

## Cannabinoids use in animals and the veterinary profession

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### **Problem statement and impact on the veterinary profession:**

The use of cannabis and cannabis-derived products (see Annex I for definition) is increasing globally. In North-America and Europe, several countries passed legislation permitting medicinal use of cannabis in humans. Some countries passed laws permitting recreational use.

As cannabis-derived products have become more available, veterinarians see more cases of animal clinical pictures of toxicity and an increased interest among clients in using these products therapeutically for their companion animals. Questions are asked about the legality, safety and effectiveness for treating medical conditions in animals.

Although cannabinoids such as CBD potentially hold therapeutic promise for example to treat osteoarthritis pain, immune-mediated and inflammatory allergic disorders, epilepsy and other pain management (oncologic, neuropathic pain), available scientific evidence around the use in animals is currently limited. Few clinical studies exist, however, most are anecdotal or based on case reports, and all of them are dedicated to companion animal usage. So far, no cannabis-derived products have been authorised as veterinary medicines in Europe. Some are, however, registered as homeopathic in the veterinary medicines legislation<sup>1</sup> or under the feed Regulation<sup>2</sup>.

Of particular concern is that a substantial portion of cannabis-derived products currently available on the market are labelled inaccurately with respect to both, the identity and amount of pharmacologically active substances found within the product, making dosing and dosage regimen very difficult to impossible. Only the composition of medical cannabis is known and controlled.

### **Recommendations for consideration**

- Studies should be promoted to investigate the potential therapeutic value and safety of cannabis-derived products for companion animals (including horses).
- Well-controlled clinical trials and pursuit of EU/national authorisation by manufacturers of cannabis-derived products should be promoted, so that

<sup>1</sup> Cardio ReVet RV 4 - Globuli für Tiere- [https://aspregister.basg.gv.at/document/servlet?action=show&zulnr=8-30100&type=DOTC\\_GEBR\\_INFO](https://aspregister.basg.gv.at/document/servlet?action=show&zulnr=8-30100&type=DOTC_GEBR_INFO)

<sup>2</sup> Anibidol Plus – Virbac - <https://www.newpetclub.pt/anibidiol-plus-canibidiol-virbac>

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high-quality products of known safety and efficacy can be made available for veterinarians and their patients.

- At least until further research have proven them safe and more research has been done, all cannabis-derived products for animals should be on veterinary prescription.
- Regulation should be put in place and the safety assessed on producing animal feed or supplements to feed with cannabis-derived products.
- Regulation should be put in place and the safety assessed on producing beddings or other care products for animals with CBD/Cannabis.

### **Warning to Veterinarians**

There are currently few regulated cannabis-derived products on the EU market (at the time of writing: one registered as homeopathic and one as feed supplement). There are, however, many companies selling “nutritional supplement” or “care products”, cannabis-derived products for dogs, cats, and horses, some of which make what clearly appears to be therapeutic claims (e.g. clinical indications as anxiety, poor appetite, etc) either in the summary product description or on the commercial product website. Be careful with these products as they do not conform to the European legislation and the ingredients (active substances) might differ in quality and/or quantity between batches. These products are not subject to any regulation and in most cases also to no independent quality control. Some products may be shown to contain illegal levels of THC or other toxic impurities (e.g. terpenoids). Any suspected breaches should be reported to Competent Authorities in the country where the event occurred.

## **Annex I: What are cannabinoids?**

Cannabis comes from the cannabis (*Cannabis sativa*) plant, of the hemp family. The part containing >0.3% THC, such as the flowering tops, is called “marijuana”, and many other names (Mary Jane, Grass, Pot, Hashish, Indian hemp, Reefer, Weed).

**Cannabinoids** are the active cannabis-derived substances that have pharmaceutical activity; over 480 relevant active substances have been isolated so far. The amount of each active pharmacologically substance contained in a sample of cannabis depends on the plant subspecies, how the leaves have been dried, the time of year the leaves were harvested, the age of the plant, and other factors.

Cannabinoids can enhance the formation of norepinephrine, dopamine, and serotonin in the brain. Two primary types of cannabinoid receptors designated as CB1 and CB2, both coupled to G-proteins, have been identified. CB1 receptors are widely distributed in the brain (central nervous system, CNS) and correlate with cannabinoid effects on cognition, appetite, emotions, memory, perception and control of movement. CB2 receptors are less frequently found in the CNS but are highly concentrated in the peripheral nervous system and immune system where they play a part in inflammation and pain regulation.

Delta-9-trans-tetrahydrocannabinol ( $\delta$ 9-THC) , more commonly called “**THC**”, is the psychoactive chemical, that makes cannabis a recreational drug. Some parts of a normal cannabis plants have up to 10% THC.

Cannabidiol, commonly referred to as “**CBD**”, is one of the cannabinoid chemicals which is not considered psychoactive and is of a more medicinal nature.

### **Abbreviations**

CBD: cannabidiol; CB: cannabinoid; CBDa: carboxylic acid of CBD;  
THC:tetrahydrocannabinol

## Annex II: Toxicity in symptoms, clinical signs and treatment (focus on dogs)

The usual pet toxicity case involves a dog that has inadvertently eaten cannabis. Toxicity in cats is less frequent seen, as they are more selective in their food intake. However, CBD oils may contain terpenes, the "flavoring substances" from the resin, which pose a particularly high risk of intoxication for cats, since cats can not metabolize them due to the conjugation defect that causes reduced glucuronjugation of these drugs.

### Symptoms/Clinical signs:

Neurological	Sleepiness
	Ataxia
	Depression
	Wobbling, pacing and agitation
	Vocalization
Eyes	Dilated pupils
	Bloodshot eyes
Gastro-intestinal	Vomiting
	Salivation
Others	Sound or light sensitivity
	Inappropriate urination
	Fast or slow heart rate
	Low body temperature

Clinical signs typically begin 30 to 90 minutes after the consumption. Because THC is stored in the body's fat deposits, the effects of marijuana ingestion can last for several days (72h). The minimum lethal oral dose in the dog for THC is greater than 3 g/kg.

*Body temperature and cardiac rate and rhythm are usually the only clinical signs that must be monitored.*

### Differential Diagnosis:

Cannabis toxicity particularly in dogs can look similar to intoxication with numerous other sedatives, but the most serious consideration is anti-freeze poisoning (e.g. ethylene glycol) or ivermectin toxicosis.

### Diagnosis:

In most cases, the diagnosis can be made based on the anamneses and the clinical symptoms. Urine testing can be performed but can give false negatives. Positive screening tests require chromatographic techniques and specifically GC-MS is used as the most reliable confirmatory method, especially when used with electron impact (EI) and chemical ionization (CI) detector modes.

### Treatment and prognosis

- As no antidote is available, treatment consists of supportive care. Because of the wide margin of safety of the cannabinoids, toxicosis is rarely fatal.
- If less than 30 minutes have passed since the consumption, vomiting should be induced and activated charcoal administered to the animal.

- If symptoms have started inducing vomiting might be difficult (due to the properties of cannabidiol) and could be dangerous if the patient is very sedated, as vomit could be inhaled and cause aspiration pneumonia.
- Fluid support and keeping the patient warm may also be needed due to low body temperature (hypothermia), with rotating the patient to prevent oedema and closely monitoring the body temperature during the treatment.
- Diazepam can be given for sedation or to control seizures.
- IV lipid emulsion therapy may be helpful in the treatment of severe cases.
- If the patient has lost consciousness, intense observation and support is needed. The chance of fatality is statistically small but possible.
- Recovery may take 24 to 72 h, or longer (up to 5 days), depending on the dose ingested.

**For references and more detail:** see publication: <https://www.mdpi.com/2076-2615/11/3/892>