

Member Advisory

November 2017, updated October 2018

Use of Medical Marijuana and related products in animals

The ABVMA office has received many calls from veterinary practices and from the general public inquiring about the use of cannabis and cannabinoids in animals. The use of medical marijuana is becoming more widespread in humans. However, the effects of cannabinoids are not well studied in animals. It appears dogs are more sensitive to these compounds than people.

The Office of Medical Cannabis, Health Canada, has confirmed that the *Access to Cannabis for Medical Purposes Regulations* do not apply to veterinarians or animals. The regulations pertain only to human healthcare practitioners and access for human patients.

The Cannabis Act comes into force on October 17, 2018. There are currently no approved CBD products for animals, meaning there is no legal pathway to obtain these products for animals in Canada. Also, research is needed to establish safety in animals.

Messages for your clients:

- Benefits of cannabinoids to veterinary patients are still theoretical with a lack of randomized clinical trials and evidence that they are safe and beneficial, further research is required.
- Long term effects of exposure are largely unknown but have significant potential to adversely affect
 - o Growth and development in young animals
 - o Behaviour and thus safety for in-contact humans. This could apply to short term effects as well
- Lack of consistency of cannabinoid composition in natural products due to:
 - o Different strains of plant
 - o Storage instability of active ingredients
 - o Processing variation (dried or fresh)
- Products available on the market are not labeled for use in veterinary species. This includes the three classes of products: recreational cannabis, medical cannabis and hemp cannabis.
- Oral administration route is currently difficult to predict bioavailability and onset to action in different preparations on the market

Further updates will occur as new information becomes available.

Resources:

- 1. Cannabis Information for ABVMA Members (attached)
- Veterinarians Caution: Medical Marijuana Exposure in Pets https://www.canadianveterinarians.net/documents/veterinarians-caution-medical-marijuana-exposure-in-pets
- Signs of Marijuana Exposure in Your
 Pethttps://www.canadianveterinarians.net/documents/signs-of-marijuana-exposure-in-your-pets

Cannabis sp. Medicinal Applications in Canine and Feline Patients Information for ABVMA Members

Many veterinary practitioners are fielding questions from clients regarding Cannabis use in their pets. This information sheet is intended to provide an initial review about what we do and do not know about the effects of Cannabis in dogs and cats.

On October 17, 2018, the Cannabis Act comes into force. This act creates a legal and regulatory framework for controlling the production, distribution, sale and possession of cannabis in Canada.

The cannabis for medical purposes regime will continue to exist to provide access to individuals who have the authorization of their healthcare practitioner to use cannabis for medical purposes (6). The Access to Cannabis for Medical Purposes Regulation (ACMPR) allows people with a health care practitioner's authorization to possess or grow a limited amount for personal use, or have someone else grow it for them on their behalf (2). This legislation does not extend to veterinarians and their animal patients, as such veterinarians are not permitted to authorize the purchase of marijuana for the treatment of animals.

History:

Although used in early centuries in China and India, it became a mainstream medicine in Britain in the 19th century as a muscle relaxant, anticonvulsant, analgesic and anti-emetic (4). By the early 20th century however it's use was in steep decline due to the following (4):

- Variable potency of herbal preparations
- Poor storage stability
- Unpredictable response to oral administration
- Availability of potent synthetic alternatives and parenteral medications
- Concern about recreational use

Discovery of the endocannabinoid system in the late 1980's and early 1990's has renewed interest in medical and veterinary applications of the many biologically active components of Cannabis. The

endocannabinoid system has been found to have receptors within and/or effects on the following systems or other applications (5):

- Central nervous system (centers involved in anxiety, pain, cognition, memory, proprioception, emotions, learning, coordination, and navigation)
- Immune system
- Metabolism
- Apoptosis and carcinogenesis
- Antimicrobial activity: antifungal and antibacterial properties

The following is a list of the most common and known cannabinoids:

- $\Delta 9$ tetrahydrocannabinol (THC): affects more receptors in the brain, and is responsible for the majority of the psychoactive effects of smoking marijuana. Nabilone is a synthetic alternative; anandamide is the endogenous receptor agonist to which THC has analogous activity.
- Cannabidiol: has most potential for medicinal use as the psychoactive effects are minimal
- Cannabinol: similar to cannabidiol, although less studied so far

Current Research Summary (not exhaustive)

Canine:

Pharmacokinetics of cannabidiol administered by 3 delivery methods at 2 different dosages to healthy dogs. Can J Vet Res. 2018 Jul;82(3):178-183

Pharmacokinetics, Safety, and Clinical Efficacy of Cannabidiol Treatment in Osteoarthritic Dogs Front. Vet. Sci., 23 July 2018 | https://doi.org/10.3389/fvets.2018.00165

Decreased glucose tolerance, increased serum ammonia levels and a decrease in plasma insulin levels Bull Narc. 1978 Jul-Sep; 30(3): 33-41

No effect on weight (gain) in marijuana smoke exposed dogs for 27 months Res Commun Chem Pathol Pharmacol. March 1976; 13(3): 465-72

IV THC Increased pulmonary vascular resistance, increased pulmonary artery pressure, and decreased heart rate in anesthetized dogs Eur J Pharmacol. July 1976; 38(1): 183-7

Small amount is metabolized directly in the lung after IV administration of THC J Pharma Pharmacol. Nov 1975; 27(11): 842-8

IV administration produced a dose dependent decrease in halothane MAC (without premedication) 1 to 3 hr after injection, even lasting up to 24 hr later, although required a dose as high as 2.0 mg/kg (average adult human smokes up to 0.05 mg/kg THC recreationally and 0.2 mg/kg produces hallucinations) Anesthesiology Jun 1973; 35(6): 521-524

Endocannabinoid receptors were found in higher concentration in skin samples from atopic dogs than from normal dogs, and associated with immunologically relevant cells such as mast cells, fibroblasts, and endothelial cells. Am J Vet Res. 2012; 73(7): 988-995

An LD50 has not been established in dogs or cats, and regardless of dose exposure, all dogs recover with supportive care within 24 hr; long term adverse effects are unknown to acute, even high dose, exposure. Suggests a low degree of toxicity. Vet ed. Jun 2002; 97(6): 437-439

Feline:

IV THC as antitussive (experimental model in anesthetized cats with electrical stimulation of superior laryngeal nerve) Eur J Pharmacol. Feb 1976; 35(2); 309-13

Rats and Mice:

Genetic variation (different rat strains) caused variation in cannabinoid-induced anxiety related behavior Life Sci. October 2010; 87(17-18):572-8

Decreased locomotor activity and anxiety related behaviour in cannabis smoke exposed rats, which was reversed by rimonabant (CB1 receptor antagonist); chronic smoke exposure lead to clinically relevant dependence. PLOS One. April 2016; 11(4) e0153327 DOI: 10.1371

Low doses (10 mg/kg) may be better than high doses (100 mg/kg) regarding anxiolytic effects; the serotonergic system is likely involved in the anxiolytic action of CBD; A review of the anxiolytic effects in mice, rats, primates, and humans Rev Bras Psiquiatr. 2012; 34(Supl1):104-117

Immune modulation effects in mouse model of multiple schlerosis. Br J Pharmacol 2011; 163: 1507-1519

Summary:

The endocannabinoid system research so far has revealed so much potential for therapeutic application of cannabinoids in veterinary patients. However, to date, the following points are not in favor of its current use in our veterinary patients:

- Benefits of cannabinoids to veterinary patients are still theoretical with a lack of randomized clinical trials and evidence that they are safe *and* beneficial, further research is required.
- Currently still illegal
- Lack of consistency of cannabinoid composition in natural products due to:
 - Different strains of plant
 - Storage instability of active ingredients
 - Processing variation (dried or fresh)
- Products available on the market are not labeled for use in veterinary species
- Oral administration route is currently difficult to predict bioavailability and onset to action in different preparations on the market

- Long term effects of exposure are largely unknown but have significant potential to adversely affect
 - Growth and development in young animals
 - Behaviour and thus safety for in-contact humans. This could apply to short term effects as well

At this time, there is no legal pathway to prescribe and dispense Cannabis, and doing so would place veterinarians at risk.

References

- 1. Controlled Drugs and Substances Act, SC 1996, c 19, http://canlii.ca/t/52wl7 retrieved on 2017-06-05
- 2. Government of Canada. Access to Cannabis for Medical Purposes Regulations. *Canada Gazette*. 150 (17), P.C. 2016-743. www.gazette.gc.ca
- 3. Government of Canada. Legalization and Regulation of Cannabis. Accessed May 14, 2017. https://www.canada.ca/en/services/health/campaigns/legalizing-strictly-regulating-cannabis-facts.html
- 4. Robson, P. (2001) Therapeutic aspects of cannabis and cannabinoids. British Journal of Psychiatry. 178 (107-115)
- 5. Silver, R.J. (2015) Medical Marijuana- What Every Veterinarian Needs to Know. Wild West Veterinary Conference
- 6. Government of Canada. Introduction of the Cannabis Act: Questions and answers. Accessed October 10, 2018.