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## **CBD treats for dogs**

*CBD (cannabidiol) is a subject of topical interest to many dog owners, fuelled by an increasing supply of CBD-infused treats. These products are claimed to mitigate inflammatory skin and joint problems, anxiety and epileptic seizures (Note 1). CBD is derived from industrial hemp crops low in the psychoactive and addictive THC (tetrahydrocannabinol), which is abundant in other hemp plants, known as marijuana. A couple of complete dog foods contain hemp seed or its oil fraction.*

*CBD dog snacks generally include CBD oils, oily extracts from hemp inflorescences mixed with the seeds' oil or another oil carrier. The CBD content of CBD oils varies markedly, while THC may be absent or substantial. Hemp whole seeds and seed oil are mostly low in CBD and THC, but a single oil may be CBD-rich. Manufacturers must allow for the variable composition of CBD oils in order to supply treats with CBD (and THC) contents that permanently meet their pre-set targets.*

*There are no available data on CBD and anxiety or inflammatory skin disease in dogs. Researching CBD's impact on joint disease and epilepsy is underway (1). As to epilepsy, preliminary affirmation has been posted (2). One well-performed study, published recently, gave conflicting results for the efficacy of CBD in dogs with joint disease. The dogs suffering from arthritis were administered CBD oil by mouth. A 20-kg dog would receive 80 mg pure CBD per day.*

*CBD oils have complex compositions, not least due to the big family of cannabinoid compounds. The naming implies that CBD is considered the chief active principle. Commercial CBD treats carry feeding instructions and may declare the amount of CBD per treat. When taking the mean for six products, a 20-kg dog gets 10 mg CBD per day. This consumption level appears safe, but does not justify health claims, at least for the time being.*

### **CBD intake**

CBD dog treats usually contain CBD oils as discriminating ingredient. CBD oils come with wide spectra of cannabinoids and terpenes, and vary considerably as to their CBD and THC concentrations. For 14 European CBD oils, the mean CBD and THC contents were 28,733 and 796 mg/kg, but the ranges were immense (3, Note 2). The CBD extracts were derived from industrial hemp with legal limit of 0.2% THC (4) in dry matter of the upper 1/3 of the crop (5).

For six CBD dog snacks of different brands, the mean declared amount of CBD per treat is 4.25 mg (Note 3). The feeding guidelines amount to a daily intake of 10 mg CBD by a 20-kg dog, which corresponds with 33 mg CBD per kg complete, dry food. Such food with 5% of the average hemp seed oil (6) would hold 4 mg CBD/kg.

### **Metabolism**

After single oral administration of CBD oil to dogs, the maximal CBD concentration in peripheral plasma was dose dependent (7, 8). Peak concentrations indicate that CBD in oils is better absorbed

(7-9) than in raw material form (10). Percent intestinal absorption is unknown. Daily administration of 50 and 200 mg CBD in a 20-kg dog, sustains plasma CBD at about 50 and 200 ng/ml (8, 11).

The dog (hepatically) transforms intravenously injected CBD into a wide array of metabolites, including hydroxylation followed by glucosylation (12-16). Less than 2% of the dose was excreted in urine as total metabolites (12). Apparently, CBD's major elimination route is fecal excretion via biliary secretion, as for THC (17). Daily intake of CBD and THC probably leads to steady-state concentrations of these cannabinoids and their metabolites in tissues (cf. 18, 19).

### **Toxicity**

No negative health effects were observed in dogs orally given CBD oil for 4 to 6 weeks, matching 4 or 20 mg CBD/kg body weight per day (7, 8). However, a mixture containing 20 mg each of CBD and THC might be harmful (11). Dogs treated orally with a single THC dose of 66 to 3000 mg/kg developed convulsions, but recovered within 24 hours (20). Likewise, cases of marijuana toxicosis in dogs generally are nonfatal (21, 22).

### **Cannabinoid receptors**

Studies with synthetic analogs of THC have identified two receptors that are part of a complex and puzzling bodily system. The CB1 and CB2 receptors are predominantly located in the nervous and immune system, respectively. Receptor up-regulation was found in canine degenerative myelopathy (23) and atopic dermatitis (24).

Arachidonoyl ethanolamine (AEA) and 2-arachidonoyl glycerol (2-AG) are endogenous ligands. THC is agonist at both CB receptors. CBD may bind to CB2 and activate CB1 through inhibition of AEA catabolism. Conceivably, CB1 and CB2 signal anti-epileptic and anti-inflammatory activity.

### **Atopic dermatitis**

Data are lacking on CBD in canine atopic dermatitis. Oral palmityl ethanolamine, an endocannabinoid, reduced the inflammatory response in *Ascaris* hypersensitive dogs (25).

### **Osteoarthritis**

One study, with double-blinded, placebo-controlled, cross-over design, addressed CBD in canine osteoarthritis (7). Oral treatment with CBD oil for four weeks (2 mg CBD/kg body weight every 12 hours) did not affect veterinarian-assessed lameness and weight bearing, but improved owner-perceived activity. 2-AG levels were higher in synovial fluid of arthritic dog knees compared with their contralateral joints (26).

### **Epilepsy**

Unrelated to direct effects at CB1, CBD acts as anti-convulsant in animal models of induced epilepsy (27, 28). A pilot study shows that CBD might mitigate naturally occurring epilepsy in dogs (2).

### **Note 1**

The health claims for CBD treats, or rather medical claims, match the reasons for which dog owners purchase various types of hemp products. Owners commonly use the products for anxiety, osteoarthritis or epilepsy in their pets, mostly diagnosed earlier by a veterinarian (29, 30).

## Note 2

### *Analysed CBD and THC concentrations in CBD-containing products*

Ref	Product	n	CBD, mg/kg		THC, mg/kg	
			Mean	Range	Mean	Range
3	CBD oil*	14	28,773	1,875 - 48,879	796	nd - 3,546
6	Hemp seed oil <sup>^</sup> ~	13	86	nd - 1,056	0.3	nd - 1.8
31	„	5	< 0.1		< 0.1	
32	„	3	11	3 - 23	6	1 - 12
31	Hemp seed <sup>~</sup>	5	nd		0.3	0.2 - 0.4 <sup>v</sup>
32	„	4	10	0.5 - 34	1.5	1 - 3
33	Galenic preparations <sup>#</sup>	3	2,644	nd - 4,901	4,378	457 - 9,376

Different analytical methods were used, but all based on mass spectrometry following a specific chromatographic separation technique.

\*Commercial formulations comprising an extract from inflorescences of industrial hemp varieties and a carrier in the form of hemp-seed oil, olive oil or MCT (medium-chain triglycerides) oil. The CBD-rich extracts are commonly obtained by supercritical CO<sub>2</sub> extraction (Note 3). <sup>^</sup> After removal of the bracts, the seeds are squashed or macerated and then subjected to cold pressing to obtain the oil. <sup>#</sup> By way of comparison, analysed compositions of galenic preparations for human use are given. The data refer to mixtures of 1 g commercial cannabis preparation in 10 ml of olive oil, simulating pharmacist-prepared tinctures on medical prescription. <sup>v</sup>Range reflects mean ± 3xSD.

~ Hemp seed (oil) does not contain intrinsic cannabinoids, but contact with resin from inflorescence and bracts left behind cause the presence CBD. In addition, decarboxylation of CBDA (cannabidiolic acid) during processing and storage leads to formation of CBD (6).

## Note 3

*Amount of CBD per treat (mg) and daily number of treats (no.) to be administered to a 20-kg dog according to the labels of commercial CBD dog treats*

Brand	Product	mg	no.	CBD-providing ingredient
Pharma Hemp	CBD Bacon Dog Biscuits	4	1.5	Hemp CBD oil
Purity Petibles	Hemp Pet Chew	5	2	CBD hemp oil
RxCBD	Big Dog Treats	5	1	CO <sub>2</sub> extracted CBD hemp oil
Pet Releaf	Edibites Peanut Butter Banana	1.5	3	Full spectrum cannabinoids
Honest Paws	Calming CBD Dog Treats	5	3	Full spectrum CBD oil
HolistaPet	CBD Dog Treats Green Apple	5	4	Pure CO <sub>2</sub> extracted CBD oil

mg = mg CBD/treat; no. = daily number of treats for a 20-kg dog

Supercritical carbon dioxide is liquid CO<sub>2</sub> that is formed above its critical temperature and pressure. By controlling temperature and pressure, the CO<sub>2</sub> becomes a solvent that specifically extracts the lipophilic cannabinoids from hemp material. CO<sub>2</sub> extraction is relatively clean and efficient.

In the US, CBD products cannot be sold legally as dietary supplement for either human or animal use. Nevertheless, many CBD products are available. Moreover, a high proportion of these products did not contain the levels of CBD they claimed (34).

#### **Note 4**

CBD treats for cats are available in the marketplace, but less ubiquitous than those for dogs. Cat owners generally use hemp products for a veterinarian-diagnosed condition, most commonly cancer, anxiety and arthritis (29). US veterinarians rarely prescribe cannabidiol-containing products for cats with chronic musculoskeletal pain due to osteoarthritis (35). In cerebral arterial smooth muscle cells of cats, the CB1 receptor has been identified (36). In a non-controlled pilot study, oral administration of a synthetic analogue of palmitoyl ethanolamide improved pruritis and erythema in cats with eosinophilic skin disease (37).

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