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# FOUR LEG NEWS



## Introduction - The Cannabis Edition!

I don't think I'd be alone in confessing that I have had owners ASK me about cannabis oil for their dogs. I don't think I'd be alone in saying I have clients that are GIVING their dogs cannabis oil (some purchased products, some home-made). Subsequently, I don't think I'd be alone in saying that I wish I had more information on the subject. Well, Voilà! This newsletter is dedicated to exactly that! Searching through PubMed, some interesting articles were found. My favourite has to be the 2016 review paper! Just check it out! Yep, more research is needed, but that holds true for so many things that are actually in use already. I'm definitely of the opinion that cannabis oil has an important future in human and animal medicine!

Enjoy the read! Cheers, Laurie

# Cannabinoids in Vet Medicine

**Landa L, Sulcova A, Gbelec P. The use of cannabinoids in animals and therapeutic implications for veterinary medicine: a review. Veterinari Medicina 61 (3), 2016: 111-122.**

## A little Cannabinoid history:

Cannabinoids have been used in traditional medicine for thousands of years. Reports of use go back to ancient China, medieval Persia, and 19<sup>th</sup> century Europe. Treatment was largely aimed at various somatic disorders such as headache, fever, bacterial infections, diarrhoea, rheumatic pain, or malaria.

## Cannabinoid classifications:

1. Endogenous cannabinoids – released in response to increases in intracellular calcium.
2. Herbal cannabinoids – chemical produced by the female plants of Cannabis sativa and are found in the resin of the herb.
3. Synthetic cannabinoids – manufactured cannabinoids that bind to cannabinoid receptors (originally created for research).

Next to know – the body has cannabinoid receptors! The two main receptors are as follows:

CB<sub>1</sub> receptors are found in the central nervous system in regions of the brain responsible for pain modulation (parts of the spinal cord, the periaqueductal gray), movement (basal ganglia, cerebellum) or memory processing (hippocampus & cerebral cortex). To a lesser extent, they can also be found in some peripheral tissues such as the pituitary gland, immune cells, reproductive tissues, gastrointestinal tissues, sympathetic ganglia, heart, lung, urinary bladder and adrenal glands.

CB<sub>2</sub> receptors are primarily found in the periphery, and highest density on immune cells, especially B-cells and natural killer cells and also in tonsils or spleen; nevertheless, their presence has also been described in the CNS.

The psychotropic effects of cannabinoids are mediated only by the activation of CB<sub>1</sub> receptors and not of CB<sub>2</sub> receptors

## Cannabinoids in humans:

Their therapeutic potential has been demonstrated in the treatment of many disorders including pain, inflammation, cancer, asthma, glaucoma, spinal cord injury, epilepsy, hypertension, myocardial infarction, arrhythmia, rheumatoid arthritis, diabetes, multiple sclerosis, Parkinson's disease, Alzheimer's disease, depression or feeding-related disorders, and many others.

*Not just for hippies anymore!!*

## THE BASICS:

### THC

=tetrahydrocannabinol

=psychotropic

### CBD =cannabidiol

=medicinal / therapeutic



As of 2015, Bangladesh, Cambodia, Canada, Chile, Colombia, the Czech Republic, India, Jamaica, Mexico, Portugal, Spain, Costa Rica, Uruguay, Germany, the Netherlands, some U.S. states, Native American Indian reservations, and cities as well as some territories of Australia have the least restrictive cannabis laws.



**Cannabinoids and animals:**

The effects of cannabinoids on animals can be found on the experimental level and were obtained during the pre-clinical testing of individual substances in mice, rats and guinea pigs (i.e. laboratory rodents). Beneficial effects of cannabinoids in these animals have been reported e.g. for disorders of the cardiovascular system, cancer treatment, pain treatment, disorders of the respiratory system or metabolic disorders.

It has been shown that the mechanism of action of cannabinoids is very complex.

The activation of cannabinoid CB1 receptors results in retrograde inhibition of the neuronal release of acetylcholine, dopamine, GABA, histamine, serotonin, glutamate, cholecystokinin, D-aspartate, glycine and noradrenaline.

CB2 receptors localized mainly in cells associated with the immune system are involved in the control of inflammatory processes. Their activation results in, among other effects, inhibition of pro-inflammatory cytokine production and increased release of anti-inflammatory cytokines.

Some cannabinoids were shown to act not only at cannabinoid receptors but also at vanilloid or serotonin 5-HT3 receptors.

<b>Table 1: Examples of cannabinoid use in rodent models</b>	
Cardiovascular disorders	Improved cardiac functions after myocardial infarction & reduced cardiac remodeling. Significantly decreased the extent of infarct size in myocardial ischemia. Suppressed cardiac contractility in hypertension. Inhibited atherosclerosis.
Cancer	Significantly reduced the number and dimensions of metastatic nodes. Slowed down the growth of various tumour xenografts (in lung, gliomas, thyroid, skin and lymphoma).
Pain	Reduction in mechanical allodynia and thermal hyperalgesia. Reduces neuropathic nociception. Elicits anti-inflammatory & peripheral analgesia. Suppresses chronic inflammatory & neuropathic pain in rodents.
Asthma	Inhibits the inflammatory response in allergic airway disease. Positive effects on induced asthma-like reactions.
Vomiting	Reduced vomiting in scenarios where vomiting would have been induced (in testing).
Diabetes	Reduced neurotoxicity, inflammation, and blood-retinal barrier breakdown. Reduced the incidence of diabetes in young non-obese diabetes-prone female mice. Ameliorated the manifestations of diabetes in non-obese diabetes-prone female, which were either in a latent diabetes stage or with initial symptoms of the disease.
Retinitis pigmentosa	Preserved cone and rod structure and function, thus showing neuroprotective effects on retinal degeneration.
Food intake / body weight	Reduced inguinal subcutaneous, retroperitoneal and mesenteric adipose tissue mass. Anorectic effects also reported.



**FUN FACTS!**

Cannabis is the largest cash crop in the U.S., exceeding corn and wheat combined –

[Source](#)

In Colorado, medical marijuana dispensaries outnumber Starbucks locations 3 to 1 –

[Source](#)

Rastafarians are legally allowed to possess marijuana in Italy due to it being a ‘sacrament’ to the religion. –

[Source](#)

During Prohibition, Pharmacies sold “Medicinal Whiskey,” much like today’s Medicinal Marijuana. –

[Source](#)

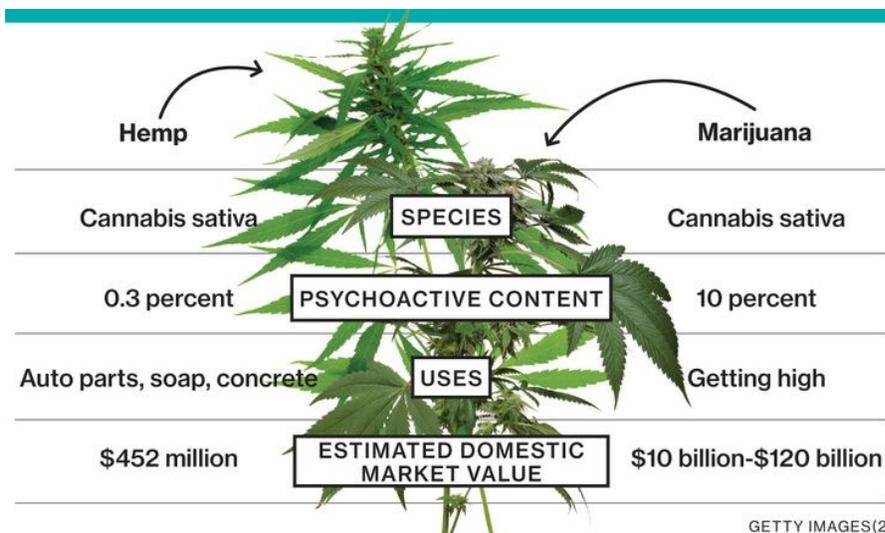
<http://www.kickassfacts.com/25-kickass-interesting-facts-about-marijuana/>

**Non-Rodent papers & findings** are less abundant. Promising research is never the less available!

- Research dating back to the 1950’s in Czechoslovakia showed antibiotic properties of cannabinoids. More recent research backs this up as well!
- The most frequently reported companion animal use of cannabinoids is for glaucoma.
- Promising results shown for inflammation and pain applications in dermatology (healing of lesions, reducing mast cell hyperactivity, and reducing allergic skin reaction) and oncology (inhibitor of angiogenesis in osteosarcoma cells, stimulation of eating, and antiemetic activity).

**Note-worthy**

- Cannabis-based medical products were introduced to human medicine in the last years in many countries (among others Austria, Canada, Czech Republic, Finland, Germany, Israel, Italy).
- Preparations approved for use in human medicine include Cesamet, Dronabinol, Sativex, Bedrocan, Bedrobinol, Bediol, Bedica or Bedrolite.
- For dogs and cats, the veterinarian-recommended, ready made hemp based supplement Canna-Pet is presently available (containing non-psychoactive cannabidiol - CBD).
- The reluctant attitude of veterinarians towards the use of cannabinoids/medical marijuana in animals could be associated with the risk that owners will make attempts to treat their animals using cannabis-based products, which can lead to intoxication.
- Legislative regulations may differ in various countries and the use of cannabinoids/ medical marijuana must be in accordance with the respective rules.



GETTY IMAGES(2)

## What about Osteoarthritis?

Injection (intra-peritoneal) or oral administration of cannabidiol (CBD) at onset of clinical symptoms of induced arthritis in mice resulted in a blocking of progression of arthritis. Both methods of administration were equally effective. Dose dependency showed a bell curve when administered: 2.5mg/kg and 20mg/kg (highest and lowest doses tested) were ineffective when given i.p., whereas 5 mg/kg was 'just right'! Orally, 25mg/kg was most effective (again a dose not the highest or lowest tested).

- Evaluation of the biochemical events following administering of CBD in this model show that there is a combined immunosuppressive and anti-inflammatory actions that result in anti-arthritic effects in induced-OA.

One study engaged in looking at the importance of CB2 receptors in the progression of OA created by destabilization of the medial meniscus in mice. They found that mice that were lacking in CB2 receptors had a more severe OA sequelae than 'normal mice' who had CB2 receptors.

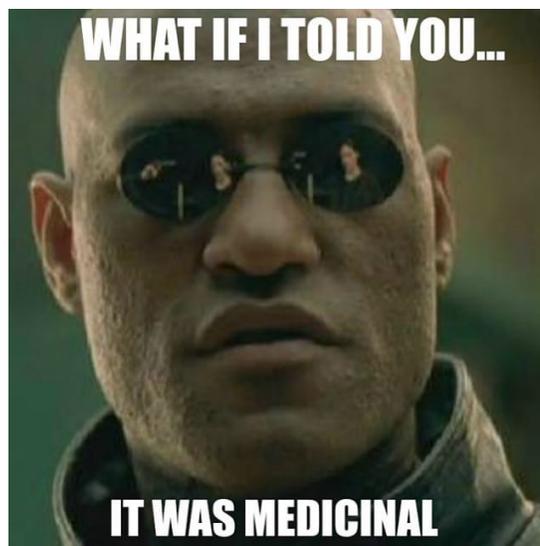
- Thus, CB2 pathways seem to play a role in the pathophysiology of OA in mice, and show that pharmacological activation of CB2 has a protective effect.

Use of a synthetic nonpsychoactive cannabinoid acid (ajulemic acid) was tested on rats with induced arthritis. Synthetic cannabinoid was found to suppress production of matrix metalloproteinases (a substance found in joint tissue of patients with inflammatory arthritis signifying cartilage degradation and bone erosion).

- Synthetic cannabinoid acid (AjA) may be useful in both rheumatoid and osteoarthritis.

### References:

1. Malfait AM, Gallily R, Sumariwalla PF, et al. The nonpsychoactive cannabis constituent cannabidiol is an oral anti-arthritic therapeutic in murine collagen-induced arthritis. *Proc Natl Acad Sci USA*. 2000, Aug 15; 97(17):9561-6.
2. Sophocleous A, Borjesson AE, Salter DM, Ralston SH. The type 2 cannabinoid receptor regulates susceptibility to osteoarthritis in mice. *Osteoarthritis Cartilage*. 2015, Sep;23(9):1586-1594.
3. Johnson DR, Stebulis JA, Rossetti RG, et al. Suppression of fibroblast metalloproteinases by ajulemic acid, a nonpsychoactive cannabinoid acid. 2007, Jan 1;100(1): 184-90.



### Description of purification of CBD from the Malfait study mentioned above:

Gaoni Y & Mechoulam R. *J. Am. Chem. Soc.*, 1971, 93 (1), pp 217-224  
<http://pubs.acs.org.cyber.usask.ca/doi/pdf/10.1021/ja00730a036>

## More Nuggets of Goodness

Gastroesophageal reflux disease (GERD) may be treated by activation of CB1 receptors in the periphery. A range of compounds demonstrated a dose-dependent inhibition of transient lower esophageal sphincter relaxation in a dog model.

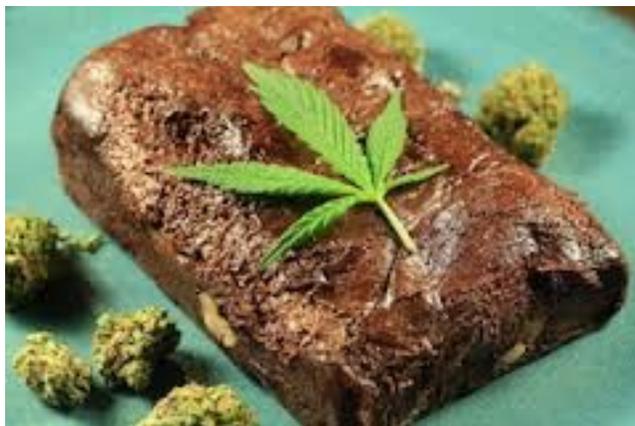
Claims of clinical efficacy in epilepsy of CBD-predominant cannabis or medical marijuana come mostly from limited studies, surveys, or case reports. The mechanism remains unclear.

Cannabinoid ligands regulate bone mass. Cannabidiol (CBD) enhances the biomechanical properties of healing rat mid-femoral fractures.

Effect of cannabidiol intradiscal injection was studied in coccygeal intervertebral discs of rats with induced disc degeneration. 120nmol of cannabidiol significantly minimized the effects of the disc damage.

### References:

1. Plowright AT, Nilsson K, Antonsson M et al. Discovery of agonists of cannabinoid receptor 1 restricted central nervous system penetration aimed for treatment of gastroesophageal reflux disease. *J Med Chem.* 2013, Jan 10,56(1):220-40.
2. Reddy DS, Golub VM. The pharmacological basis of cannabis therapy for epilepsy. *J Pharmacol Exp Ther.* 2016, Apr;357(1):45-55.
3. Kogan NM, Melamed E, Wasserman E. Cannabidiol, a major non-psychoactive cannabis constituent enhances fracture healing and stimulates Lysyl Hydroxylase activity in osteoblasts. *J Bone Miner Res.* 2015, Oct;30(10):1905-13.
4. Silveira JW, Issy AC, Castania VA, et al. Protective effects of cannabidiol on lesion-induced intervertebral



*Don't leave your Marijuana baked goods out where Fido can find them!*

Meola et al, 2012, *J Vet Emerg Crit Care* (San Antonio) found a significant correlation between the number of medical marijuana licenses and marijuana toxicosis cases seen in two veterinary hospitals in Colorado. Ingestion of baked goods made with medical grade tetrahydrocannabinol butter resulted in two deaths.

# Dog Owners are Learning More about Cannabis

Dogs Naturally Magazine had an article recently, Cannabis for your dog: How it can help.

<http://www.dogsnaturallymagazine.com/cannabis-dog-can-help/>

The article talks more about Hemp rather than Marijuana.

Both hemp and marijuana come from the plant Cannabis sativa (however, marijuana can also come from Cannabis indica). According to the article marijuana has a THC content between 10 – 15%; but hemp has only 0.3% or less. Hemp however, is higher in CBD.

Veterinarians are finding CBD hemp to be useful in treating acute ailments like sprains and strains, torn ligaments, bone breaks and even during post-operative care to reduce swelling, pain and stiffness. Apparently, as with any herbal medicine, you may not see an immediate effect. Perhaps it will help with pain within a few hours, but inflammation could take longer to respond.

CBD hemp may make your dog a little drowsy. On rare occasions, side effects have included excessive itchiness or mild vomiting.

Where to buy CBD Hemp? The article suggested the following suppliers:

[Canna-Pet](#)

[Canna4Pets](#)

[Treat Well](#)

[CannaCompanion](#)

[Auntie Dolores Treatibles](#)

## Dosing?

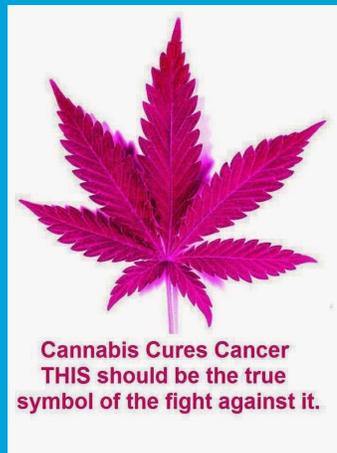
Start low and work up. 1 drop of CBD oil per 10lbs of dog's body weight per day. If that goes well, then move up to twice a day dosing. You could increase the dose every 4 – 5 days until therapeutic benefits are seen (without side effects). Watch out for disorientation, hyperactivity, vomiting, or excessive sedation. If any of these things happen, the article is clear, that one should take their animal to their veterinarian.

## MORE FUN FACTS!

In Bhutan, marijuana grows wild and is more common than regular grass. However, virtually no one smokes it. Instead it is the number one source of feed for pigs. – [Source](#)

US, Canadian and Australian consumption of cannabis per capita is more than double that of the Dutch, despite it being legal in Netherlands. – [Source](#)

Cannabis grew rampantly in Brooklyn around 1951 before being eradicated by the Sanitation Department – [Source](#)





### Did you know:

China, Egypt, France, Indonesia, Japan, Malaysia, Nigeria, Norway, the Philippines, Poland, Saudi Arabia, Singapore, South Korea, Thailand, Turkey, Ukraine, the United Arab Emirates and Vietnam have the strictest cannabis laws.

Source:

[https://en.wikipedia.org/wiki/Legality\\_of\\_cannabis\\_by\\_country](https://en.wikipedia.org/wiki/Legality_of_cannabis_by_country)




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