



Cannabis for veterinary patients gets research attention, funding

Stigma begins to lift but legal questions persist

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For The VIN News Service

More than five years after the first states legalized recreational marijuana, leading to a proliferation of cannabis products for pets and people alike, momentum is building to scientifically document whether cannabis makes good medicine for veterinary patients.

In the first study to attract substantial independent funding in the United States, a neurologist at Colorado State University College of Veterinary Medicine & Biomedical Sciences has begun enrolling patients in a clinical trial to test the effects of the cannabis compound cannabidiol on 60 epileptic dogs who respond poorly to standard treatment. The American Kennel Club Canine Health Foundation (AKC CHF) has [awarded the research \\$356,022](#).

At Auburn University College of Veterinary Medicine in Alabama, the director of the clinical pharmacology laboratory also plans a clinical trial of cannabidiol in epileptic patients, along with other cannabis-related research. Her work has received \$150,000 in analytical equipment and pilot-study funding, with a promise of more to come, from a nonprofit called Pet Conscious. The organization is associated with Canna-pet, a Washington company that sells cannabis-derived capsules, oils and biscuits for cats and dogs.

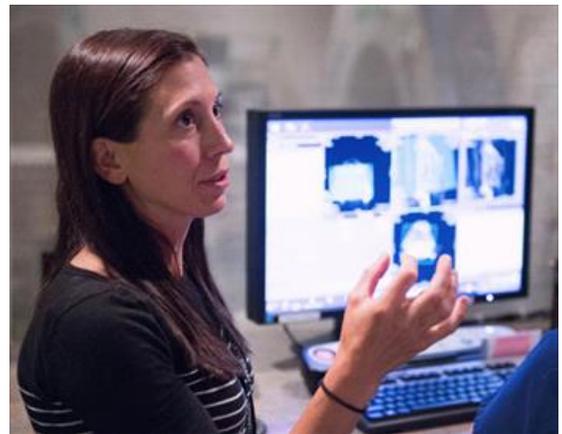
For human patients, a large body of lore and a smaller body of science support the concept of cannabis as effective medicine for an array of conditions — pain, neurological disorders, nausea, anorexia, anxiety and sleep disturbances, to name a few. A report, "[The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research](#)," published by the National Academy of Sciences in January 2017, is a comprehensive review of the hard evidence to date. In a few areas, the authors found conclusive or substantial evidence of medical benefit — specifically, for the treatment of chronic pain in adults; as antiemetics to quell chemotherapy-induced nausea; and to address spasticity in patients with multiple sclerosis.

People considering cannabis for their own ills inevitably wonder whether animal companions with similar conditions could benefit, too. There, scientific documentation has been scarce to non-existent.

Dr. Dawn Boothe, an internist and clinical pharmacologist at Auburn, 16 months ago lamented the dearth of support for cannabis research in veterinary medicine, owing to the federal government's stance that marijuana has no medical benefit. Boothe [told the VIN News Service](#) that she'd tried to obtain private funding without success. Shortly afterward, Canna-pet offered her seed money.

So far, the most likely sources of financial support are businesses that sell cannabis products. The work at Colorado State attracted the substantial AKC CHF grant only because the researcher, Dr. Stephanie McGrath, had done a safety study. That early work was funded by Applied Basic Science Corp., a Colorado company interested in producing and selling cannabis as medicine for dogs.

McGrath's promising early findings using cannabidiol oil produced by Applied Basic Science enabled the AKC CHF, a leading funder of canine health research, to support further work. "You don't just jump into a clinical trial with any product unless you have preliminary safety and dosing information specific to that species," said Dr. Diane Brown, CEO of the foundation. "All AKC CHF-



Colorado State University photo

Dr. Stephanie McGrath, a veterinary neurologist, is the first researcher to receive significant independent funding in the U.S. to document the therapeutic potential of cannabis in dogs.

funded research undergoes rigorous scrutiny through our Scientific Review Committee, and this proposal raised some unique questions."

The reviewers had to settle their nerves about supporting a study involving a plant that the U.S. Drug Enforcement Agency (DEA) regulates as a Schedule I controlled substance, meaning that the federal government considers it to have no medical benefit and a high potential for abuse. "There was a lot of discussion about the potential backlash; the politics," Brown said. "Is this going to be frowned upon? Is this legitimate science?"

The foundation concluded that in addition to anecdotal evidence that cannabis has medicinal benefits, there's a compelling safety reason to support research: "Some people are administering cannabis products to dogs based on [consulting] Dr. Google, so it really is important for the AKC CHF to take a leadership role, demonstrating responsibility and making an investment to acquire scientifically-driven data for dogs," Brown said.

Ultimately, the foundation was proud to take the step. "We are excited to be at the forefront supporting the first clinical trial for a cannabis product for drug-resistant epilepsy in dogs," Brown said.

Still, the battle for legitimacy and support for cannabis research in veterinary medicine is far from over.

Institutional resistance lingers

McGrath, the neuroscientist leading the epilepsy study in dogs, has struggled to get her pilot work on cannabis published. Her first study sponsored by Applied Basic Science examined the pharmacokinetics of cannabidiol oil in 30 research beagles — what different dosages and delivery systems looked like in the dogs' blood, and whether there were any harmful side effects. (There were not.)

When it came time to report the results, McGrath met resistance from several scientific journals in the United States.

"They did not feel that the product was federally legal, therefore, they wouldn't publish a manuscript on a product that was not federally legal. That's what they either alluded to or outright said," McGrath recounted.

She had to reach outside the country to find a receptive publication. In January, the study was accepted by the *Canadian Veterinary Journal*, which McGrath said expects to publish the research in October.

The question of legality of cannabis products in the United States, especially those containing the active agent cannabidiol — CBD in shorthand — is convoluted and confounding because the laws are inconsistent.

As explained in [guidelines](#) from the Colorado State University Office of the General Counsel and Office of the Vice President for Research, the federal Controlled Substances Act outlaws the possession, cultivation and use of *Cannabis sativa*, otherwise known as marijuana. However, the [Agricultural Act of 2014, section 7606](#), allows for the cultivation of industrial hemp, defined as "the plant *Cannabis sativa* L. and any part of such plant, whether growing or not, with a delta-9 tetrahydrocannabinol concentration of not more than 0.3 percent on a dry weight basis."

The distinction is this: Delta-9 tetrahydrocannabinol, or THC, is the psychoactive ingredient in marijuana that causes euphoria, or a "high." But THC is just one biologically active ingredient in cannabis among many that are believed to have a potentially therapeutic effect, [CBD](#) chief among them. Cannabis growers say plant strains exist that produce high levels of CBD and low levels of THC. Under the Agricultural Act definition, any cannabis plant that has little to no THC is [industrial hemp](#) that may be grown "for purposes of research conducted under an agricultural pilot program or other agricultural or academic research" in [states that have laws allowing such](#).

According to the Colorado State guidelines and fact sheet, Colorado law permits research on and commercial cultivation of industrial hemp by growers who have registered with the state Department of Agriculture. The university has state permission to grow hemp indoors and out in specified locations.

The nuance and conflict in federal law is unrecognized by a recent document prepared by the American Veterinary Medical Association's Council on Biologic and Therapeutic Agents, "[Cannabis: What Veterinarians Need to Know](#)." The guide, published in January, relays the [DEA position](#) that all derivatives of the marijuana plant, including CBD, are illegal under the Controlled Substances Act. The AVMA guide states: "Marijuana and its derivatives including CBD are federally illegal ..." and does not mention the 2014 farm bill.

Promising research ends

The AVMA council's strict interpretation of the law contributed to a halt on promising research at Cornell University.

In pilot studies requested by a company in Maine called ElleVet Sciences, Dr. Joseph Wakshlag, an associate professor of clinical nutrition and sports medicine and rehabilitation at Cornell's College of Veterinary Medicine, tested the pharmacokinetics of CBD oil produced by ElleVet. Then he tested it as a treatment for dogs with osteoarthritis and crepitus. Wakshlag said ElleVet provided about \$80,000 in funding.

Wakshlag reported resounding results: "Lo and behold, when the patients were on industrial-hemp oil with enriched CBD in it, the dogs did remarkably better. The older and more decrepit they were, the more pronounced the improvement."

The double-blinded study, which began in late 2016, involved 16 patients, each of whom received either the hemp oil or a placebo twice daily for four weeks. After a two-week break, patients who'd received the placebo were then given the hemp oil, and those who received hemp oil earlier were given the placebo, a study design known as "crossover."

Some dogs were in such bad shape that their owners were ready to euthanize, Wakshlag said. In one such case, the owner of a dog who was on the olive-oil-based placebo and not showing improvement asked, "Can we just end this?" the doctor recounted.

He asked the owner to try the second oil before giving up. After the switch, "that dog came trotting in for the two-week follow-up, and the owner was thrilled," Wakshlag reported.

In another case, within three days of starting her dog on CBD oil, the owner was "in our office, crying, thanking us for giving her her dog back," Wakshlag said.

Overall, the research showed "a significant decrease in pain and increase in activity" with no observable side effects, Wakshlag said. The experience made him a believer. In a [video](#) posted on the ElleVet website, Wakshlag predicts that CBD will "change the face of pain management probably for years to come."

But first, it has to be widely accepted as a legal product for veterinary use. Bills are pending in at least two states — [California](#) and [New York](#) — but to date, [no state has given veterinarians explicit authority](#) to discuss cannabis as medicine, much less recommend it.

"That's the sad part," Wakshlag said. "We have something out there that we think will probably help 60 to 70 percent of dogs with arthritis, and we can't recommend it."

Equally disappointing, he said, his institution's hospital director is unwilling to allow further research, owing to the DEA's statement that CBD is illegal and the AVMA's agreement. Wakshlag said he had finished the clinical trial when the DEA position, followed by the AVMA report, came out. The combination led his hospital administration to stop further research, he said. "Things are getting hairy and fuzzy, so I'm not doing it anymore."

AVMA spokesperson Sharon Granskog said the group was unaware that its report on cannabis influenced Cornell to stop a research program. The purpose of the report, she said by email, was "to help veterinarians navigate the complex issues and questions around the therapeutic use of marijuana."

Asked why the report does not mention the Agricultural Act of 2014 provision for industrial hemp, Granskog said other laws are more germane — namely, the federal

Dog owners report cannabis works

Lori Kogan has been researching marijuana in veterinary medicine for a few years now, unfettered by federal drug law.

A licensed psychologist and professor of clinical sciences at Colorado State University College of Veterinary Medicine and Biological Sciences, Kogan doesn't need to administer the drug to pursue answers to her research questions.

Kogan has been surveying pet owners online to learn who's giving marijuana or hemp products to their animal companions, why, and how they perceive their pets respond.

In a survey that ran in the U.S. from Sept. 1 to Dec. 15, about 80 percent of 1,068 respondents had bought hemp products for their dogs. Their main reasons for doing so were to treat pain, anxiety or seizures, Kogan said. And they were pleased with the results.

"People report that the stuff works," Kogan said. "Bottom line, people think it works, and they think it works better than conventional medicine."

Other findings: "People with more education were more likely to purchase these products. Gender did not make a difference. State of residence did not make a difference. If people used recreational hemp products, that was not correlated," Kogan said.

"But those who used it for personal medical use, that was correlated, which makes total sense to me," she continued. "People who see it works for them are more likely to buy it for their pet."

The survey respondents tended to be older, with more than half the group older than 45. The single largest age group, constituting some 20 percent of survey-takers, was over 60.

The majority had a four-year college degree or higher.

In short, Kogan said, "It tends to be the little bit older, more educated folks that are using these products."

Another finding that Kogan found particularly noteworthy and disheartening: "Most people are getting their information about these products from the product website. Hello? We want them to be getting information from their veterinarians, but veterinarians are afraid to talk about it. So they're getting it from these biased sources."

Collaborating with Kogan on the study were Dr. Peter Hellyer, a professor of anesthesiology at the Colorado State veterinary school; and Regina Schoenfeld-Tacher, an associate professor of veterinary educational development at North Carolina State University.

Food, Drug and Cosmetic Act, enforced by the U.S. Food and Drug Administration; and the Controlled Substances Act. "Whether hemp may be grown for food and pharmaceutical products remains a question for the FDA and/or the DEA," she said, echoing a [statement by the U.S. Department of Agriculture](#).

'It seemed crazy that there was no research'

McGrath, the Colorado State neurologist, said the AVMA historically has taken a conservative posture on cannabis but she was heartened to receive an invitation from the association to speak about her research at its annual convention in July. "I'm hoping that that at least shows that there's some more openness to their stance on the subject," she said.

McGrath credits robust support from Colorado State in making her research with veterinary patients possible. When she consulted a member of the university's legal staff at the outset, she was told, "Heck yeah, you can do studies. Just make sure it's hemp product so it's less than 0.3 percent THC."

"I do feel like I'm very protected by CSU," McGrath said. "If I were out in private practice, there's no way I would do this. I would personally not feel comfortable at all exposing myself to the potential legal repercussions."

She added: "I do spend a little bit of time feeling like, 'Gosh, I hope I'm OK doing what I'm doing.' "

Conducting pioneering studies on cannabis is nothing McGrath ever aspired to do. "I had no intention of doing this research at all," she said. "I hadn't been following any of this and had very little interest in it."

Then in 2012, voters in Colorado and Washington made marijuana legal for recreational use, marking a trend toward liberalizing attitudes on a drug that had been accepted for years in a number of states for medical use. (Today, 30 states and the District of Columbia have laws legalizing marijuana in some form, according to [Governing](#) magazine.) McGrath began fielding calls from local veterinarians and pet owners asking whether the plant's apparent medicinal effects in humans extended to other species. She looked into what was known on the topic.

"I was pretty alarmed by how little research was out there," she said. Considering that people were likely to try products on their animals regardless, McGrath thought that "with a substance that is seemingly pretty harmless — specifically, CBD — and potentially how beneficial it could be, it seemed crazy that there was no research to support that."

Her interest piqued, McGrath mused, "I wonder if I could be the one to do this research, since nobody else seems to be?"

About that time, a physician acquaintance in Colorado, Dr. Alan Shackelford, had begun to explore the anti-convulsive effects of CBD after being implored for help by the mother of a 5-year-old. The child had a severe form of epilepsy known as Dravet syndrome that caused her to have near-constant seizures.

Initially reluctant, Shackelford was persuaded by the mother's desperation. With the doctor's referral, the mother obtained a cannabis extract derived from a strain said to have high levels of CBD. She gave it to her daughter. The child "went from 300 grand mal seizures a week to none. Immediately," Shackelford said.

She had a seizure one week later, but the frequency was notably diminished. "To go from 300 a week to two to four seizures a month is an astonishing change," the doctor said.

Word spread. The girl's experience was detailed in a CNN documentary, "[Weed](#)." Parents of children suffering from seizure disorders began moving with them to Colorado to seek similar treatment.

McGrath and Shackelford discussed whether CBD might work in dogs, too. Epilepsy is the most common neurologic condition in canines, and standard drugs don't work in 20 to 30 percent of cases. "Let's see if we can find the money to do a study," Shackelford recalled saying. "This was new, of course, the very notion."

Shackelford enlisted S. David Moche, an entrepreneur who'd done real-estate deals in what he calls "the medical marijuana ecosystem" of California. Moche also had ties in Israel, dubbed "[The Holy Land of Medical Marijuana](#)" by *U.S. News & World Report* for its groundbreaking cannabis research. (It was an Israeli chemist who isolated THC and discovered that it acts on the brain by mimicking a neurotransmitter, a pioneering step toward recognizing the body's [endocannabinoid system](#).)

Kogan said the purpose of the survey is to help inform veterinarians and develop guidelines for pet owners. A report on the survey will be published in the *Journal of the American Veterinary Holistic Association*. (The same journal [published](#) the results of a similar but smaller survey by Kogan and colleagues in spring 2016.)

Kogan said she recently completed a survey of Canadian pet owners and is preparing to submit the findings for publication. In general, Kogan said, "The reasons why they got the products were the same [as in the U.S.], as was the main source of their CBD information."

In Colorado, Shackelford and Moche established Applied Basic Science and set out to obtain scientific validation of prospective products. "I was not going to put a product on the market without having the research behind it," Moche said. "Otherwise, I'd be there like every other Tom, Dick and Harry doing a big marketing game. This should not be a marketing game. You're dealing with a pet who is the most loyal, trusted, best friend. All of that is cliché, but it's true."

Results of safety study lead to clinical trials

Moche, president and CEO of the company, estimates it has contributed about \$500,000 to the science to date. To start, McGrath tested the safety of oral CBD oil on 30 research beagles. She detected no harmful effects. (The finding applies to the specific product given and cannot be extrapolated to CBD products in general. The same is true of the testing done by Wakshlag at Cornell.)

The safety data enabled McGrath's research team to apply for and receive approval from the university's Institutional Animal Use and Care Committee for a study on client-owned animals — pets. Applied Basic Science wished to test its CBD on arthritic as well as epileptic dogs, so McGrath enlisted a Colorado State colleague, Dr. Felix Duerr, a sports medicine and rehabilitation and surgery specialist, to handle the arthritis portion.

Duerr had had no particular knowledge of cannabis, and believed that any study proposal involving cannabis would be stalled in the legal gray zone. Moreover, he was accustomed to inquiries from businesses chasing cures. "I get a call from a company about every week that says, 'We've found a cure for arthritis,' he told VIN News. "I always tell them that we are open to anything as long as we know it's safe for the dogs and there's some preliminary evidence suggesting that it might be beneficial. I give them a rough estimate of what a real clinical trial costs and 95 percent of the time, they never call me again."

This proposal turned out to be one of the 5 percent that materialize.

The study involves 24 arthritic dogs, each of whom receives CBD oil for six weeks and a placebo for six weeks. Effects of each are measured through analysis of the dogs' gait, radiographs, activity monitoring and owner questionnaires. Because the research is double-blinded, Duerr doesn't know yet how well the CBD works versus the placebo. He anticipates seeing answers in May.

McGrath's pilot clinical study examining the effects of CBD on 20 epileptic dogs, now winding down, is double-blinded, too. McGrath expects to see the data in a few months. Meanwhile, her research team has begun vetting prospects for the larger AKC CHF-funded study; they aim to enroll 60 patients.

The subjects will be dogs for whom conventional epilepsy drugs don't work well or cause unacceptable side effects. The patients must be able to visit the clinic at Colorado State frequently. That requirement has not deterred out-of-state dog owners. "There's definitely people who've offered to move to Colorado for six months so their dog can take part in the study," McGrath said.

At Auburn University in Alabama, Boothe, the clinical pharmacologist, has had more difficulty getting her clinical work off the ground, owing to the legal morass.

Alabama is one of 20 states where marijuana remains illegal for any purpose, although the state in 2016 created an industrial hemp research program overseen by its agriculture department.

Boothe's research is slowed by the DEA posture that cannabis-derived products, including CBD, are subject to the same restrictions as marijuana with substantial THC content. The DEA position compelled Boothe to apply for a federal permit for research involving a Schedule I controlled substance, the classification under which marijuana (along with heroin, LSD and other narcotics) falls.

The legal landscape is dynamic. On Monday, U.S. Senate Majority Leader Mitch McConnell, a Republican from Kentucky, [announced](#) plans to introduce the Hemp Farming Act of 2018 to legalize hemp as an agricultural commodity and remove it from the list of controlled substances.

Meanwhile, Boothe said, her research team is doing work that doesn't involve them directly giving patients CBD. For example, they're measuring the presence of cannabinoid receptors in the body tissues of normal and abnormal animals as a means of understanding the biological effects of cannabinoids. They're also offering free therapeutic drug monitoring of cannabinoids in the blood of pets receiving any cannabis product.

Once they are able to work clinically with cannabinoids and animals, Boothe said one question her team will try to answer is what dose is needed in dogs, cats and horses to achieve a therapeutic response, and how best to deliver the dose.

To inquire about enrolling a dog in the Colorado State University clinical trial investigating the efficacy of cannabidiol in treating epilepsy, contact the research team at csuneurotrials@colostate.edu

To inquire about free therapeutic drug monitoring of cannabinoids in pets being given any cannabis products, [contact](#) the Auburn University College of Veterinary Medicine Clinical Pharmacology Laboratory.

With growing support for research, Boothe said she's feeling much more optimistic about the prospect of obtaining reliable, science-based information about the potency of cannabis as medicine for veterinary patients. "Ten years from now, we will have a lot settled," she predicted. After a moment's thought, she added, "I think five years might be reasonable."

Boothe is continuing to seek independent funding for research because she knows that involvement by commercial interests can detract from the credibility of findings, rightly or wrongly. "Pet Conscious has been wonderful," she said. "They have put no restrictions on what we can study, but the advantage of non-industry-sponsored studies is that it removes the perception of bias."

Without continued and wider support for research, Boothe said, veterinary medicine stands to be left behind.

"Here's the bottom line," she said: "These products are coming. There's no doubt in my mind that cannabinoids are going to prove [to be] important therapeutic interventions. What remains to be seen is for what conditions and the most appropriate doses and ways to use it. I'm convinced we need to get on this train, because it's going to go with or without us, and I'd rather it be with us."

URL: <http://news.vin.com/doc/?id=8490540>

Related resources

- [Veterinarians implore AVMA to address marijuana in animals](#) - July 25, 2017 
- [Pot for pets poses quandary for veterinarians](#) - November 4, 2016 
- [Will relaxed marijuana laws produce more stoned dogs?](#) - November 29, 2012 



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