VETERINARY CARE BASED ON THE USE OF MEDICAL CANNABIS SPP.

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ABSTRACT

Phytotherapy has been present in the daily life of humanity since the dawn of humanity, with several species of medicinal plants that are used for various purposes. However, phytotherapy aimed at veterinary medicine is still little explored, whose basis for treatments is often the transfer of knowledge applied to humans to animals. Plants of the Cannabis genus are known for the richness of cannabinoid compounds, which for some years have been explored for their therapeutic and medicinal properties. The use of Cannabis in

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treatment for animals is an extremely recent subject, in view of the controversial public opinion about plants of this genus. However, studies have revealed specific receptors for cannabinoid compounds in various animal groups, from small invertebrates to large mammals, suggesting that the therapeutic use of Cannabis can be applied to veterinary treatments. The most striking compounds cited in studies focused on cannabis treatments are Cannabidiol (CBD) and Tetrahydrocannabinol (THC), however more than 100 cannabinoid compounds are present that interact with brain receptors and can be explored in research, such as Cannabinol and Cannabigerol. Such receptors are found mainly in the central nervous system in vertebrates and are related to the regulation and maintenance of homeostasis. This chapter discusses the chemical composition, as well as the extraction and purification processes, interaction of cannabinoid compounds with endogenous CNS receptors and cannabis-based pharmaceutical formulations, seeking to contribute with a collection of current information on the use of this controversial plant in herbal treatments for veterinary use.

Keywords: Veterinary medicine. Veterinary treatment. Phytotherapy. Cannabinoids. CNS.

INTRODUCTION

The term phytotherapy is given to the therapy that uses active constituents derived from plants, or the plant itself, which originated in popular knowledge. Phytotherapy in human medicine is currently very widespread, with reports and descriptions of the use of medicinal plants since 200 BC (RODRIGUES; AMARAL, 2012). However, phytotherapy in veterinary treatments is still poorly described and, in general, the substances that are already commonly used in humans are directed to use in animals, without major research specifically focused on veterinary pharmacology (VIDAL; ANGELI, VICTÓRIO, 2023).

The plants commonly known as marijuana of the Cannabis genus, in 2017, were included as a medicinal plant in the list of Brazilian Common Denominations (DCB) through the collegiate board resolution - RDC No. 156, of May 5, 2017. This measure did not change the laws aimed at prohibiting the plant in the country, although it recognizes its medicinal value (LIMA; ALEXANDER; SANTOS, 2021). The active compounds of *Cannabis* are called endocannabinoids and bind to a specific endogenous cell signaling network that is present in various animal groups, from mammals to some invertebrate animals, such as the seahorse and mussel (ELIAM, 2022). Such compounds are membrane phospholipids that bind to the cannabinoid receptors CB1 and CB2, and are related to the regulation and maintenance of homeostasis (SANTOS, 2020; ELIAM, 2022).

Of the endocannabinoid receptors, CB1 is the most abundant, it is found mainly in the central nervous system (CNS), basal ganglia, cerebral cortex, hippocampus, cerebellum, and hypothalamus. CB2 is most commonly found in cells of the immune system (ASCENÇÃO; LESTER; SILVA, 2016). Much of the use of endocannabinoids is used to control pain in diseases such as multiple sclerosis and oncological and neuropathic pain (LIMA; ALEXANDER; SANTOS, 2021). This chapter discusses, through the bibliographic review of the medicinal use of *Cannabis*, the possibilities of using this controversial plant in veterinary treatments.

Figure 1 - Specimen of *Cannabis sativa* showing female flowering.

Cast Iron: WAITE (2022).

CHEMICAL COMPOSITION OF CANNABIS

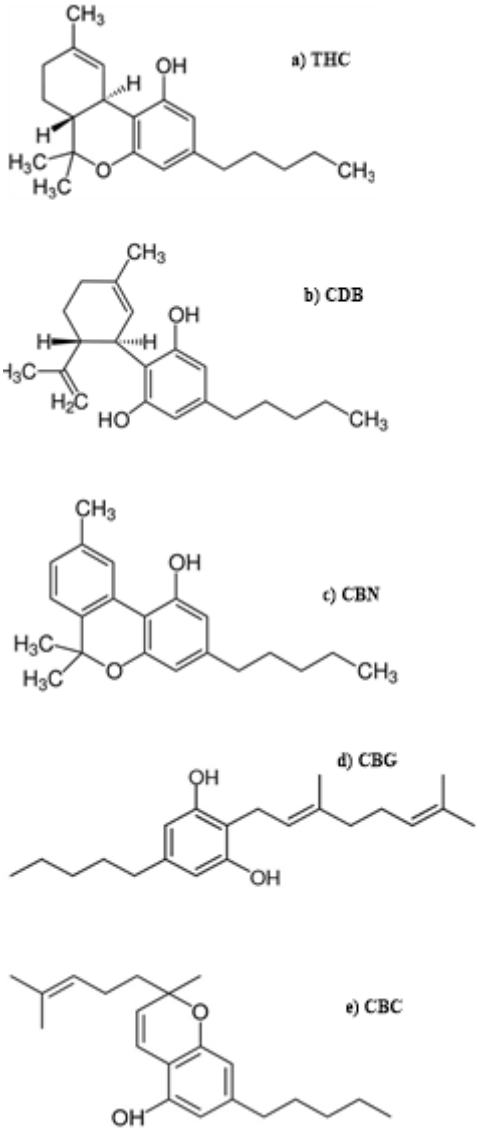
The chemical composition of cannabis is marked by the presence of more than 500 identified compounds, of which more than 100 are cannabinoids (SALAMI *et al*., 2020). The main cannabinoids include Tetrahydrocannabinol (THC), responsible for the psychoactive effects of the plant, such as euphoria and perceptual changes, and Cannabidiol (CBD), known for its therapeutic properties, such as anti-inflammatory, analgesic, anxiolytic, and neuroprotective action (HARTSEL *et al*., 2019). In addition to these, Cannabinol (CBN), Cannabigerol (CBG) and Cannabichromene (CBC) have also been the subject of study due to their therapeutic potential, which range from sedative properties to anti-inflammatory and neuroprotective effects (DELLA ROCCA; DI SALVO, 2020; RIOS *et al*., 2020; SILVA *et al*., 2024; LYONS *et al*., 2024).

In addition to these main compounds, cannabis produces a myriad of other phytocannabinoids, such as Cannabigerol (CBG), Cannabichromene (CBC), and Cannabinol (CBN), each with its own therapeutic potential, ranging from anti-inflammatory properties to sedative and analgesic effects (SCHOFS; SPARO; SÁNCHEZ BRUNI, 2021). The biosynthesis of these phytocannabinoids occurs in the glandular trichomes of the plant, where metabolic precursors such as olivetolic acid are converted by specific enzymes into acidic forms, such as THCA and CBDA, which are later decarboxylated to form the active cannabinoids THC, CBD, and CBC (HARTSEL *et al*., 2019; VASTOLO, *et al*., 2021; ALVES; FETTBACK, 2024). The interaction of cannabinoids with the cannabinoid receptors CB1 and CB2 in the human body plays a crucial role in mediating their therapeutic and psychoactive effects (SALAMI *et al*., 2020; MIRANDA-CORTÉS *et al*., 2023). While CB1 receptors are predominantly located in the central nervous system, modulating functions such as neurotransmission, pain, and memory, CB2 receptors are found primarily in the immune system, influencing inflammatory and immune responses (BRUTLAG; HOMMERDING, 2018; SCHOFS; SPARO; SÁNCHEZ BRUNI, 2021; FLORIO *et al*., 2023).

Cannabinoid biosynthesis occurs in the plant's resin glands, where metabolic precursors such as olivetolic acid and geranyl pyrophosphate are converted into acidic cannabinoids, such as THCA and CBD (GROF, 2018; ANDERSON *et al*., 2022). These compounds are subsequently activated by heat (decarboxylation) to form active cannabinoids, such as THC and CBD, which interact with the receptors of the animals' endocannabinoid system (BOOTH; PAGE; BOHLMANN, 2017; ERŽEN *et al*., 2021). Terpenes, if aromatic compounds found in cannabis, play a role not only by imparting to the plant its characteristic aroma but also by contributing to its therapeutic effects (SOMMANO *et al*., 2020). Terpenes such as myrcene, limonene, pinene, linalool, and caryophyllene

have sedative, analgesic, anxiolytic, anti-inflammatory, and even antibacterial properties, complementing the effects of cannabinoids through the so-called "*entourage effect*", where the interaction between different compounds enhances their therapeutic benefits (HANUŠ; HOD, 2020; DUGGAN, 2021; ISIDORE; KARIM; IOANNOU, 2021).

Figure 2 - Structural Formulas of the main cannabinoids of Cannabis spp. a) Tetrahydrocannabinol, b) Cannabidiol, c) Cannabinol, d) Cannabigerol and e) Cannabichromene.



Source: The Authors (2024).

CANNABINOID EXTRACTION AND PURIFICATION

EXTRACTION METHODS

The pharmaceutical industry maintains a specific niche in the market by valuing the production of isolated active ingredients, including in products based on *Cannabis* spp. This involves not only advanced extraction methods, but also refined techniques for separating and purifying compounds. This type of approach seeks to optimize yield without

compromising the quality of the final products, ensuring consistency in formulations and meeting therapeutic requirements with precision and efficacy (MAJOR; FERRISI, 2024).

Extraction technology using supercritical CO2 emerges as a promising alternative to mitigate the use of organic solvents in the selective extraction of cannabinoids and essential oils. This method makes it possible to obtain CBD-enriched products, characterized by a purity ranging from medium to high, while presenting itself as an ecologically sustainable and scalable strategy (VIEIRA, 2023). Extraction by solubilization of oil in the solvent is also widely used, it can occur in two ways: through dissolution, where the oil is released from the damaged plant cells during pressing or grinding; and by diffusion, where the oil gradually crosses the semipermeable membranes of intact plant cells to the liquid solvent medium continuously (RAMALHO; SUAREZ, 2012).

In steam drag extraction, a boiler is used to generate steam, an extractor or distiller where the raw material is placed, a condenser and a Florentine vessel to collect the condensate. The separation of phases is carried out based on polarity differences, considering that essential oils are typically nonpolar or nonpolar (STEFFANI, 2003).

PURIFICATION AND ISOLATION

The growing interest in *Cannabis* for beneficial purposes has stimulated the demand for efficient and productive methods of separating cannabinoids. These methods are categorized into chromatographic and non-chromatographic. Chromatographs include solid-liquid techniques such as batch HPLC, multi-column countercurrent chromatography (MCCC), and medium-pressure chromatography (*flash*), and liquid-liquid techniques such as countercurrent chromatography (CCC) and centrifugal partition chromatography (CPC). Non-chromatographic methods often involve extraction and recrystallization using solvents of various polarities (CITTI et al., 2020). Due to the complexity of botanical cannabis matrices, combinations of methods including decarboxylation, extraction, and purification are often employed, with additional precipitation, dissolution, and crystallization steps to treat and purify cannabinoids (FELETTI; COMPAGNIN, 2023).

Preparative single-column liquid chromatography is widely used for the purification of cannabinoids, using solid phase chromatography (SPE) or solid phase extraction techniques with stationary phases such as silica, alumina (normal phase) and C18 (reverse phase) (SIRANGELO; LUDLOW; SPADAFORA, 2022). While column chromatography improves purity and throughput, the use of large particles in SPE and flash chromatography impairs separation. Smaller particles, used in HPLC, are more effective, offering better resolution and purity. Preparative methods using C18 columns and water-alcohol mixtures

as the mobile phase can produce small amounts of pure cannabinoids with low selectivity, but still, preparative HPLC can isolate multiple cannabinoids effectively (FERRAZANO *et al*., 2022).

Gallo-Molina *et al*. (2019), in the context of THC isolation and purification, used the solid phase extraction (SPE) technique, employing a column filled with octadecyl-modified silica gel. The extract was dissolved in 0.05% trifluoroacetic acid in water and injected into the SPE column. The compounds were eluted using a linear gradient of 0.05% trifluoroacetic acid in acetonitrile, from 0% to 100%, at a constant flow rate of 1 mL/min. The fractions obtained were analyzed by thin layer chromatography (TLC) and reversed-phase high-performance liquid chromatography (RP-HPLC) to determine the presence of THC and select the THC-enriched fractions. The final fraction, after solvent removal and freeze-drying, was analyzed by RP-HPLC and nuclear magnetic resonance (NMR) to evaluate the purity of THC.

ANIMAL ENDOCANNABINOID SYSTEM

FUNCTIONING OF THE ENDOCANNABINOID SYSTEM

The endocannabinoid system is a neuromodulatory system, which has become of great importance in the last 25 years. It is composed of endogenous cannabinoids (endocannabinoids), cannabinoid receptors, and enzymes that are responsible for the synthesis and degradation of endocannabinoids (LU; MACKIE, 2016).

Cannabinoid receptors are the binding sites of an active substance, which have been classified as specific CB1 and CB2 receptors (SILVA *et al.,* 2009). CB1 receptors, the most abundant in the central nervous system, and CB2 receptors are located mainly in peripheral organs and tissues, both are responsible for modulating the psychotropic effects of cannabinoids in the brain (FONSECA *et al.,* 2013). Endocannabinoids are able to decrease neuronal excitability through several molecular mechanisms, including inhibition of Ca2+ currents and activation of K+ currents. The activation of CB1 receptors, as they are predominantly in presynaptic terminals, leads to inhibition of the release of several neurotransmitters (MATIAS; DI MARZO, 2006).

What is known about the synthesis of endocannabinoids is that their production is done on demand, and they are released through the activation of enzymes, which are triggered by a specific signal from within the cell (BELLOCCHIO *et al*., 2008), so they are transported across the cell membrane so that they can be degraded, occurring the arachidonic hydrolysis of glycerol (2-AG) or ethanolamine (AEA) (LU; MACKIE, 2021).

Among the functions of the endocannabinoid system, we can mention the maintenance of homeostatic balance, neuroprotection, modulation of nociception and control of certain phases of memory processing (PAGOTTO *et al*., 2006). With the discovery of these functions, the doors were opened for scientific research with this system, especially in the area of neurology.

THERAPEUTIC EFFECTS

Cannabis can relieve pain in several ways, including modulating the release of neurotransmitters involved in nociception. CB2 receptors can promote analgesia by releasing endorphins from keratinocytes, which act on opioid receptors to reduce the sensation of pain (KENDALL; ALEXANDER, 2009). In cases of seizures, such as epilepsy, CBD regulates the release of glutamate and increases serotonin absorption. The CB1 receptor is capable of modulating neuronal activity, contributing to the initiation and propagation of seizures (SILVA JÚNIOR *et al*., 2021).

In the text: Rocha (2010), cannabinoids have the ability to inhibit cell growth and induce apoptosis, playing a crucial role in the treatment of tumors. In addition, they can decrease the expression of matrix metalloproteinases, reducing the wear and tear of the extracellular matrix and basement membrane (ROCHA, 2010). In canine cognitive dysfunction, cannabinoids are observed to neutralize the beta-amyloid substance deposited in neurons by stimulating CB2 receptors that induce the removal of the substance by macrophages in microglia (RAMALHO, 2023).

Treatment with cannabis seeks the *entourage* effect, which combines phytocannabinoids, terpenes and flavonoids, known as *full spectrum* oil (BECHARA; ESPOSITO, 2023). The use of *full spectrum* oil reduces the side effects of isolated compounds, such as the psychoactivity of THC, which is neutralized by CBD and other phytocannabinoids due to the *entourage* effect. CBD's ability to modulate the response to THC allows for higher doses of THC, increasing clinical efficacy and improving the safety profile, especially for patients who rely on THC for significant therapeutic benefits (CHRISTENSEN *et al.*, 2023).

CANNABIS-BASED PHARMACEUTICAL FORMULATIONS

LIQUID FORMULATIONS

The liquid formulations most used for the pharmaceutical preparation of Cannabis spp.-based products are oils and hydroalcoholic solutions (tinctures). These forms, in turn, differ in terms of physicochemical characteristics (lipophilicity and stability to intrinsic and

extrinsic factors) and in terms of their pharmacokinetics (time of evolution of their absorption, bioavailability, distribution, biotransformation and excretion) (THOMAS; POLLARD, 2016).

Due to bureaucratic hurdles in some countries, there are still insufficient detailed studies on the pharmacokinetic distinction between liquid cannabis-based pharmaceutical forms in animals. However, there are some studies that point to these characteristics, such as the one carried out by Łebkowska-Wieruszewska *et al.* (2019), which evaluated the pharmacokinetics of Bedrocan®, a cannabis oil extract, in dogs. The methodology was based on the administration of Bedrocan® (containing 20% THC and 0.5% CBD) to fasting and fed dogs. The quantification of the compounds was performed using the LC/MS technique (Liquid Chromatography Coupled to Mass Spectrometry) in the blood samples of the dogs tested. THC levels in the blood were quantified from 30 minutes to 10 hours after administration, resulting in the result that fed dogs had a lower plasma concentration of THC compared to non-fed dogs (there were no significant changes in relation to CBD), concluding that the feeding state (fasted or fed) interferes with the absorption of cannabis oil and, consequently, the availability of THC in the bloodstream (ŁEBKOWSKA-WIERUSZEWSKA *et al.*, 2019).

The research conducted by Bartner *et al.* (2018) aimed to investigate how different administration methods and dosages of cannabidiol (CBD) affect its pharmacokinetics in healthy dogs. In that study, researchers utilized three methods of administering CBD – orally administered CBD oil microspheres, orally administered CBD-infused oil, and CBD-infused transdermal cream. The dogs were divided into groups to receive one of three formulations in two different dosages: 75 mg and 150 mg of CBD, administered every 12 hours for a period of 6 weeks. The study concluded that exposure to CBD is proportional to the dose administered. Oral CBD-infused oil has been identified as the most effective method of administration, providing the most favorable pharmacokinetic profile. This suggests that to maximize the therapeutic efficacy of CBD in dogs, oil infused with oral administration is the best option (BARTNER, *et al.*, 2018).

SOLID FORMULATIONS

A capsule is made by enclosing an active pharmaceutical ingredient (API) in a shell that is odorless, tasteless, easy to swallow, and easy to fill. There are two main types of gelatin capsules today: hard gelatin capsules and soft gelatin capsules, also known as *softshells*. The hard gelatin capsule can be used for dry fillers such as powder, liquids, and semi-solids, whereas the *softshell* capsule can only be used for liquids and semi-solids

(HOAG, 2017). The capsules are mainly used in dogs and cats; However, some vitamin and mineral supplement capsules are made for cattle. Tablets are another commonly used pharmaceutical form. They are less popular for animals because administration can be time-consuming, dangerous, and uncertain, as it is not possible to guarantee whether the tablet has been swallowed, spat out, or dropped from the mouth after the steward has moved away or passed it on to another animal (RAMTEKE, 2014).

The cannabinoid formulation impacts their efficacy due to variation in bioavailability and distribution. Oil-based formulations provide higher bioavailability and longer elimination time compared to other formulations. For example, liposome-encapsulated CBD oil has a superior pharmacokinetic profile to "pure" oil. When 137 veterinarians and 329 veterinary medicine students in Portugal were asked about their familiarity with the use of medical cannabis, 89.9% of veterinarians and 76.7% of students answered affirmatively. In clinical practice, veterinarians were more accustomed to tablets, capsules or microcapsules, and prescribed products available in the Portuguese market, such as Evexia® (capsules) and WeConfort® (tablets) (GASPAR, 2021).

According to an investigation on the perception of dog owners about the use of medicinal products derived from cannabis, in relation to capsules/tablets (n=68), 12 (17.6%) reported using those marketed to animals, while 3 (4.4%) reported using capsules/tablets marketed to humans (KOGAN, 2019). Polidoro *et al.* (2022) sought to analyze the pharmacokinetics of various pharmaceutical forms of cannabis in dogs. For oral administration, one tablet containing 100 mg of CBD was administered along with a small amount of highly digestible commercial canned food. CBD has low water solubility, so orally administered CBD was not detected in 50% of dogs in which it was administered as a powder inside a gelatin capsule. Therefore, if administered orally, it is best absorbed in the presence of polar fats, oils, or solvents. Oral CBD was administered inside a tablet with a small amount of wet food containing 15% fat this may explain why we observed a lower detection of CBD compared to studies using oil-based CBD, but it was still possible to observe good absorption. Thus, it is understood that the administration of solid pharmaceutical products derived from cannabis is an appropriate method of administration, and more studies should be conducted in the area seeking the formulation of new solid drugs that can be used in veterinary care (POLIDORO *et al.*, 2022)element.

CANNABIS-BASED PRODUCTS FOR ANIMALS

ADMINISTRATION AND DOSAGE

Products intended for animals often contain CBD, a non-psychoactive compound in cannabis, while THC (tetrahydrocannabinol), which is psychoactive, is avoided due to the potential for toxicity in animals. Both act on the endocannabinoid system in a similar way to endocannabinoid neurotransmitters. However, the psychoactive effect of THC, which results from its action on the central nervous system, limits clinical studies due to possible cognitive, motor, and memory alterations and the risk of long-term dependence (CARVALHO *et al.*, 2017).

For the use of cannabis-derived products, specific regulations have been established. Formulations with a THC concentration of up to 0.2% require prescription through type B prescriptions, with numbering provided by the local Health Surveillance and renewal of the prescription within 60 days. THC concentrations above 0.2% can only be prescribed to terminal patients or those who have exhausted treatment alternatives, requiring a type A prescription, valid for 30 days, provided by the local Health Surveillance (ANVISA, 2019).

There are several ways to use cannabis for medicinal purposes in veterinary and livestock production, including ointments, eye drops, extracts for oral administration, and the incorporation of seeds into the animals' diets (LANDA; SULCOVA; GBELEC, 2016).

For dogs, the recommended dosage of CBD ranges between 2 to 12 mg per kilogram of body weight, while that of THC recommended is 1.5 mg per kilogram of body weight. Before starting any cannabis treatment, it is essential to consult a veterinarian to assess the animal's health and obtain specific guidance. It is advisable to start with minimal doses and carefully monitor clinical signs to avoid any adverse effects (VAUGHN; KUPLA; PAULIONS, 2020).

SIDE EFFECTS AND SAFETY

To ensure the safety of cannabis use in dogs with spinal injuries, it is essential to determine the correct dose, utilize quality products, and have use supervised by a veterinarian to monitor the animal's response and adjust dosage as needed (LOPES; BONORINO, 2023).

According to Coelho (2021), cannabis toxicity in dogs usually appears about 60 minutes after ingestion or inhalation, with neurological, gastrointestinal, and cardiovascular symptoms varying according to dose (COELHO, 2021). Safe doses include 60 mg/kg CBD,

19 mg/kg THC, or 8 mg/kg CBD + 6 mg/kg THC (VAUGHN; KUPLA; PAULIONS, 2020). Administration of 20 mg/kg/day of CBD for six weeks is also safe (McGrath *et al.*, 2018).

Adverse effects reported in studies include diarrhea, vomiting, sedation, dermatologic and ophthalmic changes, and reduced appetite (McGrath *et al.*, 2019; VAUGHN *et al.*, 2020). Clinical signs of cannabis poisoning in dogs include ataxia, mydriasis, hyperesthesia, muscle spasms, and urinary incontinence (JANECZEK *et al.*, 2018; MEOLA *et al.*, 2012; PETERSON; TALCOTT, 2013).

An analysis of 125 cases in Colorado showed that the most common symptoms of poisoning in dogs were ataxia (88%), disorientation (53%), and urinary incontinence (47%). Two deaths were associated with the ingestion of THC-containing biscuits, indicating the sensitivity of dogs to the compound (MEOLA *et al.*, 2012).

STUDIES AND PERSPECTIVES IN VETERINARY MEDICINE

SCIENTIFIC EVIDENCE

An American study investigated the effectiveness of CBD for osteoarthritis (OA) in pet dogs. Sixteen dogs were given 2 mg/kg of CBD every 12 hours for four weeks. The results indicated a significant reduction in pain and an increase in activity in the dogs. However, 9 of the 16 dogs showed a significant increase in alkaline phosphatase (ALP), possibly due to chronic CBD dosage. The conclusion was that CBD was shown to be effective in reducing pain and increasing activity, but with elevation of liver enzymes in some cases (BRUTLAG; HOMMERDING, 2018).

Mejia *et al.* (2021) investigated the safety and efficacy of CBD in twenty-three dogs, treating them with 2.5 mg/kg of CBD every 12 hours for 6 weeks. No significant differences were found in clinical signs between the groups, although elevations of liver enzymes and vomiting were observed (MEJIA, 2021). Verrico *et al*. (2020) evaluated the effect of CBD on twenty dogs with arthritis, administering doses of 0.5 mg/kg and 1.2 mg/kg of pure CBD, in addition to 0.5 mg/kg of liposomal CBD. They concluded that both pure and liposomal CBD significantly reduced pain and improved mobility, with liposomal CBD proving effective at lower doses compared to pure CBD (VERRICO, 2020).

Mechoulam (2005) reported the use of cannabinoid acids, precursors to neutral cannabinoids such as THC and cannabidiol, for veterinary purposes in Czechoslovakia in the 1950s due to their antibiotic properties (MECHOULAM, 2005). In previous studies, Pate *et al.* (1998) administered AEA, its analogue R-alpha-isopropyl, and the non-classical cannabinoid CP-55,940 in the eyes of normotensive rabbits, demonstrating that CP-55,940 had significant ocular hypotensive effects, while the analogue R-alpha-isopropyl had minor

effects, and AEA caused an initial hypertension followed by a decrease in intraocular pressure (PATE, 1998). Fischer, Ward, and Hendrix (2013) tested the effects of topical administration of an ophthalmic solution containing THC (2%) in clinically normal dogs, resulting in a moderate reduction in intraocular pressure (FISHER; WARD; HENDRIX, 2013). Chien *et al.* (2003) used cannabinoids in normotensive and glaucomatous monkeys (*Macaca cynomolgus*), observing a significant decrease in intraocular pressure (CHIEN *et al.*, 2003). In dermatological applications, Scarampella, Abramo and Noli (2001) administered PLR 120 (analogue of PEA) to 15 cats with eosinophilic granulomas or eosinophilic plaques, observing clinical improvements in 10 of the 15 cats (SCARAMPELLA; ABRAMO; NOLI, 2001). In addition, Cerrato *et al.* (2010) isolated mast cells from skin biopsies of dogs and found that PEA significantly inhibited the release of histamine, prostaglandin D2, and canine anti-IgE-induced tumor necrosis factor-alpha (CERRATO, 2010).

CHALLENGES AND OPPORTUNITIES

Due to the frustration, disorientation and great challenge of caring for an animal diagnosed with neurological problems, many researchers in the area are looking for unconventional therapeutic options, such as treatment with the use of cannabis. Idiopathic epilepsy affects up to 5.7% of the canine population and, consequently, is considered the most common neurological condition among dogs. The first treatment should be done with phenobarbital, potassium bromide or a combination of the two, although the effectiveness of these drugs is questionable, as this treatment fails in 20% to 30% of dogs, which is one more reason for owners to opt for alternative treatments. Cannabis aids in the control of epilepsy as it has the potential to reduce, i.e., minimize sporadic or frequent seizures and also increase the total number of seizure-free days (McGrath *et al.*, 2019).

A study developed by McGrath in 2019 investigated the impacts of CBD on animals with recurrent episodes of seizures. The results of this research indicated a significant decrease in the incidence of seizures in dogs with intractable idiopathic epilepsy. In addition, CBD has antioxidant and anti-inflammatory characteristics, which can contribute to the preservation of the nervous system. Groups of animals undergoing CBD treatment have shown up to a 33% drop in seizures and the high concentration of CBD in plasma is associated with a decrease in seizure incidence (MCGRATH, 2019).

The use of phytocannabinoids in the fight against cancer can improve the patient's quality of life and can treat or delay the development of the disease. In 1975, a study was conducted that reported the antiproliferative and anticancer properties of orally

administered THC. The study describes the inhibition of the development of a lung adenocarcinoma in a rodent and an increase in the lifespan of a rat submitted to treatment compared to control rats (CITAL *et al.*, 2021).

Several beneficial effects are observed in the treatment of canine cognitive dysfunction with cannabis, due to the ability of the endocannabinoid system to regulate neuronal function by modulating calcium influx, neurotransmission, neuroprotection, and inflammatory response, and can also help suppress symptoms such as aggression and pain, thus increasing your quality of life. CBD has already been proven to aid in the regeneration of neurons in the hippocampus (B.G. WILLIAMSON *et al.*, 2021; COILE, 2016).

FINAL CONSIDERATIONS

The scenario on the use of *Cannabis* spp and its extracts is promising in the veterinary environment. However, more research is needed on its therapeutic effects and possible adverse effects for its adoption in the treatment of animals, in order to ensure its safety, efficacy, and therapeutic efficiency. Also, changes in the legislation of some countries are necessary in order to facilitate not only access to cannabis-based products that are already present in the pharmaceutical market, but also to other formulations that may be developed.

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