for ingredient quality, CBD concentration, and contamination. Unfortunately, testing revealed disappointing results. Some products contained little to no CBD, even when the labels listed a defined dose. Others contained vastly more CBD than labeled. Additionally, it was not uncommon for CBD products to be contaminated with THC, synthetic cannabinoids (potent, illegal substances that can cause seizures and other severe effects), and other, potentially harmful, non-labeled ingredients.

Can a "good quality" CBD product be harmful? CBD is considered minimally toxic although long term daily use has been well documented to increase a specific liver value called alkaline phosphatase. Diarrhea has also been documented with administration of CBD products. Additionally, CBD is metabolized in the liver by various cytochrome P450 enzymes which, in turn, can increase or decrease the rate of metabolism of other drugs and chemicals that a pet may be taking. Considerable research on drug-drug interactions with CBD is ongoing, especially in human medicine. Fetal development could potentially be negatively impacted by CBD and is not recommended for pregnant pets.

What happens when CBD is overdosed? Remember CBD is not a regulated veterinary drug, so there are no established or concrete therapeutic doses. Usage recommendations are based on limited research, anecdotal evidence, manufacturer recommendations, and veterinarians' personal experiences. A dog or cat ingesting a large amount of tincture or a full container of chews may exhibit clinical signs. Approximately half of the cases reported to Pet Poison Helpline involve a symptomatic animal. The most common effects reported in dogs are vomiting and diarrhea but some of the exposures we see are life-threatening.

Why do some patients have signs of marijuana (THC) toxicity after taking a CBD product? This is mostly due to poor quality CBD contaminated with THC or synthetic cannabinoids which, unfortunately, is quite common.

Can CBD be given with other supplements or medications? Maybe. As discussed above, there are many medications that require liver enzymes called cytochrome P450s for metabolism. CBD impacts cytochrome P450s making reactions possible. This means that some medications should not be taken with CBD while others may need to have their dose increased or decreased in order to remain safe and effective. This is one of the most important reason that pet owners should talk to their veterinarians before giving CBD to their pets. The veterinary community is becoming more aware of the possible interactions but more research is needed to aid in full understanding.

How familiar are veterinarians with CBD for use in dogs and cats? Many veterinarians were not taught about CBD in vet school and have only recently started to learn about it. As there is relatively little published research on dogs and cats, vets are struggling to understand exactly how CBD works in the body and how it can impact their patients. To complicate

matters, the sale of cannabis products, including CBD, sits in a legal quagmire evidenced by a patchwork of state regulations which differ from federal regulations. Until recently, CBD was federally classified as a schedule 1 controlled substance by the Drug Enforcement Agency (DEA). Schedule 1 substances are defined by the DEA as those with “no currently accepted medical use in the US...and potential for abuse”. Examples of schedule 1 substances include heroin, LSD, peyote, and “Ecstasy”. Because of this, prominent veterinary associations and governing bodies had discouraged vets from discussing CBD with pet owners. This left many vets confused and worried that talking about CBD with a pet owner could lead to legal repercussions or revocation of their medical license. Today, veterinary associations appear to be slowly changing their tune and trying to help vets better understand the potential therapeutic role of CBD. Vets understand that their clients want to know more about CBD and are working to bolster their own knowledge. Companies such as Veterinary Cannabis Education and Consulting may be a helpful option as their veterinarians offer case-specific consultation involving *both* the pet owner and their veterinarian.

How do you know if a CBD product is of good quality? With so many companies and products on the market, it can be overwhelming to know what is safe to buy. Look for companies that clearly discuss product quality and readily display independent, also called third party, laboratory testing of their products. Testing helps to guarantee the labeled concentration of CBD is present in their products. Testing for THC, other cannabinoids, and contaminants should also be displayed. Also look for clear labeling of the concentration of CBD in each drop of oil or dose of product so you know exactly how much is being given. Liquid products should be sold with a marked dropper or syringe to facilitate accurate dosing.

You’ve read the information and still want to use a CBD pet product. First and foremost, pet owners need to talk to their veterinarian! It is crucial that their pet be examined so they can receive a proper medical work-up and correct diagnosis. It’s possible the pet’s condition has a simple and safe therapy readily available. If CBD is potentially helpful, the pet’s current medications and supplements should be reviewed to prevent a problematic interaction. While there are still many unknowns related to the best uses for CBD, this is expected to change rapidly in coming years. Stay tuned as more research becomes available! Pet Poison Helpline will be here to keep you informed and educated.

Suggested reading:

Bartner LR, McGrath S, Rao S, Hyatt LK, Wittenburg LA (2018) Pharmacokinetics of cannabidiol administered by 3 delivery methods at 2 different dosages to healthy dogs. *Can J Vet Res.* 82(3):178-183.

Deabold KA, Schwark WS, Wolf L, Wakshlag JJ (2019) Single-Dose Pharmacokinetics and Preliminary Safety Assessment with Use of CBD-Rich Hemp Nutraceutical in Healthy Dogs and Cats. *Animals (Basel).* Oct 19:9(10). doi: 10.3390/ani9100832.

Gamble L-J, Boesch JM, Frye CW, Schwark WS, Mann S, Wolfe L, Brown H, Berthelsen ES and Wakshlag JJ (2018) Pharmacokinetics, Safety, and Clinical Efficacy of Cannabidiol Treatment in Osteoarthritic Dogs. *Front. Vet. Sci.* 5:165. doi: 10.3389/fvets.2018.00165

McGrath S, Bartner LR, Rao S, Packer RA and Gustafson DL (2019) Randomized blinded controlled clinical trial to assess the effect of oral cannabidiol administration in addition to conventional antiepileptic treatment on seizure frequency in dogs with intractable idiopathic epilepsy. *J Amer Vet Med Assn* 254:11

Pet Poison Helpline, an animal poison control center based out of Minneapolis, is available 24 hours a day, seven days a week for pet owners and veterinary professionals that require assistance treating a potentially poisoned pet. The staff provides treatment advice for poisoning cases of all species, including dogs, cats, birds, small mammals, large animals and exotic species. As the most cost-effective option for animal poison control care, Pet Poison Helpline’s per incident fee includes follow-up consultations for the duration of the treatment time. Pet Poison Helpline is available in North America by calling **800-213-6680**. Additional information can be found online at www.petpoisonhelpline.com.