Guide to CBD

vet candy

Featuring CBD Legal expert, Brian Dickerson, Esq.

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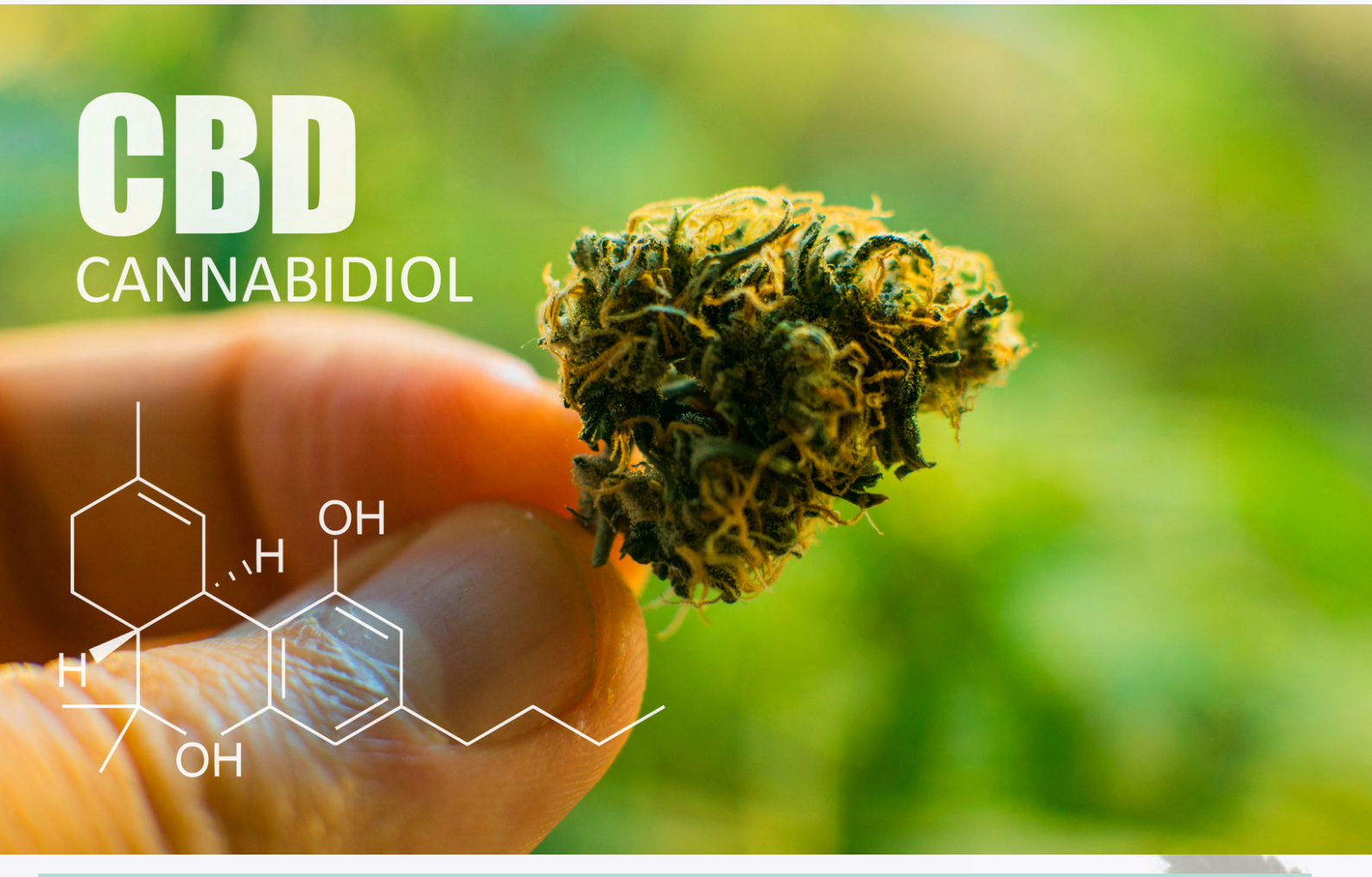
WHAT YOU NEED TO KNOW ABOUT CBD IN PETS

Dr. Jenifer Chatfield

Marijuana (*Cannabis sativa or Cannabis indica*) has been cultivated and used by humans since 500 BC in Asia. These days, people use the names hemp, marijuana, and CBD interchangeably. But are they synonymous? The short answer is no. The long answer is also no—they are not legally the same. Therein lies the rub, especially for pet owners and veterinarians searching for treatments and cures to difficult therapeutic situations ranging from cancer to arthritis to heartworm disease. Let's try to eliminate some of the haziness surrounding cannabis and pets these days.



In 2018, two critical events brought this issue front and center in every pet-owning household in the country. First, in September 2018, the U.S. Drug Enforcement Agency (DEA) reclassified drugs that contained certain cannabis components. As a result, FDA-approved drugs that contain CBD (cannabidiol) derived from cannabis and no more than 0.1% tetrahydrocannabinols (THC) are now in Schedule V, rather than Schedule I (drugs that have no currently accepted medical use and a high potential for abuse). Other Schedule V drugs include cough preparations with less than 200 mg of codeine per 100 ml (Robitussin AC), Lomotil, Motofen, Lyrica, and Parepectolin. Marijuana, as distinguished from cannabis, remained on Schedule I along with heroin, LSD, ecstasy, peyote, etc.

> There are three cannabis-related drug products that are also FDA approved, all of which are for human use and require prescriptions.

This move was huge! Currently, only a single cannabis-derived drug is FDA-approved, Epidiolex. Epidiolex contains a purified form of CBD for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients two years of age and older. That's right—only for use in people. There are three cannabis-related drug products that are also FDA-approved, all of which are for human use and require prescriptions. Well, then, why is the local gas station stocked with every flavor of CBD-containing gummy?

It has to do with who regulates what. In the land of the federal government, where a veterinarian's license to prescribe controlled substances resides with the DEA, marijuana is still illegal. Marijuana is still illegal in most states too. However, since the DEA reclassified CBD-containing products to Schedule V, it is possible for a veterinarian to legally prescribe an FDA-approved drug for use in animals containing CBD and less than 0.1% THC. Since the FDA has so far approved only a single cannabis-derived drug, however, and only in humans and only with a prescription, the reclassification did not help vets, "(nor did it allow the gas station to expand its revenue base").

Then the second critical event took place: Congress passed the Agriculture Improvement Act of 2018 (the 2018 Farm Bill). According to the US Dept. of Justice (US DOJ), this bill, which was signed into law on Dec. 20, 2018, "… changed the definition of marijuana to exclude 'hemp'—plant material that contains 0.3 percent or less delta-9 THC on a dry weight basis. Accordingly, hemp, including hemp plants and cannabidiol (CBD) preparations at or below the 0.3 percent delta-9 THC threshold, is not a controlled substance, and a DEA registration is not required to grow or research it."

interstate commerce a food (including any animal food or feed) to which has been added a substance that is an active ingredient in an approved drug product or a substance for which substantial clinical investigations have been instituted, and the existence of such investigations has been made public." There's animal food and feed! So, what are we left with?

> "The 2018 Farm Bill explicitly legalizes the interstate transport of hemp-derived products for commercial or other purposes."

The 2018 Farm Bill explicitly legalizes the interstate transport of hemp-derived products for commercial or other purposes. It further provides no restrictions on the sale, transport, or possession of hemp-derived products, so long as those items are produced in a manner consistent with the law. The proverbial floodgate was opened! So, as long as that gummy contains less than 0.3% THC, all is legal, right? Well, no.

According to July 2019 testimony from Amy Abernethy, MD, PhD, FDA Principal Deputy Commissioner, "FDA's existing authorities over foods, dietary supplements, human and veterinary drugs, and cosmetics apply to hemp products to the extent such hemp products fall within those categories." Missing from that list is dietary supplements for animals. Dr. Abernathy goes on to say, "It is unlawful under the Federal Food, Drug, and Cosmetic Act (FD&C Act) to introduce into interstate commerce a food (including any animal food or feed) to which has been added a substance that is an active ingredient in an approved drug product or a substance for which substantial clinical investigations have been instituted, and the existence of such investigations has been made public." There's animal food and feed! So, what are we left with?

All of this legalese and maneuvering leaves a somewhat grey area called animal dietary supplements. Animal drugs must still obtain FDA approval, but animal supplements do not yet exist in the federal regulatory universe, and the FDA determined in 1996, "After examining the statutory language, intent, and legislative history … the Dietary Supplement Health and Education Act (DSHEA) does not apply to animal products." As long as the label on the dog treat does not claim to prevent, diagnose, mitigate, treat, or cure any disease, and the CBD is hemp-derived through lawful cultivation (and has <0.3% THC), it is an animal dietary supplement and is not subject to regulation by the FDA. Therefore, a dog supplement containing hemp (notice I avoided saying CBD) can be labeled to support the structure and function of the animal, i.e. support joint movement or serve as a calming aid, but it cannot legally claim to treat, mitigate, or cure osteoarthritis or separation anxiety. If it were labeled thus, it would be seen by regulators as a drug and subject to FDA regulation and approval. A fine semantic line, perhaps, but semantics is the difference between legal and illegal. One more note: since pure CBD oil is currently the active ingredient in an existing FDA-approved drug (Epidiolex), pure CBD oil may not be sold without prescription.

While the DEA, FDA, and the 2018 Farm Bill all combine to make a hemp-derived animal supplement legal for over-the-counter sale at the federal level, state governments can still put the kibosh on the whole transaction. In fact, even hemp-derived products remain illegal in Idaho unless they meet additional incredibly restrictive criteria, e.g. contain 0.0% THC.

So, the next time a client comes into your practice and asks you if it is legal to give their pet a little ganja, Mary Jane, pot, or grass, the answer is still no for now. It is legal, however, to discuss supplements for pets that are hemp-based, hemp-derived, or contain hemp extract. It would be prudent to make the pet owner aware that this is a relatively new area of research in pets, and that doses may or may not be accurate. It is also prudent to remind pet owners that these supplements are unregulated—no government agency is verifying the contents or efficacy. So, yes, animal supplements containing hemp (and as a consequence likely CBD) are okay, except in Idaho, but pharmacokinetics, safety, bioavailability, and so on, are topics for another day.

LEGAL CORNER

FIVE LEGAL FACTS ABOUT CBD

Brian E. Dickerson, Esq.
Fisher Broyles

1. In 2018, the Agricultural Improvement Ac 2018, also known as the Farm Bill, reclass ied hemp as an "agricultural commodity." Hemp contains hundreds of cannabinoid, which CBD s one of the more popular.

2. The legality of hemp and CBD can vary from state to state.

3. Hemp-derived cannabinoids are legal in states that allow their use if they:

- Contain less than 0.3% THC
- Adhere to the shared state-federal regulations
- Are grown by a properly licensed grower

4. The FDA has approved one cannabis-derived and three cannabis-related drug products for human use.

5. There are no FDA approved CBD products for veterinary use. Products marketed for pets are classified as nutraceutical supplements. These products cannot make health claims.

THE TRUTH ABOUT CBD

Cannabidiol, or CBD oil, is promoted for a wide range of medical conditions in people and in pets. On one show, Dr. Jennifer Chatfield and Dr. Jason Chatfield speak with veterinary surgeon and CBD expert, Dr. Courtney Campbell. The trio review the science behind the claims, the confusion about the legality of the product, and how veterinarians can embrace this new pet-care trend.

Listen now

ALL ABOUT CBD

This episode promises an information-packed show with a focus on one of the hottest growing trends in health and wellness, Cannabidiol, also known as CBD. Interest in the compound is at an all time high, especially in the veterinary and pet care industry.

Watch now

IS CBD LEGAL?

Aaron Cadena

Is CBD legal? The short answer: Yes, CBD is legal, but ... under very specific conditions. While the legal status of CBD has become better defined with recent reforms, some laws are still unclear, and others may still be needed. Add outright misinformation to the mix, and many may have a very skewed understanding of what's legal versus what isn't.

Is CBD legal in all 50 states? It depends. The legality of CBD can vary from state to state and federally, but in general, one of the determining factors is whether the CBD is derived from hemp or marijuana.

While the two plants are very close relatives, they are classified very differently under the law, and understanding the difference is crucial to legal CBD use.

LEGALITY OF HEMP AND MARIJUANA

Hemp and marijuana are both terms used to describe different varieties of Cannabis, and both can produce an abundance of CBD. As members of the same family, hemp and marijuana share many visual similarities, but at a chemical level, the two plants have vastly different amounts of Tetrahydrocannabinol (THC), the intoxicating compound found in Cannabis.

While hemp is characterized by producing a nearly non-existent amount of THC (less than 0.3%), marijuana can produce an abundance of THC (up to 30%). Because of its high THC content, marijuana may induce severe mind-altering effects when consumed and is federally illegal in the United States and many other countries.

IS HEMP CBD LEGAL?

In 2018, President Trump passed the Agricultural Improvement Act of 2018 (also known as the 2018 Farm Bill), which removed hemp as a Schedule I substance and reclassified it as an "agricultural commodity."

A common misconception about the 2018 Farm Bill is that it legalized CBD regardless of whether it was derived from hemp or marijuana. This is not true.

Based on the DEA's guidelines, CBD is a Schedule I substance and is illegal.

If, however, the CBD is derived from hemp and adheres to the following regulations set forth in the new farm bill, it is removed as a Schedule I substance and is legal:

- The hemp must contain less than 0.3% THC.
- The hemp must adhere to state-federal regulations.
- The hemp must be grown by a properly licensed grower.

In addition, the 2018 Farm Bill also removed restrictions on the sale, transportation, and possession of hemp-derived CBD products and allowed for the transportation of hemp-derived CBD products across state lines as long as the products follow the regulations defined above.

WHAT ABOUT MARIJUANA-DERIVED CBD?

While hemp-derived CBD is federally legal as long as it adheres to the law, marijuana-derived CBD is a bit more complicated because it is derived from a plant that is illegal.

In some states, such as California and Colorado, marijuana is legal for recreational usage, and naturally so is marijuana-derived CBD. Others allow marijuana-derived CBD usage under certain conditions, such as a specific medical conditions, and some states strictly prohibit it.

STATES WHERE MARIJUANA-DERIVED CBD IS LEGAL FOR RECREATIONAL USE

As of 2020, there are ten states where Cannabis, including both marijuana and hemp, are completely legal for recreational and medicinal use. These states are Alaska, California, Colorado, Maine, Massachusetts, Michigan, Nevada, Oregon, Vermont, and Washington.

STATES WHERE MARIJUANA-DERIVED CBD IS LEGAL FOR MEDICINAL USE

As of 2020, there are a total of 47 states (including the ten states mentioned above) where marijuana-derived CBD is legal for medicinal usage. The specific regulations for such use vary from state to state with a majority of states allowing medicinal use for a broad range of conditions, while others set specific requirements for approved use (e.g. the CBD must contain less than a certain percentage of THC or the patient suffers from a specific condition).

States with regulations that permit the use of marijuana-derived CBD for a broad range of conditions include Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Hawaii, Illinois, Maine, Maryland, Massachusetts, Michigan, Minnesota, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Ohio, Oregon, Pennsylvania, Rhode Island, Vermont, Washington, and West Virginia.

States with regulations that permit the use of marijuana-derived CBD under certain circumstances include Alabama, Georgia, Indiana, Iowa, Kentucky, Mississippi, Missouri, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Utah, Virginia, Wisconsin, and Wyoming.

Read more by clicking on the link below:
The Legal Status of CBD in 2020

HOW DO U.S. VETERINARIANS PERCEIVE CBD USE IN DOGS?

Veterinary Information Network created a study to gauge U.S. veterinarians' knowledge levels, views, and experiences related to the use of cannabinoids in the medical treatment of dogs.

This study included a total of 2,130 anonymous participants' answers to an online survey. Results were analyzed based on the legal status of recreational marijuana in each participant's state of practice and the participant's year of graduation from veterinary school.

Most veterinarians (61.5%) felt comfortable discussing the use of CBD with their colleagues, but only 45.5% felt comfortable discussing this topic with clients. No differences were found based on the state of practice, and recent graduates were found to be less comfortable discussing the topic and less likely to recommend or prescribe.

Veterinarians and clients in states with legalized recreational marijuana were more likely to talk about the use of CBD products to treat canine ailments than those in other states.

CBD was most frequently discussed as a potential treatment for pain management, anxiety, and seizures. Even though veterinarians in states with legal marijuana were more likely to recommend CBD, there was no difference in prescribing in legal and non-legal states.

The most commonly used CBD formulations were oil/extract and edibles, which were helpful in providing analgesia for chronic and acute pain, relieving anxiety, and decreasing seizure frequency and severity. The most commonly reported side-effect was sedation. Participants felt their state veterinary associations and veterinary boards did not provide sufficient guidance for them to practice within applicable laws.

Finally recent graduates and those practicing in states with legalized recreational marijuana were more likely to agree that research regarding the use of CBD in dogs is needed.

Read more by clicking on the link below:
U.S. veterinarians' perceptions of CBD use in dogs

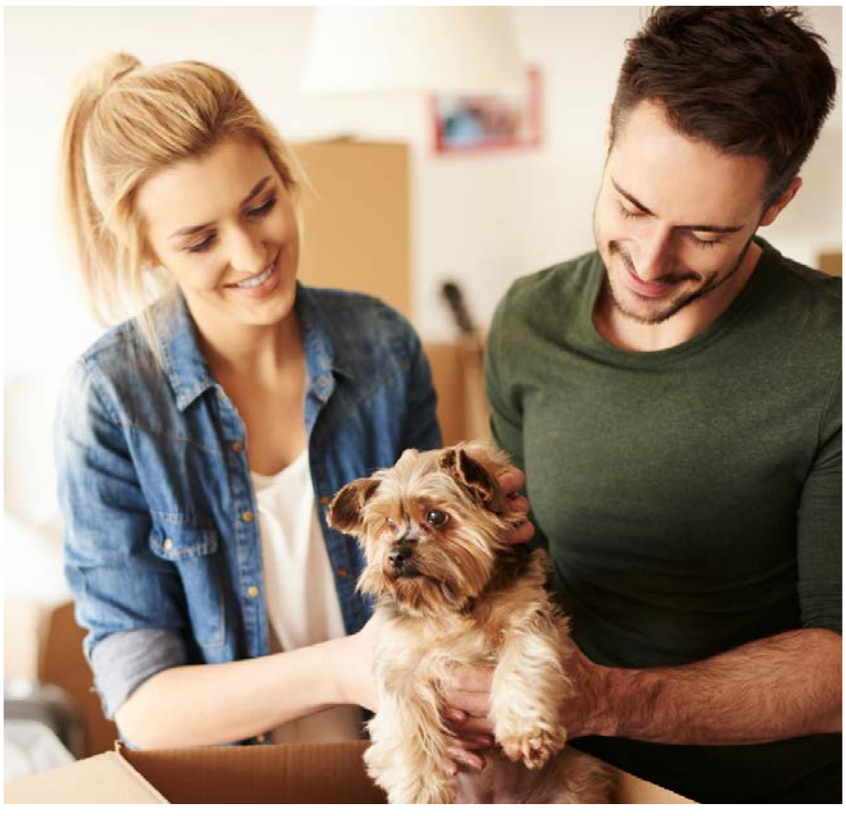
WHAT PET OWNERS THINK ABOUT CBD

CBD is not sought after only for human use; it has also become one of the leading ingredients in pet-care products. AmericanMarijuana.org surveyed 1,061 American pet owners of different ages and income levels to establish the dominant attitudes and observations of those who use CBD on their pets. This survey sought to determine who recommended that the participants use CBD for their pets and the users' main concerns about the use of CBD before they used it on their pets.

Major takeaways:

- 35% of participants said that their vets advised them to use CBD on their pets.
- Only 10% admitted that their vets doubted the efficacy of CBD for pets, while 24% were neutral on this topic.
- Half of participants said that their friends, family members, or recommended CBD for pets to them.

Read more by clicking on the link below:
CBD for Pets: 2020 Study of 1061 US CBD Consumers

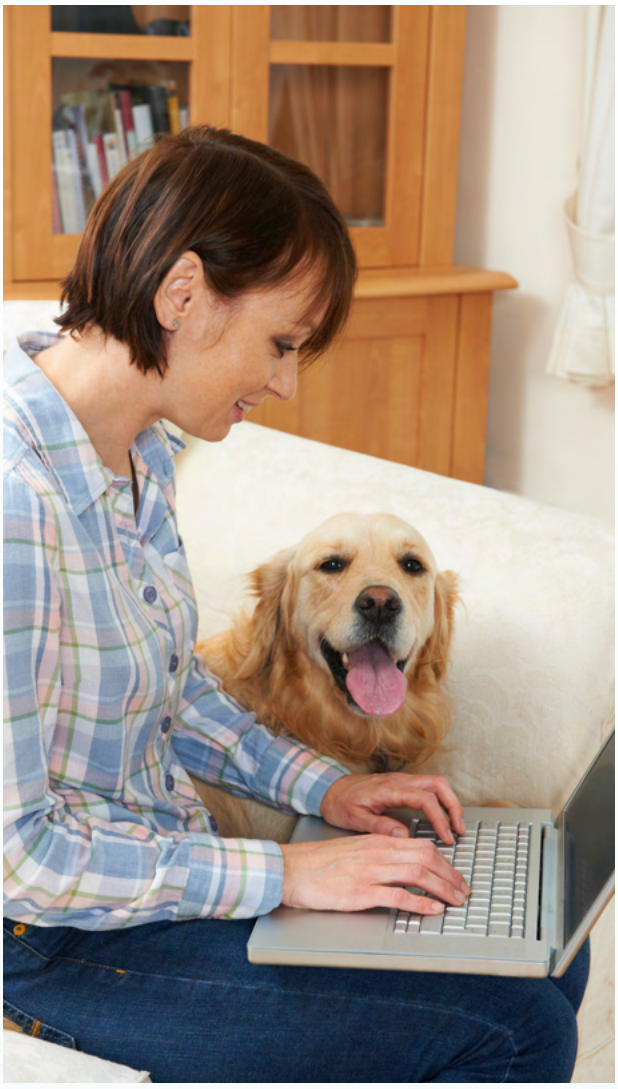


THE SCIENCE AND TRUTH OF CBD

A Veterinary Surgeon's Perspective

Dr. Courtney Campbell

It was about the third week into Bastion's recovery from his TPLO surgery, and he was already having a rough time. Bastion was a gregarious yellow Labrador who had injured his stifle about 25 days earlier. Fortunately, his family elected to have the stifle surgically reconstructed. Initially, he was recovering well from surgery, but one day in particular, he returned to the hospital because he had a brief setback. He was limping far more severely than would be normally expected at that



RESEARCHERS FIND CBD IMPROVES ARTHRITIS SYMPTOMS IN DOGS

RESEARCH CORNER

A team led by researchers at Baylor College of Medicine conducted the first scientific studies to assess the potential therapeutic effects of cannabidiol (CBD) for arthritic pain in dogs, and the results could lead the way to studying its effect in humans. Researchers focused first on these animals because their condition closely mimics the characteristics of human arthritis, the leading cause of pain and disability in the US for which there is no effective treatment.

The study first showed, both in laboratory tests and mouse models, that CBD can significantly reduce the production of inflammatory molecules and immune cells associated with arthritis. Subsequently, the study showed that in dogs diagnosed with the condition, CBD treatment significantly improved quality of life as documented by both owner and veterinarian assessments.

In the study, researchers first measured the effect of CBD on immune responses associated with arthritis, both in human and murine cells grown in the lab and in mouse models. They found that CBD treatment resulted in reduced production of both inflammatory molecules and immune cells linked to arthritis.

The 20 client-owned dogs enrolled in the study were randomly provided with identical unidentified medication bottles that contained CBD, liposomal CBD, or a placebo. Neither the owners nor the veterinarian knew which treatment each dog received.

After four weeks of daily treatment, owners and veterinarians reported on the condition of the dogs and whether they observed changes in the animals' level of pain, such as changes related to running or gait. The dogs' cell blood count and blood indicators of liver and kidney function were also evaluated before and after the four weeks of treatment.

stage of recovery. The osteotomy from his surgery had not yet completely healed, and he was still in the middle of his prescribed five weeks of strict exercise restriction. His family was trying their best, but Bastion wasn't having it. He was too active at home, and his humans were growing frustrated. They'd received anti-anxiety medications but weren't giving them. Instead, his family had decided to give him CBD oil at home. When I asked why, the client responded, "I found CBD oil at the local farmers' market, and I figured it would work just as well."

SINGLE-DOSE SAFETY ASSESSMENT OF CANNABIDIOL IN DOGS AND CATS

RESEARCH CORNER

A study evaluated the single-dose oral pharmacokinetics of cannabidiol and the safety profile of 12-week administration in healthy dogs and cats. Eight of each species were given a 2 mg/kg total CBD concentration orally twice daily for 12 weeks.

The study suggests that cats may absorb or eliminate cannabidiol differently than dogs, showing lower serum concentrations. Pharmacokinetics revealed a mean maximum concentration of 301 ng/mL and 43 ng/mL with time to maximal concentration of 1.4 hours and 2 hours for dogs and cats, respectively.

Serum chemistry and CBC results showed no significant findings in 15 animals. One cat showed a persistent rise in alanine aminotransferase (ALT) above the reference range for the duration of the trial. Cats in the study showed signs of excessive licking and head-shaking during administration.

Read full article by clicking on the link below:
Single-dose safety assessment of cannabidiol in dogs and cats

Like Bastion, an increasing number of pets are receiving cannabidiol (CBD) supplements. The popularity of CBD continues to rise, and many clients are incorporating it into the medication protocol for their pets, either as an adjunct or an alternative treatment option. Perhaps the initial interest in the benefits of CBD can be traced back to 1998, or possibly earlier, when scientists at the National Institutes of Health discovered that CBD could protect cells from oxidative stress. These findings fueled interest in the human medical field and, in large part, that appeal has been transmuted into veterinary medicine. The regard for this molecule has risen to such levels that, in many homes, CBD is being used as the sole treatment option for a variety of medical conditions.

PRELIMINARY CANNABINOID DOSE EFFICACY TESTING IN DOGS

RESEARCH CORNER

A study evaluated the safety and tolerability of escalating doses of three cannabis oil formulations, containing predominantly cannabidiol (CBD), tetrahydrocannabinol (THC), or CBD and THC (1.5:1) vs. placebo in dogs. Twenty healthy beagle dogs (10 males and 10 females) were used in this randomized, placebo-controlled, blind parallel study.

Dogs were randomly assigned to one of five treatment groups (2 males and 2 females per group): CBD-predominant oil, THC-predominant oil, CBD/THC-predominant oil (1.5:1), sunflower oil placebo, and medium-chain triglyceride (MCT) oil placebo.

Up to 10 escalating doses of the oils were planned for administration, with at least 3 days separating doses. Clinical observations, physical examinations, complete blood counts, clinical chemistry, and plasma cannabinoids were used to assess safety, tolerability, and the occurrence of adverse events which were rated as mild, moderate, or severe/medically significant.

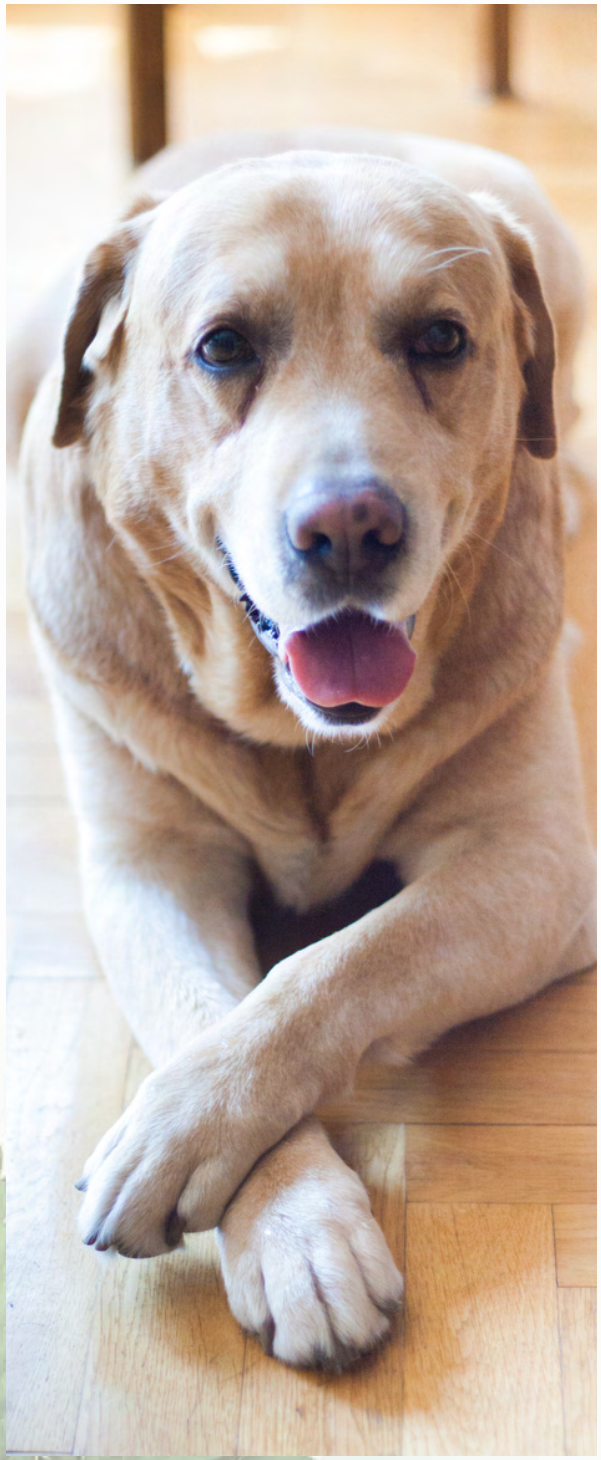
Dose escalation of the CBD-predominant oil formulation was shown to be as safe as a placebo.

Adverse events were reported in all dogs across the five groups, and the majority (94.9%) were mild. Moderate adverse events (4.4% of total) and severe/medically significant adverse events (0.8% of total) manifested as constitutional (lethargy, hypothermia) or neurological (ataxia) symptoms and mainly occurred across the two groups receiving oils containing THC (CBD/THC oil or THC oil).

Overall, dogs tolerated dose escalation of the cannabidiol oil well, experiencing only mild adverse events.

Read more on the full study here:
Preliminary cannabinoid dose efficacy testing in dogs

Veterinarians are becoming more fluent in the fascinating pharmacology regarding the use of this phytocannabinoid. A recent survey indicated that most veterinarians (61.5%) felt comfortable discussing the use of CBD with their colleagues, but only 45.5% felt comfortable discussing this topic with clients.[1] Furthermore, veterinarians and clients in states with legalized recreational marijuana were more likely to talk about the use of CBD products to treat canine ailments than those in other states.[2]



RESEARCH CORNER

PHARMACOKINETICS, SAFETY, AND EFFICACY OF CBD IN DOGS

Researchers evaluated the oral pharmacokinetics and assessed safety and efficacy of a cannabidiol (CBD) based oil in dogs with osteoarthritis (OA).

A clinical trial with client-owned dogs presenting for evaluation and treatment of a lameness due to OA was also performed. Sixteen dogs completed the trial.

The study was a randomized, placebo-controlled, owner and veterinarian double-blind cross-over trial. Dogs received each of two treatments in random order: CBD, 2 mg/kg every 12 hours, or placebo every 12 hours. Each treatment was administered for 4 weeks with a 2-week washout period between treatments. Blood was collected to repeat complete blood counts and chemistry analysis at weeks 2 and 4 for each treatment.

Pharmacokinetics revealed an elimination half-life of 4.2 hours at both doses. Clinically, the treated dogs showed a significant decrease in pain and increase in activity with CBD oil. Veterinary assessment showed decreased pain during CBD treatment.

No side effects were reported by owners, but serum chemistry showed an increase in alkaline phosphatase during CBD treatment.

The study suggests that a dose of 2 mg/kg of CBD twice daily can help increase comfort and activity in dogs with OA.

Read more by clicking on the link below:
Pharmacokinetics, Safety, and Clinical Efficacy of Cannabidiol Treatment in Osteoarthritic Dogs

Lastly, CBD was most frequently discussed as a potential treatment for pain management, anxiety, and seizures[1]. At first glance, the use of CBD has tangential or limited relevance in the world of veterinary surgery. However, as one takes a closer look at the putative—and proven—benefits, it is clear that we are just scratching the surface of its therapeutic benefits.

RESEARCH CORNER

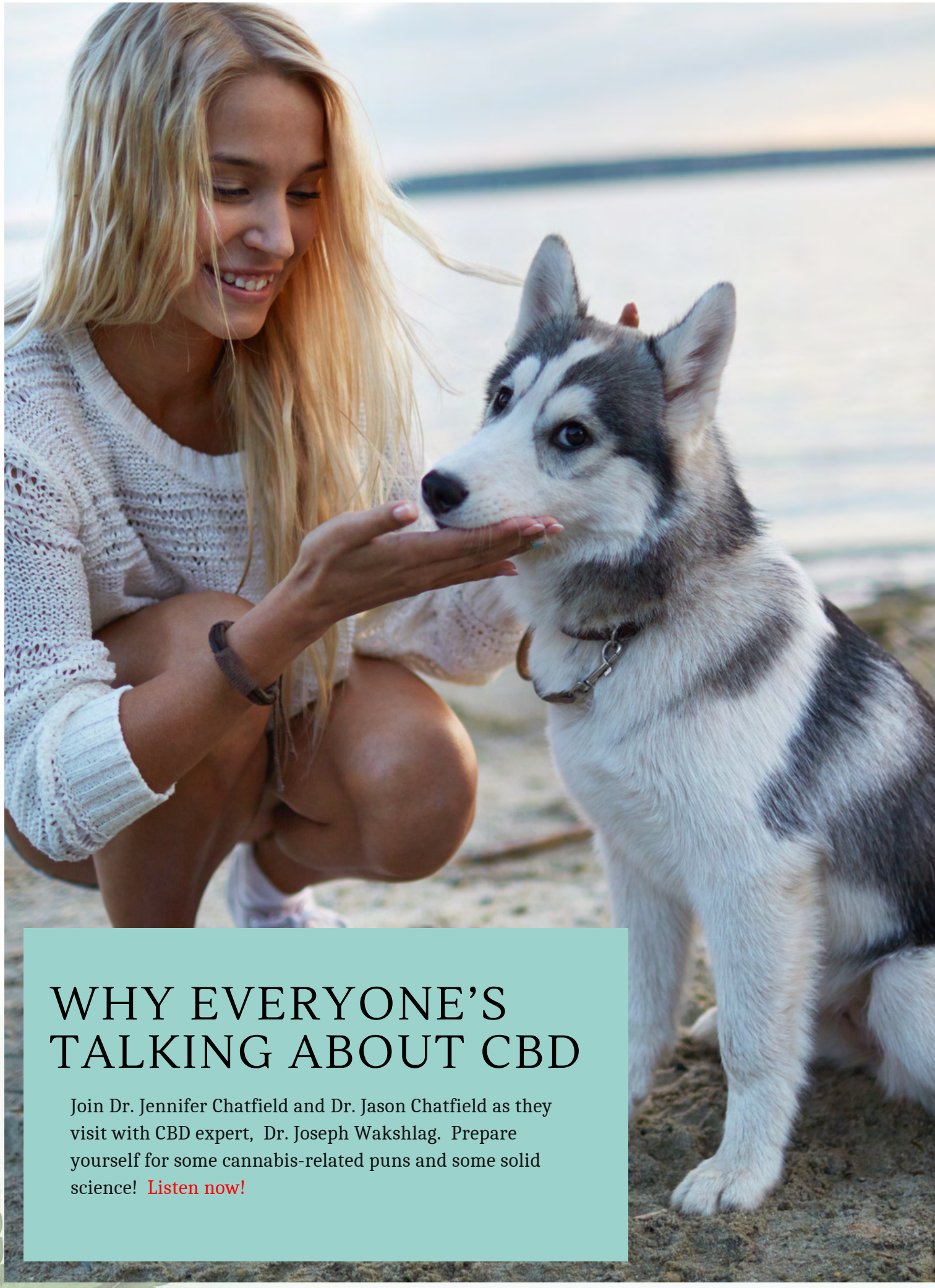
PHARMACOKINETICS OF CANNABIDIOL-INFUSED OIL IN HEALTHY CANINES

The purpose of this study was to determine the pharmacokinetics of cannabidiol (CBD) in healthy dogs. Thirty healthy research dogs were assigned to receive one of three formulations (oral microencapsulated oil beads, oral cannabidiol-infused oil, or cannabidiol-infused transdermal cream), at a dose of 75 mg or 150 mg every twelve hours for six weeks.

Serial cannabidiol blood plasma concentrations were measured over the first twelve hours and repeated at two weeks, four weeks, and six weeks. Higher systemic exposures were observed with the oral cannabidiol-infused oil formulation, and the half-life after a 75 mg and 150 mg dose was approximately 200 and 128 minutes, respectively.

Results from this study conclude that exposure is dose-proportional and that the oral cannabidiol-infused oil provides the most favorable pharmacokinetic profile.

Read the full article by clicking on the link below:
Effect of cannabidiol in healthy canines using 3 different methods

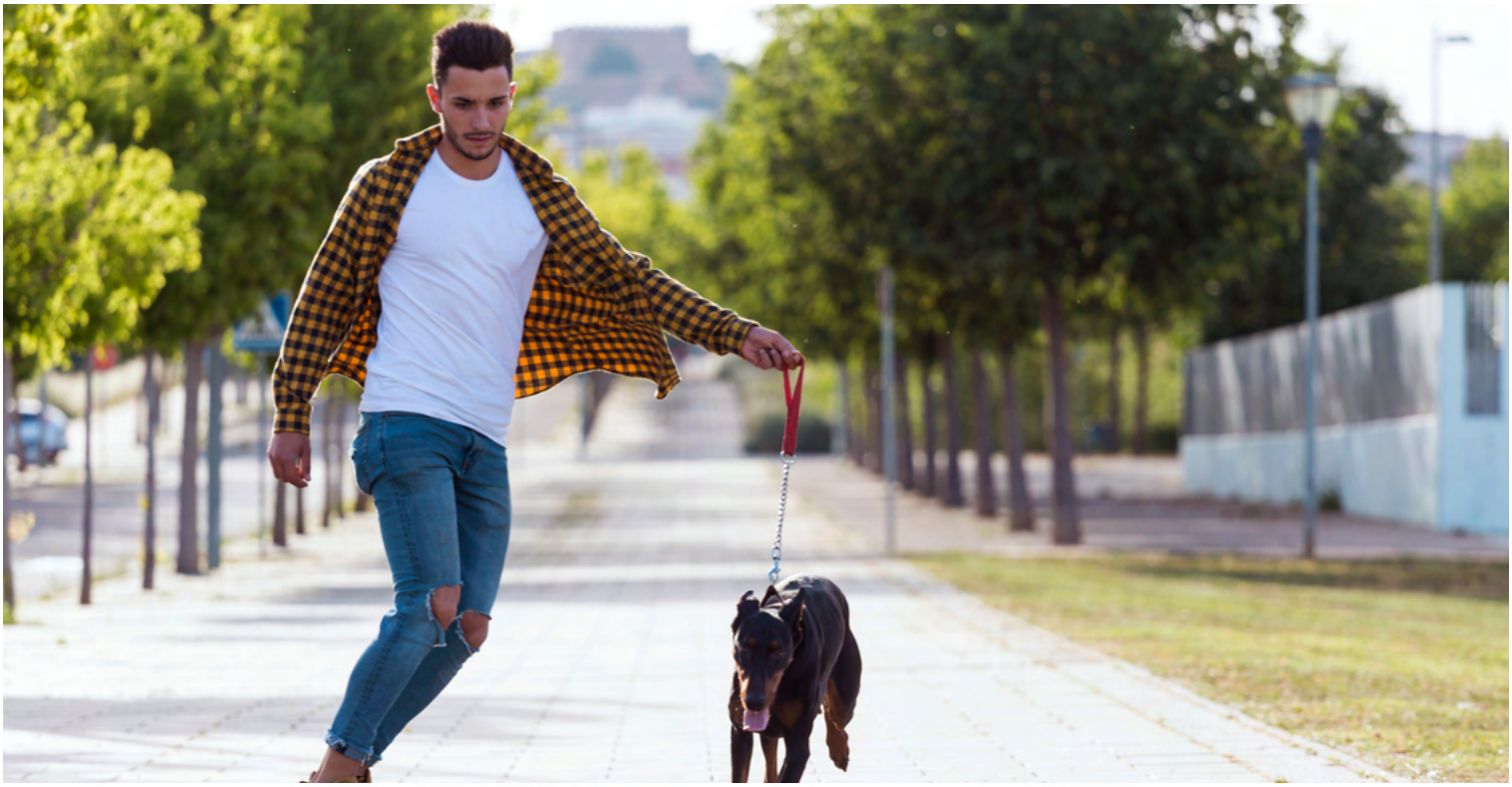


WHY EVERYONE'S TALKING ABOUT CBD

Join Dr. Jennifer Chatfield and Dr. Jason Chatfield as they visit with CBD expert, Dr. Joseph Wakshlag. Prepare yourself for some cannabis-related puns and some solid science! Listen now!

Let's take a brief dive.....

Pain



Whether you perform surgery within a specialty discipline (oncology, orthopedics, neurology, soft tissue surgery, mixed animal, oral/dental, etc.), or even if surgery is only a small part of your general practice, every veterinarian endeavors to manage pain aggressively. The first choice for pain relief among many clinicians are the medications that have been more extensively studied, including but not limited to anti-inflammatories, gabapentinoids, opioids, local anesthetics, and other analgesics (acetaminophen, amantadine, maropitant citrate, etc.).

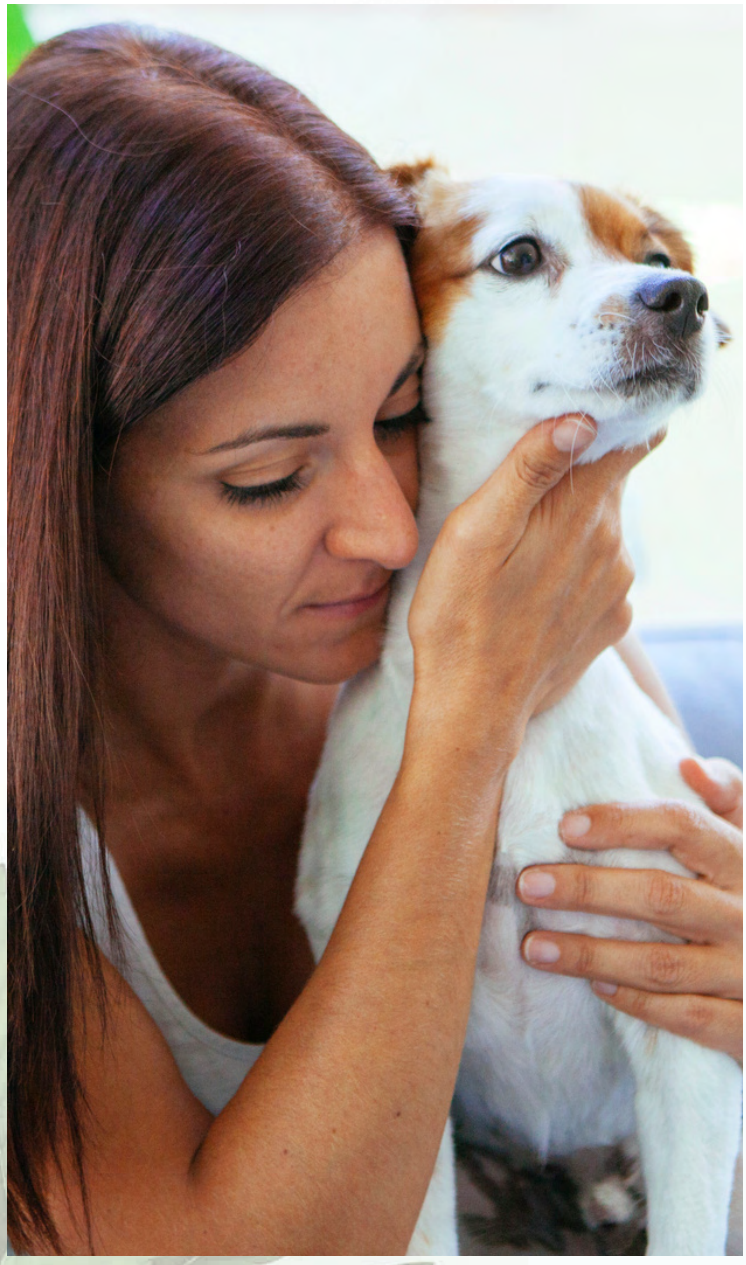
These medications or a combination thereof have been prescribed to treat pain from orthopedic surgery, soft tissue surgery, intestinal surgery, and surgical neuropathic conditions, to name just a few. In the most basic schema, pain is divided into four categories: nociceptive pain (a response to damaged tissue), neuropathic pain (a response to directly-damaged sensory or spinal nerves), centralized pain (the result of pain signals[1] being improperly amplified), and inflammatory pain.

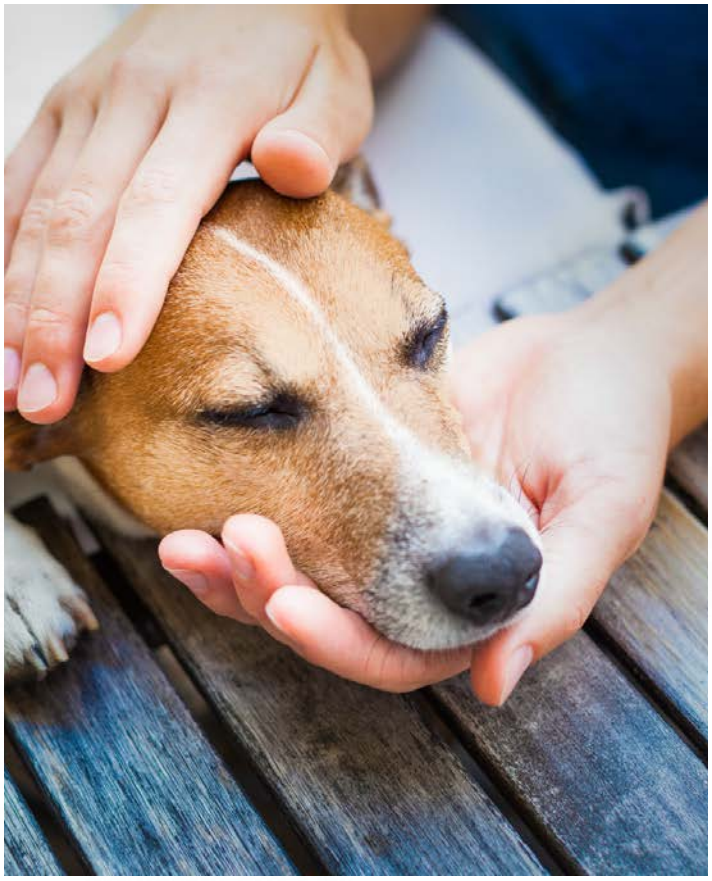
Cannabinoids may have a role to play in mediating all four of these types of pain states. When tissue is damaged, histamine, serotonin, TNF-alpha, IL-1-beta, IL-6 and Il -17 6, and interleukin 17 are released.[2] Cannabinoids bind to the CB1 receptors and attenuate the pain signal by slowing down the release of those neurotransmitters.[3]

This process can take place locally or in the central nervous system.[3] Cannabinoids have also been shown to inhibit the release of GABA, a well-known neurotransmitter associated with pain.[3] Although there is a paucity of clinical research on the use of CBD to treat postoperative pain in the veterinary medical setting, there has been heartening research conducted in humans. Indeed, the National Academies of Sciences, Engineering, and Medicine concluded that there is "substantial evidence that cannabis is an effective treatment for chronic pain in adults."

Opioids have long been the go-to option or cornerstone of pain management, but the potential for the adverse events associated with the use of opioids in veterinary patients is universally accepted.[38] I have seen how distressing it can be for a family to see their pet experiencing any of the unpleasurable side effects of opioids, including urine retention, delayed bowel movements, whining, panting, disorientation, or other manifestations of dysphoria. Those are just some of the challenges that clinicians face when using opioids for chronic pain management.

Considering the ongoing consequences of the opioid epidemic, there is a search for pain management solutions that are innovative, prone to less adverse events, and are more effective. As the scientific community begins to evaluate the evidence for use of CBD, it is clear that more research is needed.





Anecdotal reports of CBD's efficacy as a pain reliever are ubiquitous, but more practitioners are turning to scientific data for evidence of CBD's efficacy. A study in 2020 evaluating effects of CBD hemp extract on opioid use and quality-of-life indicators in chronic pain patients found that over half of chronic pain patients (53%) reduced or eliminated their opioids within eight weeks after adding CBD-rich hemp extract to their regimens.[5] Almost all CBD users (94%) reported quality-of-life improvements.[5] A recent study evaluating orally consumed cannabinoids for long-lasting relief of allodynia in a mouse model found that cannabinoids reduced hyperalgesia, and a similar effect was not found with morphine.[4] Mouse vocalizations were recorded throughout the experiment, and mice showed a large increase in ultrasonic, broadband clicks after sciatic nerve injury, which was reversed by THC, CBD, and morphine.[4] The study demonstrated that cannabinoids provide long-term relief of chronic pain states.[4] If research shows that use of cannabinoids in animals—specifically, CBD—can help to decrease the use of opioids for pain management, that would help make more animals comfortable and potentially help to fight the tragic epidemic of human prescription opioid abuse. Further research is needed in a variety of species, specifically, both the canine and feline species.

Bone Healing

Both general veterinary practitioners and veterinary surgeons commonly diagnose and treat fractures. No large retrospective study of fracture incidence in dogs in North America has been published since 1994; however, the findings from that year's study are still informative regarding the frequency of bone injuries. The study demonstrated that approximately 24% of all patients in the population studied over a 10-year period were affected by a disorder of the musculoskeletal system, with fractures contributing the largest proportion (over 29%) of all of the diagnoses of the appendicular skeletal system.[7]

Although that research is dated, the conclusions from this study, at the very least, indicate that fractures are commonplace in the clinical veterinary setting.[7] Fracture repair has gradually become more straightforward due to improvements in technology. Because of these innovations, specialty surgeons and general practitioners who repair fractures have begun to see better surgical outcomes. So whether you primarily stabilize fractures with implants, or if external coaptation of fractures with the intention to refer (or perhaps as the primary means of fixation) is your treatment of choice, all veterinary practitioners aim to help fractured bones heal quickly.

Despite these technological improvements, bone healing can be protracted or non-existent with some fractures. There are a variety of options at a veterinarian's disposal to kick-start the healing process, but perhaps in the near future, CBD may be added to that armamentarium. The effect of CBD in fracture healing has been investigated evaluating bone callus formation in femur fractures in a rat model.[8] The findings demonstrated enhanced biomechanical properties of healing fractures in those given CBD compared with a control group.[8] This effect was not found in those given only Δ9-THC.

Moreover, the bone-forming (osteogenic) effects of CBD were weakened when test subjects were given equal amounts of CBD and Δ9-THC.[6] Another in vivo research study indicated that when CBD is incorporated into a surface that promotes bone growth (osteoconductive scaffold) it can stimulate stem cell migration and osteogenic differentiation.[9] Further studies are needed to better evaluate the role of CBD in healing and bone metabolism of companion animals so that these findings can be applied in the clinical setting.

Additionally, cannabis has been shown to be a useful addition in treatment plans to improve bone health in laboratory studies. Studies have endeavored to better understand the role of CB2 receptors in maintaining bone health. CB2 receptors in bone cells have been linked to maintaining bone density and stimulating growth and may therefore have a part in reversing the effects of osteoporosis. One study evaluating the role of CB2 receptors found CB2 receptors found that mice whose genes had been altered to remove the CB1 or CB2 receptors developed signs of bone weakness that were far more pronounced than those in the control group.[12] Another study in 2009 investigated the relationship between CB2 expression and bone disease in humans. It found that people with dysfunctional CB2 receptors have significantly weaker hand bones.

Arthritis

Osteoarthritis (OA) affects many dogs, large and small. Most often, OA is the consequence of a developmental orthopedic disease that affects a single joint or a pair of joints and, less often, affects multiple joints. It is axiomatic that "Mother Nature likes symmetry," thus developmental orthopedic diseases frequently affect both left and right joints. For example, hip dysplasia is reportedly bilateral in >60% of affected dogs,[13] and elbow dysplasia is bilateral in approximately 50% of affected dogs.[14] Osteoarthritis occurs secondary to a myriad of primary orthopedic conditions that affect a variety of joints including: the hip (most common causes of OA in the hip: hip dysplasia, Perthes disease); stifle (patellar luxation, cranial cruciate ligament disease, osteochondritis dissecans [OCD]); elbow (elbow dysplasia, elbow OCD, fragmentation of the medial coronoid process, incomplete ossification of the humeral condyle); shoulder (shoulder OCD, developmental shoulder subluxation); tarsus (OCD of the talus), and carpus (carpal laxity, carpal subluxation secondary to chondrodystrophy); and metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joint degenerative osteoarthritis (digital osteoarthritis).

Cannabinoids were found to treat pain secondary to inflammation in a variety of studies on humans. Some of the most compelling research has shown that cannabis can reduce the inflammation in the joint caused in human patients diagnosed with immune-mediated arthritis.[15] One study found that cannabinoids could simultaneously reduce the secretion of cytokines involved in inflammation from one type of T immune cells, which were being under-produced, while also increasing their numbers to correct their scarcity.[15]

Furthermore, in a study in 2003, researchers found that plant-based cannabinoids could suppress the expression of interleukin-1beta—one of the most prominent markers for inflammation in patients with rheumatoid arthritis—by as much as 50%.[16] And finally, in 2006, transdermal applications of CBD were shown to decrease biomarkers that can contribute to neurogenic inflammation in a sample of arthritic rats."

A report published in The Journal of PAIN and written by researchers at Baylor College of Medicine revealed the results of a large, double-blinded, placebo-controlled study on the positive effects CBD had in the fight against osteoarthritis.[18] The study was designed with two main goals: The first portion of the research studied the effect CBD had on the inflammatory molecules and cells in mice.[18] The second portion of the study investigated whether CBD improved the quality of life in dogs diagnosed with osteoarthritis.

In lab tests and in mouse models, CBD significantly decreased the production of natural chemicals that promote inflammation, and it increased the natural chemicals that fight inflammation.[18] Essentially, they saw a drop in proinflammatory cytokines and an increase in anti-inflammatory cytokines.[18] For dogs with osteoarthritis, CBD significantly decreased pain and increased mobility in a dose-dependent fashion. Importantly, a lower dose of liposomal CBD was as effective as the highest dose of non-liposomal CBD, indicating that the effect of CBD was quicker and more powerful when CBD was delivered encapsulated in liposomes than without.[18] Blood samples indicated no significant harmful side effects or adverse events over the 4-week analysis period.[18]

In the veterinary population, use of cannabidiol and other alternative treatments has the potential to obviate the need for other medications and thus spare patients from adverse effects associated with their use. More likely, the use of cannabinoids could be additive or synergistic in a multimodal treatment strategy and could increase quality-of-life issues associated with painful arthritic conditions.

Intervertebral Disk Disease

As our patients age, discs in their spines undergo degenerative changes. Thus, degeneration of intervertebral discs is inevitable. This process of degeneration is multifactorial, and it involves hypoxia, inflammation, neoinnervation, accelerated catabolism, and reduction in water and glycosaminoglycan content.[39] The magnitude and severity of disc degeneration can vary widely between patients. The most common locations of clinically relevant disc disease are the cervical spine, thoracolumbar spine, and lumbosacral spine.[40]

Although there are various manifestations of disc disease, broad classifications of Hansen Type I and Type II are typically used to describe the condition. In short, disc material may either extrude (acute herniations) or protrude (chronic herniations), both of which compress the spinal cord, which can ultimately cause pain, paresis, paralysis, and other neurological deficits.[40] The prevalence of thoracolumbar disc disease in dogs has been estimated at 3.5%.[40] Depending on the neurologic examination, diagnosis, severity, prognosis, and other factors, surgery may be recommended to decompress the spinal cord. After surgical decompression, there is a host of challenges that the patient, the family, and the surgeon may have to work through, including a potentially protracted recovery, recurrence of neurological signs, post-surgical pain, spinal instability, urinary disorders, (cystitis, urinary tract infection, urinary retention, micturition disorders), ascending myelomalacia, and others.[41] Could CBD play a part in helping to improve those affected by disc disease pre-, intra-, or post-operatively, and what types of spinal disorders could benefit from CBD?

A study conducted on the use of CBD in mice with degenerative disc disease showed promise in mitigating the effect of disc damage and wear.[19] Instead of being ingested orally, CBD was injected at the site of the disc. Researchers investigated the effects of cannabidiol intradiscal injection using a combination of MRI and histological analyses.[19] A puncture was created in the disc, and then CBD was injected into the disc (30, 60 or 120 nmol) shortly after.[19] The effects of intradiscal injection of cannabidiol were analyzed within 2 days by MRI.[17] Fifteen days later, the group that received cannabidiol 120 nmol was resubmitted to MRI examination and then to histological analyses after the cannabidiol injection.[19] They found that cannabidiol significantly decreased the effects of disc injury induced by the needle puncture.[19] These results suggest that this compound could be useful in the treatment of intervertebral disc degeneration, perhaps using a novel route of administration. Unfortunately, the exact mechanism for how CBD oil helped alleviate disc damage is still being investigated. The hope is that the neuroprotective properties of cannabidiol can also be found in the study of canine and feline disc disease to ultimately improve functional recovery.

Neuropathic Pain

Fortunately, more effort, research, and attention is being paid to treating pain in veterinary medicine. Nociceptive pain is caused by external pressure, cold, heat, or internal trauma, stimulated by the release of compounds like bradykinin, prostaglandins, or leukotrienes.[20] Humans may describe this pain as a sharp, aching, or throbbing sensation. In veterinary patients, nociceptive pain may be manifested by limping, sharp movements, lip smacking, panting, vocalization, or, in select cases, no obvious response. The function of nociceptive pain in humans, and presumably in pets, is to alert them that they are injured and hopefully prevent further injury.[20]

Neuropathic pain, caused by direct damage to sensory or spinal nerves, allows aberrant pain signals to be sent to the brain.[21] In veterinary patients, a common example of neuropathic pain that I diagnose commonly is sciatic or radial nerve hyperpathia, but lumbar or cervical foraminal radiculopathies can also be relatively frequent causes of neuropathic pain.[21] Neuropathic pain syndromes are often secondary to intervertebral disc disease, static and dynamic nerve foramen impingement, vertebral instability, recent surgery, trauma, abnormal conformation, abnormal gait, and chronic joint pain. A classic example of neuropathic pain in humans is diabetic neuropathy.

Unfortunately, there are some challenges to diagnosing and understanding neuropathic pain in the veterinary setting, particularly in the presence of an otherwise normal orthopedic exam. To be sure, neuropathic pain can be evoked by low- or high-intensity stimuli; it can be spontaneous and not stimulus-dependent; it is maladaptive (maintained in the absence of tissue trauma), and it responds poorly to opiates and anti-inflammatory drugs.[21]

CBD use has shown promise in the treatment of neuropathic pain. In a 2010 study, researchers looked at a sample of diabetic rats and administered daily doses of Cannabis sativa ranging from 25 to 100 mg/kg of body weight.[22] After fourteen days, the rats exhibited significant reductions in tingling, heat, and pain in the extremities associated with advanced diabetes.[22] Another study, from 2015, compared descriptions of spontaneous pain among sixteen patients with painful diabetic peripheral neuropathy in a randomized, double-blinded setting.[23] The study subjects were administered four single-dosing sessions of placebo or cannabis. Significant reduction in pain intensity varied directly with the size of their dose.[23]

As we begin to understand neuropathic pain in animals more clearly, treatment strategies and pharmaceutical alternatives will more adequately address their pain, possibly including the use of CBD or CBD alternatives. Additional research will hopefully actualize the promise and potential that CBD may have in treating the veterinary population in neuropathic pain.

Anxiety

Exercise restriction is a critical component for successful surgical outcomes in many elective orthopedic surgeries. For example, post dynamic stifle stabilization surgery, I frequently recommend a minimum of five to eight weeks of strict monitoring and exercise restriction. This recommendation can be extremely challenging for families, because many of the animals are inclined to be active, are frequently powerful and athletic, and are young and unaccustomed to confinement. Implant failure or a poor surgical outcome overall can many times be ascribed to the challenges related to activity restriction. Difficulties with this process may lead to protracted recovery or even surgical treatment failure, necessitating a second surgical procedure.

Common pharmaceutical strategies employed to help with exercise restriction include the use of Trazodone and Acepromazine.[24] However, both of these medications can have variable effects depending on the individual, and in some cases, there are undesirable adverse effects (e.g. excessive sedation and paradoxical excitation with Acepromazine, serotonin syndrome with Trazodone, etc.).[24]

Could CBD or CBD derivatives enhance calmness and alleviate anxiety in animals? Based on CBD's proposed mechanism of action in mitigating anxiety, the answer may be encouraging. Higher levels of natural endocannabinoids in the human body are associated with an antidepressant effect.[25] Cannabinoid receptors are found throughout the central nervous system and play a key part in maintaining our sense of well-being. They are particularly numerous in cells tasked with manufacturing serotonin where it is needed.[25]

Cannabidiol may also have an effect on the hippocampus, which is a region of the brain responsible for memory and mood. Glucocorticoids are secreted during stress, which may cause the hippocampus to atrophy.[26] That shrinking process plays a role in diminished memory and depressed mood.[26] Cannabinoids have shown an ability to counter this process through the phenomenon of hippocampal neurogenesis (regrowth and development in nerve tissue), which can be activated by the expression of cannabinoid type-1 receptors.[26] Both natural endocannabinoids and plant-based cannabinoids have both been shown to accelerate this process.[26]

In another random-controlled trial performed on humans, subjects receiving a 600 mg CBD supplement also reported less subjective anxiety symptoms during public speaking than those who'd taken a placebo.[27] CBD also shows activity specific to the limbic system in the brain. A study evaluating that effect on the limbic system found that CBD administration helped to reduce symptoms in people with social anxiety disorder.[28] Indeed, the National Academies of Sciences, Engineering, and Medicine specifically referenced CBD's effects in a statement about anxiety disorders, "... there is evidence that cannabidiol is an effective treatment for the improvement of anxiety symptoms, as assessed by a public speaking test in individuals with social anxiety disorders."[30]

A 2019 study in mice simulated to have an anxiety disorder, (Fragile X Syndrome—a neurodevelopmental disorder that affects intellectual, social, and physical development due to a mutation of the FMR1 gene) were shown to have fewer anxiety-related behaviors across tests when given CBD.[31] Furthermore, CBD decreased the anxiety response of all mice tested while not affecting their cognitive performance.[31]

The potential for CBD to be efficacious in treating anxiety in other species will be important to study, but its use as an anxiolytic and sedative is growing in popularity despite the paucity of research specific to this indication. As previously mentioned, anxiety was one of the most common reasons for veterinarians to discuss CBD.[1] The most commonly used CBD formulations were oil/extract and edibles for the putative benefits of relieving anxiety, among others. As CBD[1] research continues to gain steam, more attention will hopefully be directed towards how the full ensemble of cannabinoids, terpenes, and flavonoids seem to complement each other, working through multiple receptors at once, and often enhancing each other's signals to the body.

Wound Healing

When it comes to wounds, all medical professionals are generally united in a common purpose: we want wounds to heal faster. Indeed, products that promote or accelerate wound healing have been of interest to veterinarians and physicians since the advent of wound treatment. Wound healing products and topical agents may target different phases of wound healing, including debridement, wound contraction, epithelialization, and granulation. Many products promote the formation of granulation tissue, while others are more effective after granulation tissue has formed (e.g. hyaluronic acid). For this reason, adapting the topical dressing specific to the stage and progress of wound healing is of utmost importance.

CBD has shown efficacy in the maturation phase of wound healing and some inflammatory skin conditions.[33] In a 2019 study of 20 patients with two most frequent skin disorders—psoriasis (5 patients), atopic dermatitis (5), and resulting outcome scars (10)—the subjects were instructed to administer topical CBD-enriched ointment to lesioned skin areas twice daily for three months.[33] The results showed that topical treatment with CBD-enriched ointment significantly improved the skin parameters and the symptoms associated with the skin condition.[33] This study concluded that the topical administration of CBD ointment, without any THC, is a safe, effective, and non-invasive alternative for improving the quality of life in patients with some skin disorders, especially inflammatory ones.[33] Another study in 2019 investigated the potential effect of a Cannabis sativa L. ethanolic extract standardized in cannabidiol as anti-inflammatory agent in the skin.[34] The study found that the extract inhibited the release of mediators of inflammation involved in wound healing and inflammatory processes occurring in the skin.[34] The down-regulation of genes involved in wound healing and skin inflammation was at least in part due to the presence of cannabidiol.[34] The findings provided new insights into the potential effect of Cannabis extracts against inflammation-based skin diseases.

Bacterial infiltration can negatively influence wound healing. Another area in which topical cannabis treatments show a great deal of potential is in the treatment of bacteria-related skin disorders. One study from 1976 indicated that isolates of THC and CBD were effective in reducing samples of staphylococci and streptococci, two bacteria associated with acne.[35] Another study from 2008 found that the plant-based CBD, CBC, CBG, THC, and CBN were substantially potent against a variety of Staphylococcus aureus strains, which were resistant to the antibiotic methicillin (MRSA).[36]

However, a recent study perhaps underscores the importance of adjusting topical therapy according to the stage of healing. In 2020, the Australian Veterinary Journal reported a study on horses with wounds that were created in a laboratory setting and then deliberately contaminated. Each wound was assigned to a treatment group that contained 1% cannabidiol in three different manuka honey formulations.[37] Treatments were applied topically daily for a total of 42 days. The results indicated that irrespective of the treatment, wounds did not retract as expected in the first seven days after wound creation.[37] There was no difference in wound area, daily healing rate, or days to complete healing between treatment groups.[37] This study highlights the importance for continued study on the correct time, concentration, and best practices when using CBD to accelerate wound healing.

CONCLUSION

Though the overall potential for cannabidiol to address specific surgical conditions is encouraging, strong double-blinded, placebo-controlled studies with large sample sizes are lacking. Based on the research that's available in animal models and among human patients, there are large pockets of convincing research that inspire hope and promise in the use of CBD in veterinary surgery and veterinary medicine writ large. To be sure, the concept of scientific integrative medicine should be considered along with other first-line treatments for veterinary patients. Evidence-based solutions should be prioritized when treating disease, but innovative or novel treatments may have to be considered in patients with neuropathic pain, disc disease, anxiety, or debilitating arthritis. New discoveries in the world of cannabis-based medicine may be just what the doctor ordered for an effervescent Labrador like Bastion.

CONTINUING EDUCATION INFORMATION

This program 1487-43959 is approved by the AAVSB RACE to offer a total of 2.0 CE Credits, with a maximum of 2.0 CE Credits being available to any individual veterinarian or veterinary technician/technologist. This RACE approval is for the subject matter categories of medical and non medical using the delivery method of lecture/seminar .This approval is valid in jurisdictions which recognize AAVSB RACE; however, participants are responsible for ascertaining each board's CE requirements. This program is also approved in the State of New York for 2.0 CE Credits.

The American Association of Veterinary State Boards RACE committee has reviewed and approved the program referenced above as meeting the Standards adopted by the AAVSB.

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