CANDID TAILS

TAKING CARE OF YOUR BEST FRIEND

PET CBD

Candidtails.com

candidtails.com

Our pets are our family.

Our mission is to **break with the traditional system of pet wellness** by offering **natural and ecological alternatives** to improve and maintain their quality of life.

"Our dog, Chika, has always been an energetic Border Collie. However, at the age of 8, she was hit by a car and suffered a serious injury. Painkillers provided temporary relief but caused serious side effects. We already knew CBD helped her a lot with her thunderstorm anxiety. We then started giving CBD daily, and we realized this also helped her a lot with her mobility. Chika was again like her younger self, which inspired us to start CandidTails..“

Sander & Anton Rijk, co-founders of CandidTails

Main health problems in cats and dogs

In Europe

	1. ANXIETY	2. DERMATITIS	3. ARTRITIS	4. CANCER	5. GINGIVITIS
89.9M *dogs* 	72%	15%	25%	25%	65%
110.1M cats 	25%	13%	45%	20%	80%

Advances in veterinary care and nutrition, have **increased the life expectancy of pets**, leading to an **increase in the population of senior pets**. While this is undoubtedly good news for pet parents, it has also led to **more frequent health problems**, particularly chronic conditions such as **arthritis** and age-related diseases such as **cancer**.

Source: BMC; NIH; AVMA, NC State & Colorado State University; Covetrus

Existing solutions have side effects in 25% of the cases:

- Stomach problems (e.g., vomiting)
- Digestive problems (e.g., diarrhea)
- Incompatibility with other medication
- Prolonged use may cause serious adverse reactions

The shift towards a natural alternative

70%

of millennials prefer **natural and organic alternatives for their pet**

~3X

more likely to choose **natural remedies for anxiety related issues**

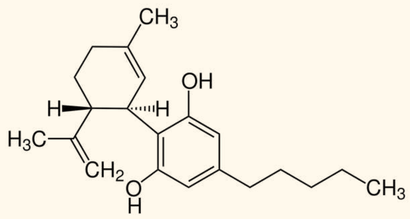
~2X

more likely to choose **natural remedies for chronical pains**

Source: BMC; NIH; Frontiers (Pharma)

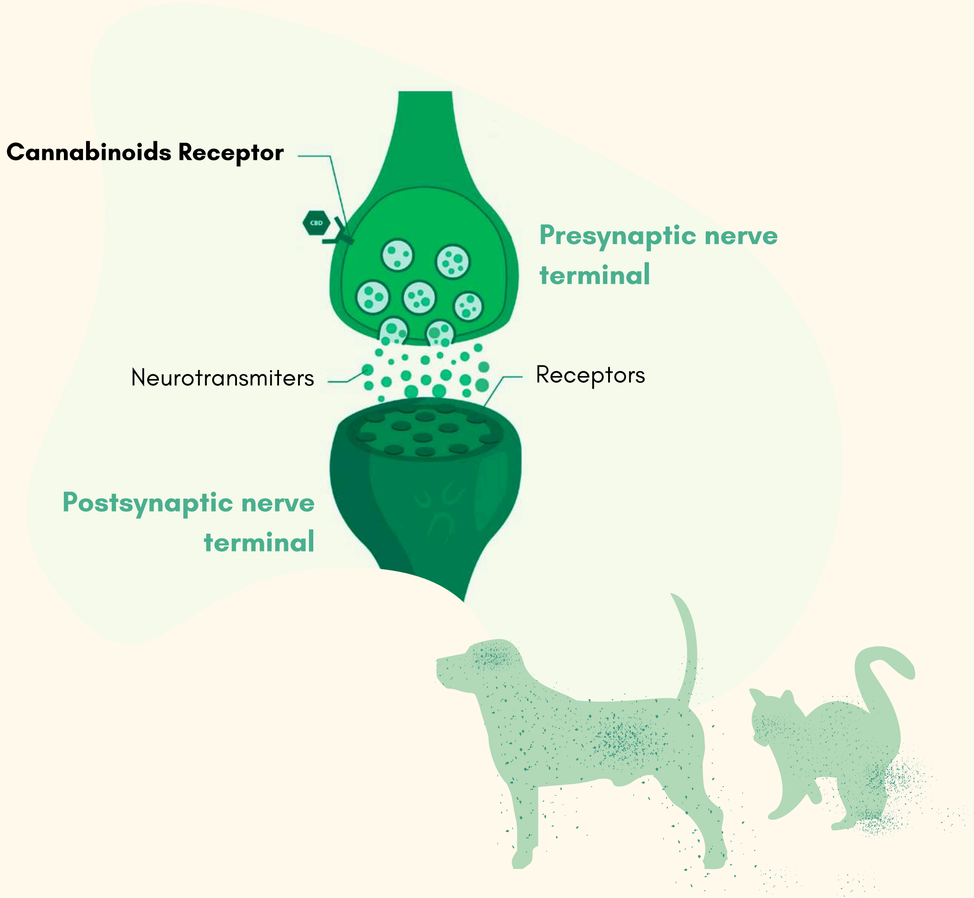
How can CBD help pets?

Cannabidiol (CBD) is a natural substance found in **cannabis sativa plants**. The **hemp plant**, a subspecies, has a **higher concentration of CBD**.



CBD is your natural alternative, without side effects

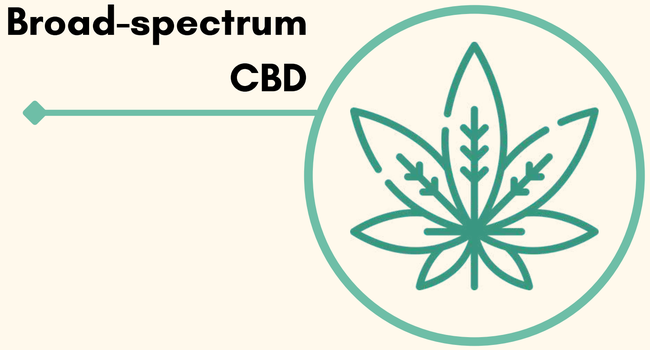
The hemp plant presents us with a variety of cannabinoids, of which CBD is the most abundant. **CBD is a natural and safe substance that can enhance the health and well-being of your pet.**



CBD acts on the endocannabinoid system (ECS), the most widely distributed **network of chemical signals and cell receptors** that are densely distributed in the mammalian brain. The **main function** of this system (ECS) is to **regulate the homeostasis (balance) of the organism.**

Can CBD make pets high?

No. This is because we use broad-spectrum CBD oil. This type of CBD oil contains nearly all the compounds naturally present in the hemp plant except THC (the psychoactive compound of the hemp plant).



All other beneficial compounds like Cannabinoids (**CBDA, CBG, CBN, CBC, CBDV**...), **Terpenes** and **Flavonoids** (components that provide aroma and flavor to the product) are still present. This way, we take advantage of the synergy between the different constituents, optimizing their therapeutic potential.

***Clinical studies can be found at the end of the brochure.**

Source: Pisanti S. eta al Cannabidiol: State of the art and new challenges for therapeutic applications, Pharmacology & Therapeutics 175 (2017) 133–150)

The Candid products

For dogs, cats and horses

Third-party lab tested

Free of THC

Natural

Approved by veterinarians

Petibidiol - CBD Oil for Cats

Petibidiol - CBD Oil for Dogs

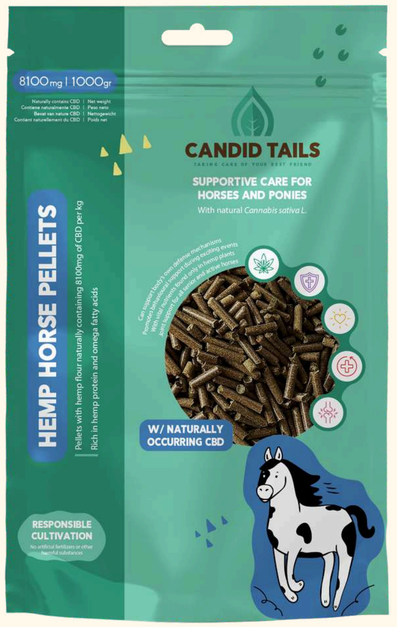
Candid Brush

CBD Balm

Hemp Snacks with CBD

Snacks for Mobility and Relaxation

Hemp Shampoo & Conditioner 4S



Horse Hemp Pellets

Petibidiol Oils

For dogs and cats

✓ **No Sugar** ✓ **Cold Pressed** ✓ **Lab Tested** ✓ **Omega 3, 6 and Vitamin E**

250mg CBD Oil

for cats

Product description

Our **Petibidiol 250mg** is not only a **broad-spectrum CBD oil free of terpenes**, but also a healthy **supplement for your cat**. It is formulated with the highest quality CBD and other cannabinoids in combination with salmon oil. This means that it can help your cat to maintain a sense of calmth, as well as healthy joints and skin.

Ingredients per 10ml*:

Cold-pressed hemp oil and hemp flour macerat (53%), Salmon oil (42,7%), vitamin E(4,3%), naturally contains 250 mg CBD in 10 ml.
Analytical constituents: Crude fat 99%, crude protein 0%, crude ash 0%, crude fibre 0%. Free of terpenes.

*Natural variations may occur.
Certificates of analysis available.

350mg CBD **700mg CBD** **1000mg CBD**

small dogs <10kg medium 10-25kg big >25kg

Product description

Our **Petibidiol (350mg, 700mg and 1000mg)** is a **broad spectrum CBD oil for dogs.** It is formulated with the highest quality CBD and other cannabinoids in combination with hemp seed oil. It is rich in omega 3 and 6 for its broad immunological properties. We have also added chamomile to the formulation, for its soothing and anti-inflammatory properties.

Ingredients per 10ml or 20ml*:

Cold-pressed hemp oil and hemp flour macerat (53%), Salmon oil (42%), Chamomile oil (0,7%), vitamin E (4,3%).
Contains CBD naturally. Analytical constituents: Crude fat 99%, crude protein 0%, crude ash 0%, crude fiber 0%.

Hemp Snacks with CBD

Supplementary feed for dogs

With **native CBD from hemp flour**

Developed and **tested** by **veterinarians**

Carefully formulated for **maximum bioavailability and functionality**

Hypoallergenic due to use of insect and chicken liver protein. Also **sugar free**

Mobility+ *Snacks*

***6 active natural ingredients** for maintaining **healthy joints** of dogs

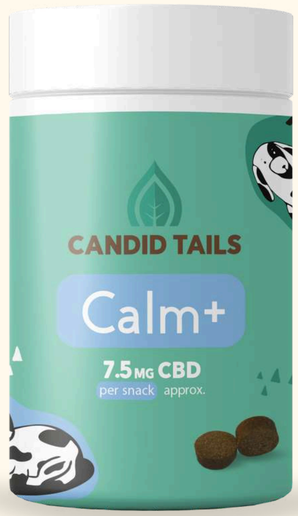
May help with **joint discomfort** often present in **senior dogs**

Product description

Mobility+ is specially developed for **very active and senior dogs** (or for other dogs with **reduced mobility and/or less desire to move**). This is because its **natural ingredients** and **high-quality CBD** can help to maintain joint health. You will find the recommended amounts on the back of the pack.

Ingredients (450mg of CBD / 150g):

Composition: Sweet potato, vegetable glycerin, insect protein, hemp flour, fermentation-derived glucosamine (4%), hydrolyzed chicken liver protein, chondroitin sulfate (2%), hemp expeller cake, parsnip powder, psyllium husk, turmeric, chamomile, incense resin (Boswellia serrata), methylsulfonylmethane (MSM). Analytical Constituents: Crude protein 19.0%, crude fat 5.0%, crude fiber 5.0%, crude ash 5.0%. Naturally occurring 450mg CBD per pack. Net weight 150g.



Calm+ *Snacks*

***4 active natural ingredients** that can help dogs maintain a **sense of calm**

Useful for dogs during **loud-noise events, separation , car rides** and other exciting events

Product description

Relax+ is specially developed to **help dogs maintain a state of calm** during emotional events. They are used especially when there are **loud noises, fireworks, trips of all kinds or loneliness.** All ingredients are natural. You will find the recommended amounts on the back of the pack.

Ingredients (450mg of CBD / 150g):

Sweet potato, vegetable glycerin, insect protein, *hemp flour, hemp protein, hydrolysed liver, psyllium husk powder, *rose root (2mg/2.5g), *lemon balm (2mg/2.5g), *chamomile flowers. Additives: Rosemary CO2 extract. Analytical constitutes: Crude protein 16.5%, crude fat 9.0%, crude fibre 3.5%, crude ash 6.0%; Naturally contains 450mg CBD per pack. Net weight 150g.

Note: This product should not be administered to pregnant animals nor cats and we recommend consulting your veterinarian.
*Natural variations may occur.

Candid Hemp Snacks

Supplementary feed for dogs

Functional food supplement for **dogs** with **native CBD** from hemp flour

Delicious snack suitable for **training**

Contains 40+ **sugar free** snacks per package

Useful for dogs during **loud-noise events, separation, car rides** and other exciting events

May help with **dogs** that have a **reduced desire to move**

It can help **soothe irritated skin** and keeping it healthy

Product description

Candid Hemp Snacks are **40+ functional snacks** that **naturally contain 2.5 mg of CBD** per snack. **Hemp, insect and chicken proteins** were chosen to supplement your dog's daily diet. These snacks can potentially help **stabilise behaviour**, **reduce itchiness** and **improve mobility**. Quantity indications can be accessed by scanning the QR code on the back of the packet.

Ingredients (100mg of CBD / 100g):

Sweet potato 40 %, vegetable glycerin 24 %, insect protein 18 %, hemp flour 6 %, hemp crude protein 5 %, chicken liver hydrolyzate 3 %, herbal mix 2% (chamomille, rosemary,sage, nettle, fennel), carrot powder 1 %, parsnip powder 1 %

Note: This product should not be administered to pregnant animals nor cats and we recommend consulting your veterinarian.
*Natural variations may occur.

CBD Balm

For nose, paws, scars and elbows

Bee wax
Natural exfoliating protective layer.

Aloe vera
Moisturises and soothes itching. Helps to heal sores or treat skin irritations.

Broad spectrum CBD

Rosemary oil
Antibacterial properties help to soothe the skin.

Hemp oil
Nourishes dry skin and can help soothe it. Protects against sunburns.

Honey
Natural antibacterial with moisturising and nourishing characteristics

Product description

Our **CBD balm** has been carefully formulated to help pets suffering from **dry and cracked noses, elbows and paws**. It can also be used on **wounds, skin irritations, scars and hotspots**. In addition, topical application of CBD can help relieve **muscle and joint stiffness.** We recommend applying the balm 3 times a day.

When should I apply the CBD balm on my pet?

Cracked noses and paws
All the ingredients work together to hydrate, nourish and protect your pet's paws while the CBD may help with cracks in the pads.

Sunburned noses
Aloe vera, CBD and hemp are perfect for treating burned skin, promoting skin regeneration and providing sun protection.

Grazed elbows
The CBD balm will help soothe grazed elbows.

Itchy skin
Many of the CBD balm ingredients are soothing and reduce itchiness.

Dry ears
The CBD balm will help with dry ears and damaged spots.

Joint stiffness
Applying CBD balm to joints and muscles can help to make them less stiff.

4S Hemp Shampoo

+ Conditioner and Broad Spectrum CBD

1. Shine

Hemp seed oil, avocado, chamomilla recutita

2. Softness

Hemp seed oil, avocado, grapefruit

3. Smell

Coconut oil

4. Skin

250mg de CBD de amplio espectro

Broad spectrum CBD

According to studies, CBD soothes and protects the skin and helps with itching caused by seasonal allergies.

Product Description

Our **4S Hemp Shampoo and Conditioner** has been specially created for those pets with **sensitive skin and skin irritations** that require special care. Therefore, 4S shampoo is **enriched with broad-spectrum CBD**, due to its **multiple benefits for skin health**.

Other ingredients (250ml):

Aqua (Water), Sodium Coceth Sulfate, Sodium Chloride, Cannabidiol, Cannabis Sativa Seed Oil, Cocamide Dea, Cocamidopropyl Betaine, Parfum (Fragrance), Glycerin, Propylene Glycol, Citrus Grandis (Grapefruit) Fruit Extract, Persea Gratissima (Avocado) Fruit Extract, Rosmarinus Officinalis (Rosemary) Leaf Extract, Urtica Diotica (Nettle) Extract, Betula Alba (Birch) Leaf Extract, Equisetum Arvense (Horse Tail) Extract, Tussilago Farfara (Coltsfoot) Leaf Extract, Achillea Millefolium (Yarrow), Extract, Thymus Serpillum (Wild Thyme) Extract, Foeniculum Vulgare (Fennel) Fruit Extract,Humulus Lupulus (Hops) Extract, Melissa Officinalis Leaf Extract, Viscum Album (Mistletoe) Leaf Extract, Chamomilla Recutita (Matricaria) Flower Extract, Hydrolyzed Jojoba Esters, Cocos Nucifera (Coconut) Fruit Extract, Aloe Barbadensis Leaf Juice, Sorbitol, Sodium Benzoate, Urea, Allantoin, Citric Acid, Benzyl Alcohol, Potassium Sorbate.

Note: Cats suffering from skin irritations can also use these products; we recommend shaking the shampoo bottle before use.

Candid Brush

Dispenser and massager

Our Candid Brush has a **dual function**, as a **shampoo dispenser** and a **massaging brush**. The brush is **safe**, **durable** and will provide a sense of **comfort and pleasure for your pet.**

Cap

A cap to pour the shampoo into the brush.

Hand-grip

Non-slip handle for a comfortable grip when washing your pet.

Dispenser

Shampoo dispenser that works by squeezing the brush.

Open the cap and **pour in your Candid shampoo**. Close the cap tightly. **During washing**, gently **squeeze the brush** to **dispense the shampoo** into your dog's coat. You can pour a little water into the shampoo to dilute it.

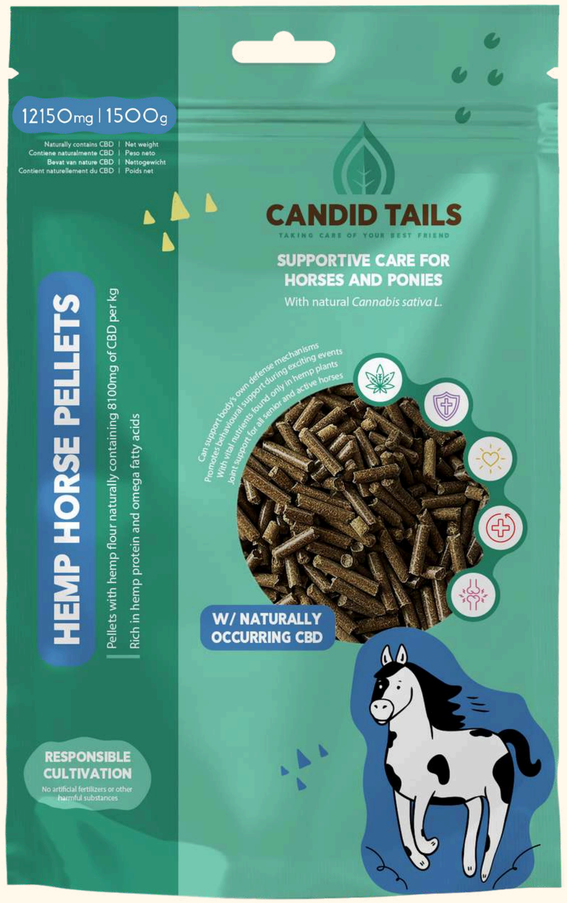
- Allows you to massage your pet, which improves blood circulation
- Enhances the skin and coat benefits of our shampoo.
- Takes care of your pet's skin and fur
- Eliminates frizz

Hemp Pellets with CBD

Complementary feed for horses

Supplement that can support the body's own **defense mechanisms**

Support **behavioural management** during **exciting events**



Provides **essential substances and nutrients** found only in hemp

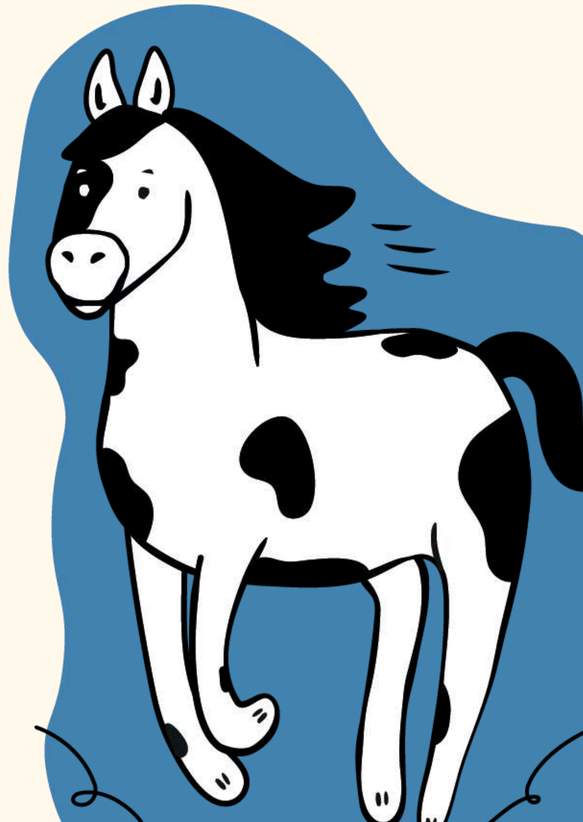
Can provide **joint support** for senior and high performance horses

Product description

Candid **Horse Hemp Pellets** are made **100% of hemp**, naturally containing **12150 mg of CBD per pack of 1500g.** Hemp pellets are a great supplement to your horse diet, providing vital nutrients found only in the hemp plant. The Candid Pellets can provide **emotional support during exciting events** like transportation, hoof trimming and vet visits. Additionaly, ir promotes **joint support** for senior and high performance horses, aiding them in **recovery** after training. Quantity indications can be accessed by scanning the QR code on the back of the packet. **One Pack will last 30+ days for a horse of 500kg**

Ingredients (8100mg of CBD / 1000g):

Hemp flour (100%). Analytical constituents: Crude protein 58.0%, crude fat 7.0%, crude fiber 12.5%, crude ash 11.6%. Net weight 1500g.



Dosage table

Oils:

This is the daily recommendation for our cannabis **oils with CBD**.
You can access it by scanning the **QR code** on the lid of the box of the oils.

Snacks:

This is the daily recommendation for our **CBD hemp snacks.**
You can access it by scanning the **QR code** on the label of the snack box.

	Week 1 (2mg/kg)				Week 2+ (1mg/kg)			
	Activation Dose (incl. situational triggers, acute itching)				Maintenance Dose			
	250mg CBD	350mg CBD	700mg CBD	1000mg CBD	250mg CBD	350mg CBD	700mg CBD	1000mg CBD
5	☀ 4 💧 ☾ 4 💧	☀ 4 💧 ☾ 2 💧	☀ 4 💧 ☾ 2 💧	☀ 2 💧 ☾ 2 💧	☀ 2 💧 ☾ 2 💧	☀ 2 💧 ☾ 1 💧	☀ 2 💧 ☾ 1 💧	☀ 1 💧 ☾ 1 💧
10	☀ 8 💧 ☾ 8 💧	☀ 6 💧 ☾ 6 💧	☀ 6 💧 ☾ 6 💧	☀ 4 💧 ☾ 4 💧	☀ 4 💧 ☾ 4 💧	☀ 3 💧 ☾ 3 💧	☀ 3 💧 ☾ 3 💧	☀ 2 💧 ☾ 2 💧
15	☀ 12 💧 ☾ 12 💧	☀ 10 💧 ☾ 8 💧	☀ 10 💧 ☾ 8 💧	☀ 6 💧 ☾ 6 💧	☀ 6 💧 ☾ 6 💧	☀ 5 💧 ☾ 4 💧	☀ 5 💧 ☾ 4 💧	☀ 3 💧 ☾ 3 💧
20		☀ 12 💧 ☾ 12 💧	☀ 12 💧 ☾ 12 💧	☀ 8 💧 ☾ 8 💧		☀ 6 💧 ☾ 6 💧	☀ 6 💧 ☾ 6 💧	☀ 4 💧 ☾ 4 💧
25		☀ 14 💧 ☾ 14 💧	☀ 14 💧 ☾ 14 💧	☀ 10 💧 ☾ 10 💧		☀ 7 💧 ☾ 7 💧	☀ 7 💧 ☾ 7 💧	☀ 5 💧 ☾ 5 💧
30			☀ 18 💧 ☾ 16 💧	☀ 12 💧 ☾ 12 💧			☀ 9 💧 ☾ 8 💧	☀ 6 💧 ☾ 6 💧
35				☀ 14 💧 ☾ 14 💧				☀ 7 💧 ☾ 7 💧
40				☀ 16 💧 ☾ 16 💧				☀ 8 💧 ☾ 8 💧
45				☀ 18 💧 ☾ 18 💧				☀ 9 💧 ☾ 9 💧

Kg	Hemp	Calm+	Mobility+
5	☀ 1/2 snack ☾ 1/2 snack	☀ 1/2 snack ☾ 1/2 snack	☀ 1/2 snack ☾ 1/2 snack
10	☀ 1 snack ☾ 1 snack	☀ 1 snack ☾ 1/2 snack	☀ 1 snack ☾ 1/2 snack
15	☀ 2 snacks ☾ 1 snacks	☀ 1 snacks ☾ 1 snacks	☀ 1 snacks ☾ 1 snacks
20	☀ 2 snacks ☾ 2 snacks	☀ 1 +1/2 snacks ☾ 1 + 1/2 snacks	☀ 1 + 1/2 snacks ☾ 1 + 1/2 snacks
25	☀ 3 snacks ☾ 2 snacks	☀ 2 snacks ☾ 1 + 1/2 snacks	☀ 2 snacks ☾ 1 + 1/2 snacks
30+	☀ 3 snacks ☾ 3 snacks	☀ 2 snacks ☾ 2 snacks	☀ 2 snacks ☾ 2 snacks

Interested in learning more about CBD?

Follow us on social media

@candidtails

Clinical Research on CBD

Study: **The Use of Cannabidiol-Rich Hemp Oil Extract to Treat Canine Osteoarthritis-Related Pain: A Pilot Study**
The clinical trial consisted of a 90-day open pilot study with no placebo control group that enrolled 37 dogs suffering from chronic maladaptive pain. Dogs received a CBD oil product at a dose of 0.25 mg/kg delivered on food for 3 days and then every 12 hours; the CBD dose was adjusted as needed. The objective was to determine whether CBD could positively influence pain relief and overall function in dogs experiencing chronic maladaptive pain from osteoarthritis.

RESULTS:

- 95% of the dogs experienced decreased pain and improved mobility and quality of life after ingesting CBD oil
- Other pain-related medication already in use was eliminated in 43.5% of patients and reduced in 47.8% due to CBD contribution
- Quotes from patients: “She’s more like a puppy”; “He is acting like a much younger dog”; and “I haven’t seen him play like this for a long time.”

The Use of Cannabidiol-Rich Hemp Oil Extract to Treat Canine Osteoarthritis-Related Pain: A Pilot Study
Kogan, P. Hellyer, R. Downing
2020

Study: **Transdermal Cannabidiol Reduces Inflammation and Pain-Related Behaviours in a Rat Model of Arthritis**
Of the 54 rats included in the study, 21 were used as control and 23 were subjected to adjuvant-induced monoarthritis. Vehicle gel or CBD gel was applied in the skin. The doses of CBD were: 0.62 mg, 3.1mg, 6.2mg, 62mg. Criteria: joint circumference; spontaneous pain; hindpaw heat sensitivity; and animal behavior. The levels of immunomodulator molecules and immunoreactivity were also determined. The objective of the study was to examine the in vivo efficacy of transdermal CBD to reduce inflammation and pain-related behaviors.

RESULTS:

- Topical CBD proved to be an effective symptomatic, anti-inflammatory and anti-hyperalgesic treatment in arthritis
- A dose of 6.2mg/day of CBD significantly reduced swelling and synovial thickness
- Transdermal CBD use improved pain, reducing the median score from 4 to 1.5 (0-5 scale)
- Only after 2 days of CBD treatment, there was a significant improvement of heat hypersensitivity, which persisted throughout the experiment
- Pro-inflammatory activity dropped as low as non-pathological levels after using CBD
- The subjects didn’t suffer any alteration in their activity levels or motor abilities.

Transdermal cannabidiol reduces inflammation and pain-related behaviours in a rat model of arthritis
C. Hammell, L. P. Zhang, F. M, S. M. Abshire, S. L. McIlwrath, A. L. Stinchcomb, K. N. Westlund
2016

*These studies are provided for informational purposes. CandidTails does not claim their products will diagnose, cure or prevent any of the discussed diseases. These studies should not be used as a substitute for the advice of medical experts.

Study: **A Randomized, Double-Blind, Placebo-Controlled Study of Daily Cannabidiol for the Treatment of Canine Osteoarthritis pain**
In this study, 20 dogs were randomly assigned to 1 of 4 groups: placebo, 0.5 mg/kg of CBD, 1.2 mg/kg of CBD, or 20 mg/day liposomal CBD. Before treatment initiation and at day 30, each dog was evaluated by a veterinarian who assessed locomotion on a 5-point scale (1 = best). Owners also evaluated dogs before treatment and at weeks 4 and 6 using the Helsinki Chronic Pain Index (HCPI). The present study aimed to validate whether CBD might positively impact the development and progression of osteoarthrithis

RESULTS:

- 50 mg/day of CBD or 20 mg/day of liposomal CBD significantly reduced pain in dogs suffering from osteoarthritis
- Movement indexes (standing, walking and running) were all improved after administration of both 50mg/day CBD and 20 mg/day liposomal CBD
- Dog’s quality of life increased after CBD treatment
- CBD showed efficacy in relieving arthritic pain and improving dog’s activity levels
- No detrimental impact of CBD administration was reported

A randomized, double-blind, placebo-controlled study of daily cannabidiol for the treatment of canine osteoarthritis pain
D. Verrico, S. Wesson, V. Konduri, C. J. Hofferek, J. Vazquez-Perez, E. Blair, K. Dunner Jr, P. Salimpour, W. K. Decker, M. M. Halpert
2021

Study: Pharmacokinetics, Safety, and Clinical Efficacy of Cannabidiol Treatment in Osteoarthritic Dogs
The study consisted of a randomised, placebo-controlled, double-blind, owner-veterinarian crossover trial involving 16 dogs. Dogs received each of two treatments in random order: CBD, 2 mg/kg every 12h or placebo every 12h. Each treatment was administered for 4 weeks with a 2-week washout period between treatments. The main objective was to study the short-term efficacy and safety of CBD-based oil in dogs with osteoarthritis.

RESULTS:

- During CBD treatment, dogs’ pain decreased, with pain scores dropping from 21 to 14 (0-50 scale)
- Use of CBD oil result in a 12% increase in dogs’ activity
- No side effects were reported by owners
- The use of 2 mg/kg CBD twice a day increased the comfort and activity of dogs suffering from osteoarthritis

Pharmacokinetics, Safety, and Clinical Efficacy of Cannabidiol Treatment in Osteoarthritic Dogs
L. Gamble, J. M. Boesch, C. W. Frye, W. S. Schwark, S. Mann, L. Wolfe, H. Brown, E. S. Berthelsen, J. J. Wakshlag
2018

Clinical Research on CBD

Study: A single dose of cannabidiol (CBD) positively influences measures of stress in dogs during separation and car travel
The present study aimed to understand the impact of being left alone and traveling in a car on measures of canine stress, and establish whether CBD could positively influence any measures of stress. 40 healthy dogs were included in the study, with 19 of them experiencing the separation event and 21 the car travel. Before the event, dogs either received placebo or one single dose of 4mg/kg of CBD.

RESULTS:

- First, it was evident that these events, separation and car travel, elicited a negative emotional response in dogs;
- During car travel, dogs that received CBD CBD were less "sad," and had a smaller decrease in "relaxed" ratings when compared to the placebo treated dogs; they also had significantly lower serum cortisol concentrations than dogs that received a placebo;
- When considered collectively, the results suggest that a single dose of CBD has a positive effect on reducing multiple aspects of canine stress during a car journey;
- Dogs who received CBD were less "stressed," "sad," "tense," and "uncomfortable" and more "explorative" during the separation event than dogs who received the placebo;
- Dogs who received the CBD also exhibited less whining and sitting behavior and traveled further when they were left alone. Collectively these characteristics are suggestive of a more relaxed emotional state in CBD treated dogs.

A single dose of cannabidiol (CBD) positively influences measures of stress in dogs during separation and car travel
A. B. G. Hunt, H. E. Flint, D. W. Logan, T. King
2023

Study: **Cannabidiol as a Potential Treatment for Anxiety Disorder**
The current study is a review to determine CBD's potential as a treatment for anxiety-related disorders, assessed by evidence from existing studies.

RESULTS:

- 68.75% of the studies demonstrated the anxiolytic effects of CBD
- CBD reduced experimentally-induced anxiety in healthy subjects and reduced anxiety in patients with social anxiety disorders (SAD)
- CBD reduced acute increases in heart rate and blood pressure produced by states of heightened anxiety
- CBD blocked reconsolidation of unpleasant memories in rats and enhanced extinction of fear memories in healthy humans
- Human experimental studies put into evidence CBD's excellent safety profile and minimal sedative effect

Cannabidiol as a Potential Treatment for Anxiety Disorders
E. Blessing, M. M. Steenkamp, J. Manzanares, C. R. Marmar
2015

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Study: **Anxiety: CBD May Reduce Agressive Behaviour Towards Humans in Shelter Dogs**
The purpose of this study was to determine whether CBD treatment can decrease disturbed, stressed and aggressive behaviors in shelter dogs. 24 sheltered dogs with various kinds of behavioral troubles were alternately assigned forming 2 groups (treated and control) of 12 dogs each. The treatment group received 5% CBD based oil (1 drop/2kg) and the placebo group received olive oil, dispensed daily for 45 days. Behavioral observations were performed at 3 moments and consisted of more than 100 behavioral patterns.

RESULTS:

- After CBD administration, aggressive behavior towards humans showed a significant decrease
- Dogs in the study did not show any of the symptoms referable to CBD intolerance
- CBD treatment did not decrease the activity nor level of attention towards the environment of the dogs studied, as already highlighted for other species

Anxiety: CBD May Reduce Aggressive Behaviour Towards Humans in Shelter Dogs
Corsetti, S. Borruso, L. Malandrucco, V. Spallucci, L. Maragliano, R. Perino, P. D'Agostino, E. Natoli
2021

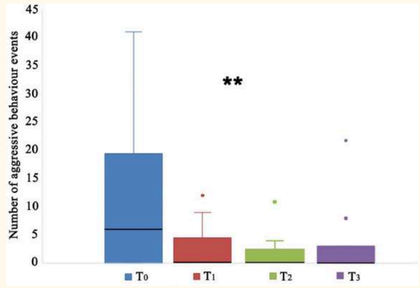

Figure 1: Number of aggressive behaviors following CBD treatment at the start of the study (T0), after 15 (T1) and 45 (T2) days from the beginning of the treatment, and 15 days after the end of the administration of CBD (T3)

Study: **Cannabidiol Blocks Long-Lasting Behavioural Consequences of Predator Threat Stress: Possible Involvement of 5HT1A Receptors**
The current study is a review to determine CBD's potential as a treatment for anxiety-related disorders, assessed by evidence from existing studies.

RESULTS:

- CBD can prevent the long-lasting anxiogenic effect promoted by traumatic events
- When compared to the control group, the reduction in anxiety behavior was greater with CBD than with the common antidepressant used in PTSD treatment
- CBD anti-stress effects could depend on serotonin (5HT1A) receptor activation; serotonin contributes to the feeling of well-being

Cannabidiol blocks long-lasting behavioral consequences of predator threat stress: Possible involvement of 5HT1A receptors
C. Campos, F. R. Ferreira, F. S. Guimarães
2012

Clinical Research on CBD

Study: **Cannabidiol in Anxiety and Sleep: A Large Case Studies**
The present retrospective study was conducted at a psychiatric clinic involving adult patients treated with CBD for anxiety or sleep as an adjunct to treatment, with the purpose of studying the effects of CBD on anxiety or sleep disturbances. Nearly all patients were given CBD 25 mg/d in capsule form. The main objectives were to determine whether CBD is helpful for improving sleep and/or anxiety and to comprehend tolerability and safety concerns.

RESULTS:

- 79.2% of the patients exhibited an improvement in anxiety in the 1st month
- The decrease of anxiety levels was sustained during the rest of the treatment period
- 66.7% of the population experienced less sleep-related problems in the 1st month
- The mean anxiety score dropped from 23.87 to 16.36 in the population whose primary concern was anxiety
- The patients presenting with a primary concern of sleep had a reduction from 13.08 to 9.33 in the mean sleep-problems score

Cannabidiol in Anxiety and Sleep: A Large Case Series
Shannon, N. Lewis, H. Lee, S. Hughes
2019

Study: **Polyphenols and Cannabidiol Modulate Transcriptional Regulation of Th1/Th2 Inflammatory Genes Related to Canine Atopic Dermatitis**
Atopic dermatitis (AD) is associated with multiple immune cells and mediators encoded by specific genes whose expression is increased in dogs suffering from AD. In this study, immune and skin cells from dogs' skin biopsies with both spontaneously occurring and induced atopic dermatitis were treated with the cannabidiol and polyphenols. The purpose of the study was to test the effects of a CBD + polyphenols in reverting the upregulation of AD canine key genes.

RESULTS:

- Cannabidiol was able to downregulate key actors involved in the development and progression of this dermatological disease
- Treatment with CBD + polyphenols showed an ability to revert the overexpression of canine AD key inflammatory genes
- This study's results provide groundwork for CBD application in sustained drug therapy or relapse prevention in atopic dermatitis

Polyphenols and Cannabidiol Modulate Transcriptional Regulation of Th1/Th2 Inflammatory Genes Related to Canine Atopic Dermatitis
Massimini, E. D. Vedove, B. Bachetti, F. Di Pierro, C. Ribecco, C. D'Addario, M. Pucci
2021

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Study: **Effect of Cannabidiol (CBD) on Canine Inflammatory Response: An Ex Vivo Study on LPS Stimulated Whole Blood**
The study used an ex vivo model where whole blood from healthy dogs was stimulated with LPS and then treated with CBD or vehicle. The study then focused on the levels of the major regulating molecules. IL-6 and TNF-α are the major pro-inflammatory molecules and both are overproduced in atopic dermatitis and also associated with the pathogenesis of arthritis in dogs. IL-10 is an anti-inflammatory molecule and immune-regulating mediator. The balance between TNF-α and IL-10 is important for immune homeostasis maintenance. Furthermore, the study evaluated the effect of CBD on Nf-κB (key regulator of inflammatory response that regulates the expression of several pro-inflammatory mediators) and COX-2 expression. COX-2 plays a fundamental role in the inflammatory cascade, and thus in acute and chronic inflammation.

RESULTS:

- CBD reduced the secretion of TNF-α and IL-6 in an ex vivo model of inflammation in canine blood cells
- Treatment with CBD restored the TNF-α to IL-10 ratio to a healthy balance
- CBD also reduced NF-κB activation
- Finally, administration of CBD to the inflamed cells resulted in a lower COX-2 (which is upregulated in inflammation) expression

Effect of Cannabidiol (CBD) on Canine Inflammatory Response: An Ex Vivo Study on LPS Stimulated Whole Blood
Gugliandolo, P. Licata, A. F. Peritore, R. Siracusa, R. D'Amico, M. Cordaro, R.Fusco, D. Impellizzeri, R. Di Paola, S. Cuzzocrea, R. Crupi and C. D. Interlandi
2021

Study: **Cannabinoid Receptor Type 1 and 2 Expression in the Skin of Healthy Dogs and Dogs With Atopic Dermatitis**
The study enrolled 5 healthy and 5 dogs with atopic dermatitis. Collection of skin samples was performed in order to study CB1 and CB2's expression and distribution.

RESULTS:

- The cannabinoid receptors are overexpressed in atopic dermatitis, making them a target for treatment
- This study reports that cannabinoids, such as CBD, can be a treatment option for AD and other inflammatory diseases in companion animals

Cannabinoid receptor type 1 and 2 expression in the skin of healthy dogs and dogs with atopic dermatitis
Campora, V. Miragliotta, E.Ricci, L. Cristino, V. Di Marzo, F. Albanese, M. F. della Valle, F. Abramo
2012

Clinical Research on CBD

Study: **Research Priorities for Idiopathic Epilepsy in Dogs: Viewpoints of Owners, General Practice Veterinarians, and Neurology Specialists**
An online survey was conducted and respondents were asked to report the potential for 10 nondrug therapies to positively impact upon the management of IE in dogs, on a scale of 0 (no impact), 1 (little impact), 2 (some impact), 3 (great impact) and 4 (major impact). The therapies explored were: cannabidiol (CBD) oil, medium-chain triglyceride (MCT) oil, raw food diet, hypoallergenic diet, vagus nerve stimulation (VNS), deep brain stimulation (DBS), gene editing, behavioral management, seizure trigger avoidance, transcranial magnetic stimulation (TMS) and epilepsy surgery.

RESULTS:

- CBD treatment is in the top 3 of highest potential positive impact on epilepsy management in dogs, among nondrug therapies
- 77% of responders reported that CBD had a positive impact in controlling epilepsy

Research priorities for idiopathic epilepsy in dogs: Viewpoints of owners, general practice veterinarians, and neurology specialists
M. C. Jones, H. A. Volk, R. M. A. Packer
2021

Study: **Randomized Blinded Controlled Clinical Trial to Assess the Effect of Oral Cannabidiol Administration in Addition to Conventional Antiepileptic Treatment on Seizure Fequency in Dogs With Intractable Idiopathic Epilepsy**
9 dogs in the CBD group and 7 in the placebo group were included in the analysis. The CBD group received 2.5 mg/kg twice daily for 12 weeks in addition to existing antiepileptic treatments, and the placebo group received non infused oil under the same conditions. Seizure activity, adverse effects, and plasma CBD concentrations were compared between groups.

RESULTS:

- Dogs treated with CBD had a significant reduction in seizure frequency, compared with the placebo group
- No adverse behavioral effects were reported by owners
- CBD had no reported proconvulsive effects
- Side effects like somnolence, loss of appetite, and diarrhea were not reported in the present study

Randomized blinded controlled clinical trial to assess the effect of oral cannabidiol administration in addition to conventional antiepileptic treatment on seizure frequency in dogs with intractable idiopathic epilepsy
McGrath, L. R. Bartner, S. Rao, R. A. Packer, D. L. Gustafson
2019

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Study: **Cannabidiol in Patients With Treatment-Resistant Epilepsy: An Open-Label Interventional Trial**
The study is a prospective trial with patients with severe, intractable, treatment-resistant epilepsy of which 162 were included in the safety analysis and 137 in the efficacy one. Cannabidiol at a dose of 2–5 mg/kg/day divided in twice-daily dosing was added to the baseline antiepileptic drug regimen, then up-titrated until intolerance or a maximum daily dose of 25 mg/kg or 50 mg/kg was reached.

RESULTS:

- CBD oil treatment showed a favorable safety and adverse event profile
- There was a 36.5% reduction in motor seizures frequency over the treatment period and a reduction of 35.5% in seizures of all types
- For motor seizures, 39% of patients had a reduction of 50% or more, 21% of 70% or more and 9% had a reduction of 90% or more
- For all seizure types, 37% of patients had a reduction of 50% or more, 22% of 70% or more, and 8% had a reduction of 90% or more
- Most patients who achieved seizure freedom or a reduction of 90% had never experienced a previous antiepileptic drug regimen that was as efficacious as CBD oil

Cannabidiol in patients with treatment-resistant epilepsy: an open-label interventional trial
Devinsky, E. Marsh, D. Friedman, E. Thiele, L. Laux, J. Sullivan, I. Miller, R. Flamini, A. Wilfong, F. Filloux, M. Wong, N. Tilton, P. Bruno, J. Bluvstein, J. Hedlund, R. Kamens, J. Maclean, S. Nangia, N. S. Singhal, C. A. Wilson, A. Patel, M. R. Cilio
2015

Study: Expression of cannabinoid and cannabinoid-related receptors in the oral mucosa of healthy cats and cats with chronic gingivostomatitis
The study investigated the expression of cannabinoid receptors type 1 (CB1R) and 2 (CB2R), and cannabinoid-related receptors G protein-coupled receptor 55 (GPR55), transient receptor potential ankyrin 1 (TRPA1) and serotonin 1a receptor (5-HT1aR), in the oral mucosa of healthy cats to determine whether there was altered expression and distribution in cats with chronic gengivostomatitis.

RESULTS:

- The findings of the study support the hypothesis that the endocannabinoid system in cats may play a role in the maintenance of oral mucosa homeostasis;
- There is an upregulation of receptors of this system in the oral mucosa of cats suffering from gengivostomastitis, possibly making these cannabinoid receptors an interesting potential therapeutic target for this disease;
- Phytocannabinoids, like CBD, could be useful in modulating the inflammation and pain associated with FCGS.

Expression of cannabinoid and cannabinoid-related receptors in the oral mucosa of healthy cats and cats with chronic gingivostomatitis
G. Polidoro, G. Galiazzo F. Giancola, S. Papadimitriou M. Kouki, S. Sabattini, A. Rigillo, R. Chiocchetti
2020

Clinical Research on CBD

Study: Placebo-Controlled Trial of Daily Oral Cannabidiol as Adjunctive Treatment for Cats with Chronic Gingivostomatitis
This study evaluated the clinical efficacy and safety of a CBD oral formulation as an adjunctive treatment for pain management for feline chronic gingivostomatitis (FCGS). 22 cats were included; study group received a fixed dosage of 4mg of CBD per cat every 12h for 15 consecutive days, and the control group received a placebo of similar features.

RESULTS:

- Cats with chronic gingivostomatitis that received CBD showed a significant improvement in Stomatitis Disease Activity Index (SDAI) scores compared to the placebo group;
- Cats in the CBD group scored an average of 3 points less on the Composite Oral Pain Scale for cats and dogs (COPS-C/F) compared to the placebo, suggesting cats receiving CBD may have experienced less pain, although this difference was not statistically significant;
- Cats in the CBD group required lower amounts of rescue analgesia than cats in the placebo group, indicating potential benefits of CBD in managing pain and inflammation.

Placebo-Controlled Trial of Daily Oral Cannabidiol as Adjunctive Treatment for Cats with Chronic Gingivostomatitis
J. Coelho, N. Bento da Silva, M. R. Bronze, L. A. Mestrinho
2023

Study: **Multicenter, Double-Blind, Randomized, Placebo-Controlled, Parallel-Group Study of the Efficacy, Safety, and Tolerability of THC:CBD Extract and THC Extract in Patients with Intractable Cancer-Related Pain** + **Extension Study to Investigate the Long-Term Safety and Tolerability**
177 patients with cancer entered a 2 week trial and were randomized to receive THC+CBD, THC only or placebo. The endpoints were the changes in Numerical Rating Scale (NRS) pain score and use of concomitant analgesia. Moreover, the study assessed the use of opioid background medication, sleep quality, nausea, memory, concentration, and appetite. The study compared the efficacy of a THC:CBD and a THC-only extract with placebo, in relieving pain in patients with advanced cancer and moderate or severe cancer-related pain. The follow-up study focused on the long-term safety and tolerability.

RESULTS:

- 43% of participants experienced a ⩾30% reduction in pain intensity after cannabinoid treatment
- After 2 weeks of receiving CBD+THC in addition to all other treatments, there was a statistically significant reduction in pain severity when compared with placebo
- The addition of CBD resulted in a increase of 20% in the response rate
- A greater proportion of patients in the CBD treatment group reduced other pain medication doses whereas the highest proportion of increases in dose was in the placebo group
- Administration of THC+CBD was well tolerated and no safety concerns were identified
- Long-term use of cannabinoids was well tolerated and no loss of effect was perceived. Patients did not seek to increase cannabinoids dose nor did they seek any other treatment for pain relief
- Insomnia and fatigue improved with CBD and no harmful cognitive effect was observed

Multicenter, Double-Blind, Randomized, Placebo-Controlled, Parallel-Group Study of the Efficacy, Safety, and Tolerability of THC:CBD Extract and THC Extract in Patients with Intractable Cancer-Related Pain
R. Johnson, M. Burnell-Nugent, D.Lossignol, E. D. Ganae-Motan, R. Potts, M. T. Fallon
2010

Study: **Enhancing the Therapeutic Efficacy of Cancer Treatment With Cannabinoids**
Cultures of lung cancer cell lines, from both human and mouse and pancreatic cancer mouse cell lines were grown. Later on, these colonies were counted and a percent survival was calculated. In the in vivo study, cancer mouse models were randomized into different cohorts: intratumoral injection of CBD (5 mg/kg); methanol injection in one control group; SRBs loaded with CBD (5mg/kg); SRBs loaded with methanol in the other control group.The main objective of the study was to explore the potential for enhancing the effectiveness of pancreatic and lung tumor cell kill via combination of CBD with RT.

RESULTS:

- Superior tumor cell killing was achieved with CBD than with 4 Gy (unit of radiation dose) of RT alone
- Results support a greater effectiveness in killing tumor cells when combining CBD and radiotherapy (RT)
- CBD use in combination with RT increased the survival rates of the studied mice
- There is a clear demonstration of a bigger survival rate of CBD-treated mice comparing with the control group (no treatment)
- In situ (in the exact local) delivery of CBD with smart biomaterials allows bigger concentrations of CBD to reach its target
- CBD treatment occasioned an 80% survival rate (vs 50% in the control group) in mice with tumors, whereas the use of smart biomaterials loaded with CBD resulted in a 100% survival rates

Enhancing the Therapeutic Efficacy of Cancer Treatment With Cannabinoids
Yasmin-Karim, M. Moreau
2018

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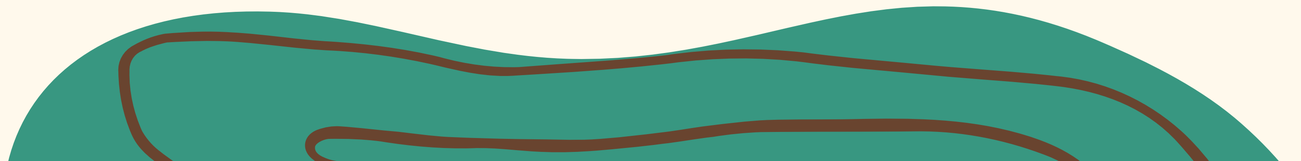

Clinical Research on CBD

Study: **Randomized, PLacebo-Controlled, 28-day Safety and Pharmacokinetics Evaluation of Repeated Oral Cannabidiol Administration in Healthy Dogs**

The study consists of a trial with 20 healthy Beagles. Dogs were were randomly assigned to a different treatment condition (CBD oil at 1, 2, 4, or 12 mg CBD/kg or placebo oil). The following outcomes were assessed: animal health observations, veterinary examination results, food consumption, 24-hour activity, body weight, intraocular pressure, tear production, SAP and ECG parameters.

RESULTS:

- Repeated CBD administration was well tolerated by dogs and no clinically relevant changes were observed related to the administration of any dose of CBD
- Veterinary examinations revealed no clinically important abnormal findings
- No observable differences between groups were detected in motor activity, ophthalmologic examinations, systolic arterial blood pressure (SAP), ECG and complete blood count (CBC)
- All adverse effects were mild and self-limiting, required no intervention, and occurred across all treatment groups, including the placebo group
- There was a greater frequency in side effects in the 12mg/kg group with hypersalivation being the most common one
- The most notable change was the increase in serum ALP (liver enzyme) activity; these increases began to decrease after 2 weeks of treatment and not all dogs developed this change, suggesting that such increase may not be a hallmark of CBD administration but an adaptive response. The dogs that had higher ALP activity didn´t show any sign of hepatocellular degeneration indicating it is an adaptive rather than adverse response to drug exposure

Randomized, placebo-controlled, 28-day safety and pharmacokinetics evaluation of repeated oral cannabidiol administration in healthy dogs
M. Vaughn, L. J. Paulionis, J. E. Kulpa
2020

Study: **Single-Dose Pharmacokinetics and Preliminary Safety Assessment with Use of CBD-Rich Hemp Nutraceutical in Healthy Dogs and Cats**

8 healthy dogs and cats were included in the study and each of them was provided a 2mg/kg total CBD concentration orally twice daily for 12 weeks. The study aimed to assess the safety and adverse effects of CBD in healthy dogs and cats.

RESULTS:

- CBD administration had no effect on food intake and body weight
- No abnormal physical examinations, changes in behavior or organ dysfunction were detected after CBD administration in both dogs and cats
- The administration of 4mg/kg of CBD daily to dogs and cats was well tolerated and not harmful
- CBD consumption by healthy dogs and cats did not alter blood analysis nor serum chemistry, supporting the secure and harmless profile of CBD

Single-Dose Pharmacokinetics and Preliminary Safety Assessment with Use of CBD-Rich Hemp Nutraceutical in Healthy Dogs and Cats
A. Deabold, W. S. Schwark, L. Wolf and J. J. Wakshlag
2019

Study: **Preliminary Investigation of the Safety of Escalating Cannabinoid Doses in Healthy Dogs**

The study was a randomized trial that enrolled 20 healthy dogs. The dogs were randomly assigned to one of five treatment groups: CBD-predominant oil, THC-predominant oil, CBD/THC-predominant oil (1.5:1), sunflower (SF) oil placebo, MCT (medium chain triglycerides) oil placebo. Up to 10 escalating doses were administrated (the daily maximum doses administered were: 62 mg/kg of CBD, 49 mg/kg of THC and 12 mg/kg CBD + 8 mg/kg THC).

RESULTS:

- CBD oil administration had little effect on food intake and physical activity
- There was no difference in the adverse effect profile of CBD oil when compared to its control
- Administration of CBD oil up to a dose of 62mg/kg per day resulted in mild side effects only and these side effects were also detected in the corresponding placebo group
- No moderate or clinically significant adverse effects were reported after administration of CBD oil up to 62mg/kg daily
- There was a clear distinction in the safety profile of the CBD oil when compared to THC or CBD+THC oil, with CBD oil being the most well tolerated
- The study supports the safe and tolerable profile of CBD oil even when administered up to 62mg/kg daily, which is a much higher dose than would be anticipated for clinical use

Preliminary Investigation of the Safety of Escalating Cannabinoid Doses in Healthy Dogs
Vaughn, J. Kulpa and L. Paulionis
2020

Study: Equine Research on the Short-Term Effects of Cannabidiol for the Treatment of Chronic Pain and/or Anxiety

The objectives of this study were to determine whether a single concentration dose of CBD would demonstrate improvements in movement, lessening of perceived pain and decrease in anxiety scores in 41 horses. Short-term safety was also measured through reporting any adverse events to the dosing regimen.

RESULTS:

- There is significant evidence of an association of CBD with an improvement in health and a reduction of pain observed in horses;
- The study demonstrated a continual improvement in pain response through the course of the study;
- Horses taking CBD demonstrated a trend towards improvement in the anxiety score, but did not demonstrate statistical significance for improvement across all participants at the dose utilized in this study;
- In those horses taking CBD that demonstrated lower anxiety, the effect was more profound, with an improvement by 3 units.

Equine Research on the Short-Term Effects of Cannabidiol for the Treatment of Chronic Pain and/or Anxiety
J. Baumgartner, L. Dukes
2020

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