

AVMA Council on Biologic and Therapeutic Agents

CANNABIS: WHAT VETERINARIANS NEED TO KNOW

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INTRODUCTION

With the increasing interest in cannabis as a therapeutic agent both in human medicine and veterinary medicine, veterinarians are fielding more questions about the use, dosing, and adverse effects of cannabis. Since there is little evidence-based information about the use of cannabis in pets, veterinarians are left with relying on anecdotal reports, client reports, or manufacturer's claims about its use. For these reasons, the AVMA offers the following current information to attempt to clear up confusion regarding the use/prescribing of marijuana-based products in pets.

Table of Contents

INTRODUCTION	2
MARIJUANA, CANNABINOIDS, AND HEMP	4
MARIJUANA.....	4
CANNABINOIDS.....	4
THC versus CBD.....	4
Mechanism of Action: Cannabinoids function via receptors.....	5
Synthetic Cannabinoids	5
HEMP.....	5
Industrial Hemp	5
Animal Food/Feed.....	6
TOXICOLOGY	6
MARIJUANA TOXICOSIS	6
Exposure.....	6
Diagnosis.....	7
Clinical Signs.....	7
Treatment	7
ADDITIONAL INFORMATION	8
DEA SCHEDULING.....	8
Scheduling and Drug Availability for Research	8
Marijuana products in animals	9
Dietary Supplements.....	9
CONTRIBUTORS.....	10

MARIJUANA, CANNABINOIDS, AND HEMP

MARIJUANA

Marijuana (*Cannabis sativa*) - All parts of the plant *Cannabis sativa* L.—the seeds; the resin extracted from any part of the plant; and every compound, manufacture, salt, derivative, mixture, or preparation of the plant, its seeds or resin. The term marijuana does not include hemp,¹ Marijuana is classified by the DEA as a Schedule 1 Controlled Substance—most restricted category for drugs with no current acceptable medical use.

- Marijuana and its derivatives are ILLEGAL and not approved by the FDA for ANY medical use.
- Illegal for veterinarians in ANY state to prescribe or recommend as a treatment.
 - Marijuana and its derivatives including CBD are federally illegal, even though more than half of the states have legalized marijuana for human medical use. There are NO FDA-approved marijuana or hemp products for use in animals, and thus the legality of veterinarians recommending any unapproved products can be confusing.
 - Even in states where medical marijuana is legal, such as the State of Colorado, it is illegal for a veterinarian to prescribe marijuana for animal use. Furthermore, any discussion regarding any therapeutic regimen should be consistent with a valid Veterinarian-Client-Patient-Relationship (VCPR)

CANNABINOIDS

Cannabinoids, such as tetrahydrocannabinols (THC) and cannabidiols (CBD), are found in the flowering tops, resin, and leaves of the marijuana plant. Cannabinoids are not found in hemp, except for trace amounts (typically, only parts per million). Therefore, extracts that contain more than trace amounts of cannabinoids must be from the parts of the cannabis plant that are defined as marijuana and regulated as Schedule 1 controlled substances. Furthermore, if using only the parts of the cannabis plant that are excluded from the CSA definition of marijuana to produce products such as hemp seed oil, the industrial processes used to clean cannabis seeds and produce seed oil would likely further diminish any trace amounts of cannabinoids that end up in the finished product. ([DEA, 2017](#)) A more complete discussion on hemp follows in the section below.

THC VERSUS CBD

- Both are cannabinoids that originate from the *Cannabis sativa* plant. The 2 main cannabinoids are tetrahydrocannabinolic acid (THCA) and cannabidiolic acid (CBDA). THCA when dried is converted to tetrahydrocannabinol (THC), the psychoactive cannabinoid. Carboxylation of CBDA yields cannabidiol (CBD).
- While CBD may not produce the typical euphoria seen with THC in humans, it does affect the nervous system in mammalian species. The specific mechanisms and effects remain unknown.
- CBD products often indicate a hemp source, leading many to believe that the products are legally marketed, when in fact they are not. CBD is promoted as having antianxiety, antipsychotic, antispasmodic, antibacterial, and many of the same properties as THC-containing marijuana products without the euphoric properties. THC products are sourced from marijuana

¹ The CSA states: "The term 'marihuana' means all parts of the plant *Cannabis sativa* L., whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin. Such term does not include the mature stalks of such plant, fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture, or preparation of such mature stalks (except the resin extracted therefrom), fiber, oil, or cake, or the sterilized seed of such plant which is incapable of germination." [21 U.S.C. § 802\(16\)](#)

and purport analgesic, anti-inflammatory, antiemetic, antioxidant, antipruritic and cholinergic in addition to known euphoric properties.

MECHANISM OF ACTION: CANNABINOIDS FUNCTION VIA RECEPTORS

- CB1 receptors are found on neurons and in the GI tract, causing release of GABA (inhibitory neurotransmitter). High concentrations of receptors are present in the canine cerebellum.
- CB2 receptors are expressed on cells of the immune system.
- Non-receptor interactions also exist.
- Medicinal properties include: anti-inflammatory, anticonvulsant, analgesia, antioxidant, anti-seborrheic, anti-MRSA, antifungal, antidepressant, neuroprotective in Parkinson's disease.

SYNTHETIC CANNABINOIDS

Synthetic cannabinoids (dronabinol and nabilone, synthetic THC) are available for humans as Schedule II Controlled Substances under the trade names Cesamet[®] and Syndros[®]. Nabilone (Syndros[®]) should not be used in dogs due to potentially lethal toxic effects. Chronic cannabinoid toxicity varied between species tested but dogs exhibited ataxia, muscle incoordination.² Marinol[®] (a different formulation of dronabinol) is available as Schedule III. Veterinary prescribing of these products under the [Extra Label Drug Use](#) regulations are not expressly prohibited by AMDUCA.

HEMP

Hemp (excluded from the DEA definition of marijuana) is "the mature stalks of such plant, fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture, or preparation of such mature stalks (except the resin extracted there from), fiber, oil, or cake, or the sterilized seed of such plant which is incapable of germination,"³ and is not a significant source of THC or CBD, as noted in the above section on cannabinoids. Furthermore, the DEA has issued a clarification that while they indeed recognize industrial hemp research and its products as legal, this protection does not extend to CBD products, which remain illegal, regardless of the source.⁴

INDUSTRIAL HEMP

Industrial hemp may ONLY be grown in accordance with an agricultural pilot program in a state where state law allows for industrial hemp to be produced legally to study its growth, cultivation, or marketing by licensed and registered cultivators. The term includes any part or derivative of *Cannabis sativa L.* including the seeds that is used exclusively for industrial purposes (fiber and seed) with a THC concentration of < 0.3% on a dry weight basis.⁵

² [Fundam Appl Toxicol.](#) 1987 Aug;9(2):185-97. A species comparison of the toxicity of nabilone, a new synthetic cannabinoid. [Hanazono GK](#)¹, [Sullivan HR](#), [Gries CL](#), [Jordan WH](#), [Emmerson JL](#).

³ The CSA states: "The term 'marihuana' means all parts of the plant *Cannabis sativa L.*, whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin. Such term does not include the mature stalks of such plant, fiber produced from such stalks, oil or cake made from the seeds of such plant, any other compound, manufacture, salt, derivative, mixture, or preparation of such mature stalks (except the resin extracted therefrom), fiber, oil, or cake, or the sterilized seed of such plant which is incapable of germination." [21 U.S.C. § 802\(16\)](#)

⁴ Drug Enforcement Administration Diversion Control Division. In *Clarification to the New Drug Code (7350) for Marijuana Extract. s.l.*, 2017.

⁵ https://www.federalregister.gov/documents/2016/08/12/2016-19146/statement-of-principles-on-industrial-hemp?utm_campaign=pi+subscription+mailing+list&utm_medium=email&utm_source=federalregister.gov

ANIMAL FOOD/FEED

Hemp has not undergone the required scientific review to ensure its safety and utility for use in animal food and therefore has not been approved as an ingredient for animal food.⁶ Furthermore, potential safety concerns related to the presence of cannabinoids (including THC and CBD) still need to be addressed.

Under section 301(II) of the FD&C Act, it is prohibited to introduce or deliver for introduction into interstate commerce any food (including any animal food or feed) to which has been added a substance which is an active ingredient in a drug product that has been approved under 21 U.S.C. § 355 (section 505 of the Act) or a drug for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public. There are exceptions, including when the drug was marketed in food before the drug was approved or before the substantial clinical investigations involving the drug had been instituted or, in the case of animal feed, that the drug is a new animal drug approved for use in feed and used according to the approved labeling. However, based on available evidence, FDA has concluded that none of these is the case for THC or CBD. FDA has therefore concluded that it is a prohibited act to introduce or deliver for introduction into interstate commerce any food (including any animal food or feed) to which THC or CBD has been added.⁷

TOXICOLOGY

MARIJUANA TOXICOSIS

Marijuana toxicosis is most commonly due to our canine patients' predilection for dietary indiscretion. The majority of cases reported have occurred in young dogs (less than 1 year old), although cases have also been recorded in cats.^{6,7} Toxicosis in dogs is most commonly associated with edibles, often those made with chocolate, while cats are more likely to directly consume the plant material. This complicates the clinical picture in dogs, who may also be suffering from other toxicities, such as chocolate, raisins, xylitol, or a foreign body from concurrently eating packaging material.

EXPOSURE

It is also important to consider how marijuana exposure occurred. Effects from ingesting marijuana products tend to have a slower onset. In most cases, clinical signs appear within 1-3 hours of exposure; however, clinical signs have been reported to manifest in as little as 5 minutes or as long as 96 hours.^{7,8} This variation may be due to many factors, including lipid content within the gastrointestinal tract, body condition score, quantity and concentration of cannabinoids consumed, and individual variation in absorption. Furthermore, dogs have a more complex excretion profile than humans with hepatic uptake and biliary excretion resulting in different metabolites than in humans.

Many edible marijuana products contain ingredients toxic to dogs, potentially resulting in concurrent toxicoses from marijuana and other ingredients, such as chocolate, raisins, or xylitol and resulting in a poorer prognosis. Toxicosis from these ingredients is associated with clinical signs different from that of marijuana toxicity, complicating clinical diagnosis; concurrent toxicoses may not become apparent unless included in the history or determined through monitoring clinical signs over time. Additionally, it

⁶ AAFCO Guidelines on Hemp in Animal Food March 2017

⁷ https://www.fda.gov/NewsEvents/PublicHealthFocus/ucm421168.htm#enforcement_action

is common for dogs to inadvertently ingest the packaging that the marijuana is contained in. This may result in a foreign body requiring additional diagnostics, treatment and surgery.

DIAGNOSIS

Diagnosis of marijuana toxicity is almost solely based on history and clinical signs. Human urine tests are available, but have not been validated in pets. They are reported to have high specificity but low sensitivity. This means that, while a positive test can be trusted, false negatives are likely. False negatives may result if testing is done too early after intoxication: THC metabolites need to be formed in order for the test to return a positive result. Furthermore, false negatives may occur as a result of testing procedures designed for human use that detect only human metabolites. Differences in metabolism of THC have been documented in several species that are kept as companion animals and there are multiple metabolites formed in dogs that are not formed in humans,⁹ which available screening tests may not detect. Additionally, collection errors may occur due to THC's proclivity to bind to glass and rubber stoppers.^{5,11} Due to these challenges with diagnostic testing and lack of pathognomonic clinical signs in these cases, a reliable history from the owner is extremely important. To facilitate the discussion, some veterinarians have found it helpful to explain the cost of additional tests needed to rule out other forms of toxicosis, if marijuana cannot be determined as the likely causative agent from the history. Clients should also be reminded that veterinarians have no ethical or legal obligation to report marijuana toxicosis to any authorities; their focus is on patient care, which requires an accurate history. In addition, the veterinarian could provide the owner several opportunities to provide a complete and accurate history when marijuana toxicity is suspected.

CLINICAL SIGNS

ASPCA Poison Control Center reports that pets that ingest CBD products develop the same clinical signs as those that are exposed to THC products. It is unknown if this is due to quality control or unknown content of unregulated products; metabolism of CBD; or the varying amount of CBD despite label claims.

There are a wide range of clinical signs that have been associated with marijuana toxicosis, with the most common being ataxia, depression, mydriatic pupils, hyperesthesia, and urinary incontinence.⁵ A typical owner may describe their pet as dull and dribbling urine, seemingly falling asleep while standing. Other signs include vomiting, hypothermia, hypotension, bradycardia or tachycardia, tremors, seizures, incoordination, anorexia, weakness, hypersalivation, disorientation, and death; some animals may simply present recumbent or comatose.^{5,7,8} Several deaths have been reported in the literature and appear to be the result of associated complications, such as aspiration. Anecdotally, additional deaths have been reported related to marijuana exposure.

Marijuana toxicity can look similar to intoxication with numerous other sedatives, but the most serious consideration is anti-freeze poisoning. Therefore, it is important to consider marijuana along with other depressants.

TREATMENT

Treatment of marijuana toxicosis is primarily supportive, based on clinical signs. If an animal presents with a history of marijuana ingestion, but is not currently symptomatic, emesis can be performed if within 2 hours of ingestion and if there are no CNS signs. Administration of activated charcoal (1-2g/kg)

Q8 for at least the first 24 hours may be indicated as THC undergoes enterohepatic recirculation.⁶⁻⁸ These treatments should not be pursued in animals showing severe CNS signs as the risk of aspiration pneumonia is greatly increased. Other treatments may include fluid therapy if there is evidence of dehydration, monitoring of temperature and respiratory rate, atropine for bradycardia, and diazepam (0.25-0.5mg/kg IV) if exhibiting hyperexcitability.⁶ An anti-emetic, such as Maropitant (1mg/kg SQ Q24) or Ondansetron (0.1-0.2 mg/kg IV Q8) is indicated if vomiting has occurred or if activated charcoal has been given.⁸ Intravenous lipid emulsion therapy has been used in some cases, although effectiveness of this treatment has not been fully established. The use of metoclopramide to increase gastric emptying has also been proposed.¹² Selection of appropriate supportive care interventions, based upon clinical signs and exposure history, in addition to vigilant monitoring, is imperative for management of marijuana toxicosis cases. While relatively few deaths have been reported in relation to marijuana exposure, those that have occurred have appeared to be related to complications from toxicosis rather than the marijuana itself. These complications are commonly due to asphyxiation from vomiting but also include sub-clinical disorders that become clinical after marijuana toxicosis.

Acute marijuana toxicosis can cause severe clinical signs in companion animals, and even death in rare instances. As more states legalize medicinal and recreational use in humans, it is likely that marijuana toxicosis cases presented to veterinary hospitals will continue to increase as well. The ability to obtain a complete exposure history, as well as recognition of associated clinical signs, is critical to the practicing veterinarian for optimal case management. Initiation of appropriate supportive care measures can facilitate recovery and mitigate complications, which will further reduce the risk of death in these cases. Having an open dialogue between veterinarian and the client will help to facilitate the most detailed history and thus proper animal care.

ADDITIONAL INFORMATION

DEA SCHEDULING

Drugs and other substances that are considered controlled substances under the Controlled Substances Act (CSA) are divided into five schedules. An updated and complete list of the schedules is published annually in [Title 21 Code of Federal Regulations \(C.F.R.\) §§ 1308.11 through 1308.15](#). Substances are placed in their respective schedules based on whether they have a currently accepted medical use in treatment in the United States, their relative abuse potential, and likelihood of causing dependence when abused. Substances in Schedule 1 have no currently accepted medical use in the United States, a lack of accepted safety for use under medical supervision, and a high potential for abuse.

SCHEDULING AND DRUG AVAILABILITY FOR RESEARCH

There is a significant amount of interest in reclassifying marijuana from a Schedule 1 drug to a Schedule 2 drug to facilitate research opportunities for veterinary and human medical uses. However, despite attempts to verify, examples of marijuana and associated products being unavailable for research purposes have not been documented. Several hundred marijuana researchers are registered with DEA suggesting that the lack of product availability is a common misconception. However, it is acknowledged that Schedule 1 drug research is more difficult than other types of drug research due to rigorous requirements for approval and lack of research funding. While there have been reports of several veterinary researchers evaluating marijuana therapies, no results have been reported in the literature.



Typically, DEA scheduling is based upon the drug compound (active ingredient) rather than by individual products. However, if a marijuana product is found to be a safe and effective treatment for one or more diseases/conditions, and that product has been approved by the FDA as such, then the individual product would likely be classified as a Schedule II drug.

Marijuana products in animals

Marijuana products are being marketed to treat diseases in animals. While both marijuana and industrial hemp products are available, no studies, doses, or uses in veterinary medicine have been determined. Furthermore, FDA has not approved the use of marijuana or hemp in any form in animals, and the agency cannot ensure the safety or effectiveness of these products. For these reasons, FDA and AVMA cautions pet owners against the use of such products. Many of these products are marketed as CBD oil or chews. These products, despite contrary claims, are illegal for use in pets.

Dietary Supplements

There is no FDA approval process for animal supplements, including marijuana products marketed as nutritional supplements. Animal products are regulated as either animal drugs or animal feed ingredients. For humans, FDA has concluded that THC and CBD products are excluded from the dietary supplement definition. If a substance (such as THC or CBD) is an active ingredient in a drug product that has been approved or has been authorized for investigation as a new drug, then products containing that substance are outside the definition of a dietary supplement.⁸ Therefore, neither THC nor CBD can be legally marketed as a human or animal supplement.

Despite the fact that CBD cannot be sold legally as a dietary supplement in the U.S., many CBD products are available. The FDA has issued numerous warning letters to companies selling products containing cannabidiol. Many products did not contain the levels of CBD they claimed-some containing .0025% CBD while others 25-35% CBD similar to doses used in clinical trials.⁹

⁸ https://www.fda.gov/NewsEvents/PublicHealthFocus/ucm421168.htm#enforcement_action

⁹ <https://www.fda.gov/NewsEvents/PublicHealthFocus/ucm484109.htm>

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