

HIGH TIME FOR CANNABIS RESEARCH

Researchers Aim to Determine the Efficacy and Safety of Cannabis in Dogs

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AS OF DECEMBER 2017, 29 STATES and the District of Columbia had laws legalizing marijuana in some form. As more people experience the apparent medical benefits of cannabis, many pet owners are left wondering if the plant might be useful in treating various conditions in veterinary medicine, too. And many of those people are turning to their veterinarians for advice.

"When it became legal in Colorado, we got an influx of telephone calls from local veterinarians and clients inquiring into using cannabis for their pets," said Stephanie McGrath, MS, DVM, DACVIM (Neurology), assistant professor at the Colorado State University (CSU) College of Veterinary Medicine and Biomedical Sciences. "Because now, of course, we had people that were getting medical marijuana for themselves, and oftentimes finding it to be helpful for their ailments, and so why not give it to their pets?"

The *Cannabis sativa* L. plant contains more than 113 compounds. It's been proven that tetrahydrocannabinol (THC)—the compound in cannabis responsible for the "high" feeling—is toxic to dogs in certain doses. That's why McGrath and her colleagues at CSU were interested in testing another compound in the plant—cannabidiol (CBD)—on dogs.

S. David Moche, cofounder and CEO of Applied Basic Science Corporation (ABSC), knew that strains of cannabis high in CBD and low in THC were being used to treat various human health conditions, including epilepsy in pediatric patients. He wanted to develop a similar strain for animal patients, but he wanted science to back up his product, which is where McGrath came in. "He and I both felt that there was such a huge lack of any sort of research behind the use of CBD in animals that he was turning to CSU as the contact for him to be able to do some research," McGrath explained.

And so, with funding from Moche and approval from CSU, cannabis studies on dogs were officially underway.

The Research

Phase 1 Study: Is CBD Safe for Dogs?

Before McGrath could test CBD on client-owned dogs, she had to determine if it was safe and, if so, in what forms and at what doses. The Phase 1 study, conducted in 2016, tested the safety, toxicity, and pharmacokinetics of CBD on canine patients. Thirty healthy dogs—beagles from a research facility who lived at CSU during the study—were randomly assigned to receive various doses and delivery methods of CBD for six weeks.

The dogs were divided into six groups. Two of the groups received CBD via a transdermal cream, which was applied to the ears. Two groups received capsules with a powder form of CBD, and two groups received oil tinctures. For each delivery method, one group received 150mg daily, and one group received 300mg daily.

Throughout the study, researchers took daily observational notes and conducted periodic CBD plasma concentrations and routine bloodwork.

The study revealed that of the three delivery methods, oil tinctures had the highest and most stable bloodstream absorption rates. It also revealed that the high dosages of CBD came with some side effects, including elevations in liver enzymes (with no clinical evidence of liver disease). All 30 dogs developed diarrhea during various times of the study.

"To be fair, we were using higher dosages than we would expect to use clinically, since it was for a safety toxicity study," explained McGrath. "We definitely took it seriously and wanted to make sure to closely monitor for those side effects in our clinical trials."

At the conclusion of the Phase 1 study, the team at CSU determined that the CBD product from ABSC was tolerable and measurable, which was just what they needed to get approval to conduct the first-ever cannabis clinical trials on client-owned dogs.

Clinical Trials: Does CBD Have Medical Benefits for Dogs?

In late 2016, two CBD clinical trials on client-owned dogs began at CSU and are now nearing completion. Both studies are placebo controlled and double blinded, which means neither the pet owners nor the researchers know which dogs are receiving the placebo and which are receiving the CBD.

Canine Epilepsy Clinical Trial

The goal of the epilepsy trial is to determine if CBD reduces seizure activity in epileptic dogs with poorly controlled seizures. Only dogs on standard anticonvulsant therapy qualify to participate, and all participants go through a 12-week period on either the placebo or 5 mg/kg CBD daily.

Canine Osteoarthritis Clinical Trial

How CBD Is Thought to Help Dogs

Researchers are still learning CBD's specific effects on dogs, but here's how the compound is thought to work:



Dogs have an endocannabinoid system (ECS), just like humans.

The ECS is a network of cellular activators and receptors in the body that regulate physiological processes, including pain, mood, inflammation, stress, and more.

CBD binds to and activates the vanilloid, adenosine, and serotonin receptors in a dog's ECS and helps to regulate pain perception, inflammation, temperature, and more. It also boosts dopamine levels, helping to reduce anxiety and improve mood.

CBD also blocks GPR55 signaling, which decreases cancer cell reproduction.

CBD can help improve:



Allergies



Anxiety and fear



Appetite loss and digestive problems



Arthritis, joint, and mobility issues



Cancer and tumors



Skin issues



Seizures and epilepsy



Inflammation



Glaucoma



Spasms

Source: greencamp.com/cbd-for-dogs

The goal of the osteoarthritis trial is to determine if CBD reduces pain associated with the disease. To be included in the study, dogs have to present with visually identifiable lameness in any or all limbs, have a radiographically confirmed osteoarthritis diagnosis, and be on a conventional pain management protocol. Unlike the epilepsy trial, the osteoarthritis trial is a crossover study, so each participant received 5 mg/kg CBD or the placebo for six weeks and then the opposite for six weeks.

Researchers hope for study results by the end of 2018. And although both studies are double blinded, some preliminary observations look promising. McGrath said none of the dogs have developed diarrhea or other severe adverse side effects. And, Moche said, many of the dog owners who have completed their 12 weeks have elected to purchase the CBD product after their clinical trials end.

"One [owner] recently told me she knows her dog was on a placebo during the study because the minute she got our product, there was a noticeable difference in her dog," Moche described. "We have people weeping with happiness over the reduction of seizures. One owner has taken her dog off the classical drugs and is only giving him our tincture."

For McGrath, the owner of a geriatric dog with osteoarthritis, the proof will be in the results of these current and future studies. She and her team at CSU recently began a larger, three-year epilepsy and CBD study, which is being funded by a grant from the American Kennel Club's Canine Health Foundation. She hopes to study the effects of CBD on other conditions in the future, including chronic neuropathic pain (dogs with sciatica or bulging or slipped discs in their backs), anxiety in dogs, and various cancers—both on the cancers themselves and as an appetite stimulant for dogs undergoing cancer treatments. She'd also like to begin studies with cats.

"Whether it will be effective for the diseases we're studying, I honestly don't know," she said. "As a scientist, I need that evidence to feel comfortable recommending it to pet owners."

The Anecdotal Evidence

"So, I have three cats . . ." began Casara Andre, DVM, cVMA, owner of Veterinary Cannabis, an education and consulting company, as well as Cultivate Veterinary Wellbeing, a coworking community for veterinary professionals near Denver, Colorado.

Andre started giving her 15-year-old cat, Mattie, hemp about two years ago in an effort to improve her arthritis, appetite, and inflammatory bowel disease.

Six months later, as Mattie's conditions began to improve, Andre watched as her boyfriend's father struggled with end-stage cancer and used medical marijuana to relieve his pain. "That led me to explore medical marijuana for Mattie," she explained. "I bought tinctures from a medical dispensary, and after a couple of weeks, I saw even more dramatic progress in her playfulness, willingness to go outside, and her ability to jump on things and groom herself more effectively."

In October 2017, Andre hosted the first-ever Cannabis in Veterinary Medicine Symposium. Held in Denver, Colorado, the all-day event was attended by veterinary professionals, pet owners, and those in the cannabis industry. Robert Silver, DVM, MS, CVA, chief medical officer of Rx Vitamins and author of *Medical Marijuana and Your Pet: The Definitive Guide*, was one of the speakers.

"I hear so many stories of the beneficial effects of CBD on dogs with arthritis and epilepsy," said Silver, who also spoke at the North American Veterinary Community's VMX conference in February about how cannabis has been shown through research to impact cancer cells and improve the quality of life in cancer patients.

One study Silver referred to was a 1974 National Institutes of Health study that revealed that THC slowed the growth of experimentally induced cancers in mice and increased survival times by 36%.

Some of the testimonials from pet owners and veterinary colleagues that Silver describes are powerful, including that of a dog with fibrosarcoma who avoided amputation and experienced a decrease in tumor size with cannabinoid therapy, a dog in hospice whose appetite increased and had a more comfortable end-of-life experience with hemp oil, and many others.

Andre has similar success stories but emphasized that cannabis medicine is individualized medicine—a holistic approach that is different for each animal. She adapts Mattie's cannabis protocol each day. "I change her dosage based on the day. I have different ratios of tinctures containing different amounts of THC, and I use those based on the weather," she explained.

"It's definitely been a life saver for her. It's why I'm such a proponent of exploring this more."

And by "this," Andre means researching the whole-plant approach and not limiting it to CBD. "I think there are a lot of medicinal benefits that we may be missing if we're only studying CBD," she said. "The more specific, more powerful tools tend to be in the whole plant, including THC . . . all of that."

The Legal Implications

"Right now, it's more legal for a random person off the street or an employee of a recreational dispensary to give a pet owner advice about cannabis," said Andre.

"As veterinarians, we know the ins and outs of what's going on with an animal. If pet owners have questions about using cannabis on their pets, veterinarians should be able to answer those questions and make recommendations specific to that animal's condition. But we have to dance carefully around the wording."

And that's because marijuana is federally illegal, classified as a Schedule 1 substance under the Federal Controlled Substances Act.

"Schedule 1 controlled substances are substances that Congress has found to be dangerous, to have no medical benefit, and no safe or effective use," explained Garrett Graff, JD, of Hoban Law Group in Denver, Colorado. "It is the most severe categorization under the Controlled Substances Act."

The cannabis plant is the broader description for both marijuana and hemp. Marijuana is federally illegal, but what about hemp products and hemp-derived CBD?

"Cannabis, or *Cannabis sativa* L. specifically as the species, is referred to as part of the definition of marijuana. Under the Controlled Substances Act, 'marihuana' refers to certain portions of the *Cannabis sativa* L. plant, including the flowers, the leaves, and the viable seeds," said Graff.

Other parts of the cannabis plant, like the stalks, stems, nonviable seeds, and fibers, are exempt from the legal definition of "marihuana." In 2014, Congress established "industrial hemp" as a defined term under federal law pursuant to the Agricultural Act of 2014, also known as the Farm Bill. There, hemp is defined as all parts of the *Cannabis sativa* L. plant below 0.3% THC by dry weight.

As more states legalize the use of marijuana—either medically, recreationally, or both—will the federal government amend its classification of marijuana? Graff believes it will happen eventually, but it's likely years away.

"I suspect we'll continue to see the status quo for a number of years ahead as additional states legalize either medical or adult use of cannabis," he explained. "And eventually, we will see a tipping point where there are simply too many states for the federal government to pretend any longer, as if an evolution of legalization is not upon them."

But until that happens, pet owners will have questions about cannabis, and Andre wants to be able to provide harm reduction for her clients.

“Veterinarians need to be the safety mechanism,” she said. “If we stay silent, and it’s the commercials, marketing, dispensaries, and companies attempting to educate pet owners, I think that’s really dangerous. There are bad ways to use it. It has interactions with other drugs. Every veterinarian has seen an overdose or toxicity. So, if we aren’t there on the frontlines, I’m concerned about where our patients might be without our oversight.”

According to Graff, practitioners should refer to their respective boards of licensure, “as many boards have put forth guidance, and those boards are the governing authority for a practitioner’s license.”

Graff referred to the Colorado Veterinary Medical Association’s position that practitioners may not prescribe cannabis, but they may have discussions with patients in the context of, and governed by the laws concerning, the practitioner-patient relationship.

“Many practitioners also hold [Drug Enforcement Administration] licensure,” he explained, “which could be implicated given marijuana is federally illegal; however, to date, we are not aware of these occurrences.”

Andre loves that studies are underway at CSU and has plans for her own studies as well, but she says, “We need to be active participants in the education of pet owners while we wait for the studies.”

“I think we have the potential to gain access to a huge new side of our toolbox,” she continued. “One that, potentially, both complements everything we’re already doing as well as expands our ability to treat some conditions that we don’t have great resources for right now.”

Cannabis: An Unregulated Industry

In states where medical and recreational marijuana is legal, dispensaries are not hard to come by. But, do you really know what you’re getting when you purchase a cannabis product? A recent study* showed that only 17% of cannabinoid products are accurately labeled; 23% indicated they had less THC than they actually did, and 60% indicated they had more THC than they did. “The only product we’ve tested is ABSC’s product, so in theory, all of the other products should go through their own testing,” said McGrath. “Think about any other drug that’s out there, whether it’s Tylenol or aspirin or something else, they’ve all gone through their own [Food and Drug Administration] testing on animals and humans. Every drug should go through what ABSC is going through now with these studies.”

**Journal of the American Medical Association*, June 23/30, 2015 Volume 313, Number 24 2491–2493

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