THE USE OF CBD IN PETS

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Cannabis science is still in its infancy

CANNABIS REMOTE HISTORY

- 8000 BC - Asian archaeology finds
- Middle Ages - Hemp sails & rope for navy
- 1553 - King Henry VIII passes an act that requires landowners to dedicate ¼ acre to cannabis plant
- 1619 - 1st New World (Jamestown) Marijuana legislation - settlers required to grow cannabis
- 1700s - A main crop at George Washington's Mount Vernon estate

Hemp rope pattern on a Chinese artifact dated 4800 BC

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CANNIBIS RECENT HISTORY

- **1839 -** Irish physician and medical researcher, William O'Shaughnessy, publishes a study on the cannabis' therapeutic effects
- **1937 -** Marijuana Tax Act levies tax on many aspects of the plant product
- **1940 -** American Harvard trained chemist Roger Adams isolates the CBD compound
- **2006 -** Charlotte Figi born with intractable life-threatening seizures related to a rare genetic disorder - "medical marijuana" or "Charlotte's web" with low THC/high CBD suppresses her seizures
- **2018 -** Epidiolex (purified CBD) receives FDA approval for rare genetic seizure disorders

World Health Organization

- In humans, CBD exhibits no effects indicative of any abuse or dependence potential.
- There is evidence that CBD may be a useful treatment for several medical conditions.
- CBD is generally well tolerated with a good safety profile. Reported adverse effects may be the result of drug-drug interactions.
- To date, there is no evidence of recreational use of CBD, or any other health-related problems associated with the use of pure CBD.

SAHPRA
South African Health Products Regulatory Authority

- On 23 May 2019, the Minister of Health excluded cannabidiol (CBD), one of the naturally occurring non-psychoactive cannabinoids found in the cannabis plant.
- Government Notice No. 586, Government Gazette No. 43347, issued on 22 May 2020, the Minister of Health has amended the Schedules as follows:
- Cannabidiol (CBD) is listed in Schedule 4, except:
  - *in complementary medicines containing no more than 600 mg cannabidiol per sales pack, providing a maximum daily dose of 20 mg of cannabidiol, and making a general health enhancement, health maintenance or relief of minor symptoms (low-risk) claim.*

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HEMP VS. CANNABIS

What's the Difference?

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CBD BASIC TERMS & DEFINITIONS

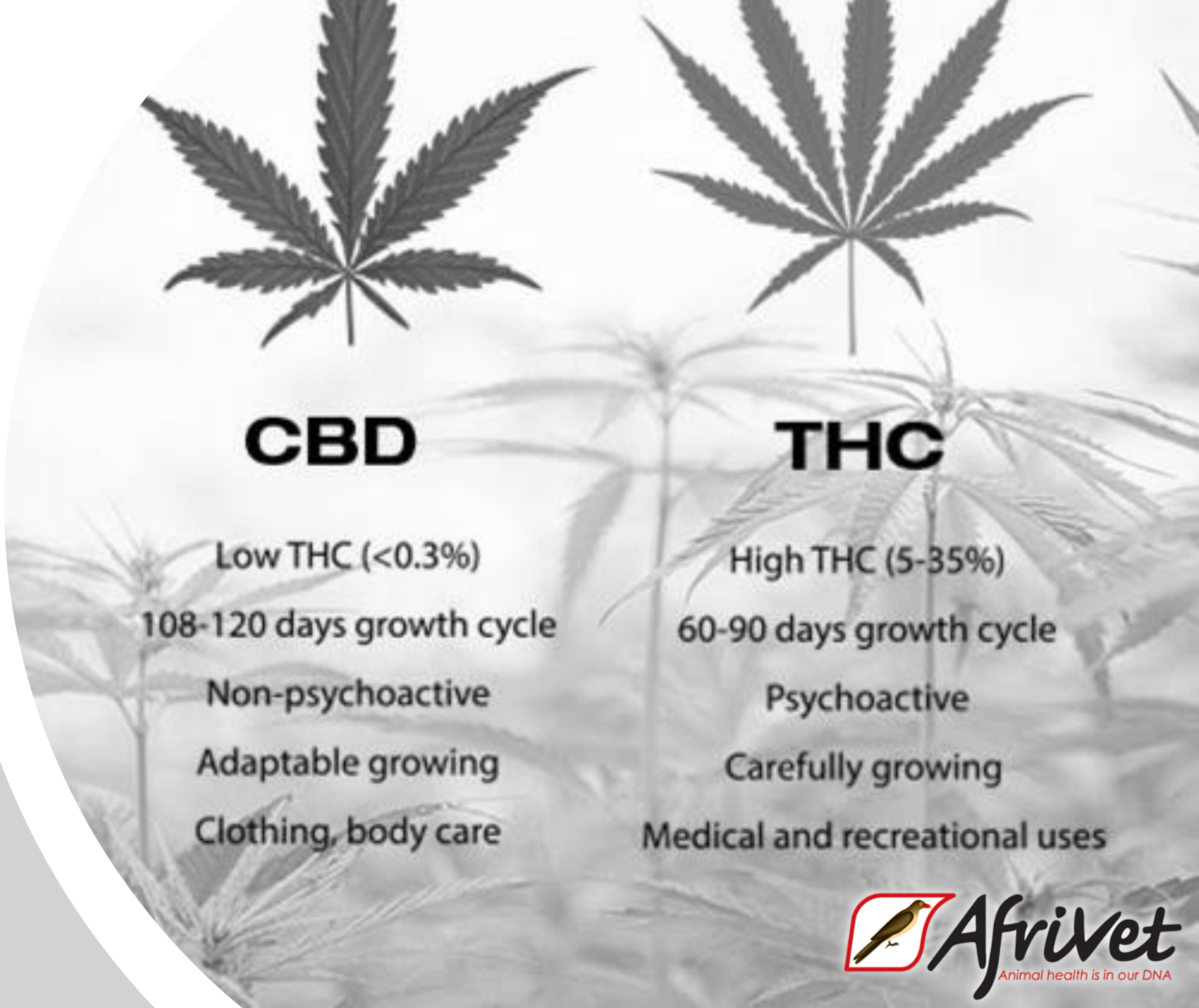
Cannabinoid:

- A class of chemical compounds that act on cannabinoid receptors;
- The active constituents of cannabis.

There is 100+ cannabinoids that have been isolated from the cannabis plant.

Tetrahydrocannabinol (THC) – The psychoactive cannabinoid; responsible for the "high".

Cannabidiol (CBD) – a non-psychoactive cannabinoid.



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SCIENTIFIC CLASSIFICATION

Cannabaceae
FAMILY

Cannabis
GENUS

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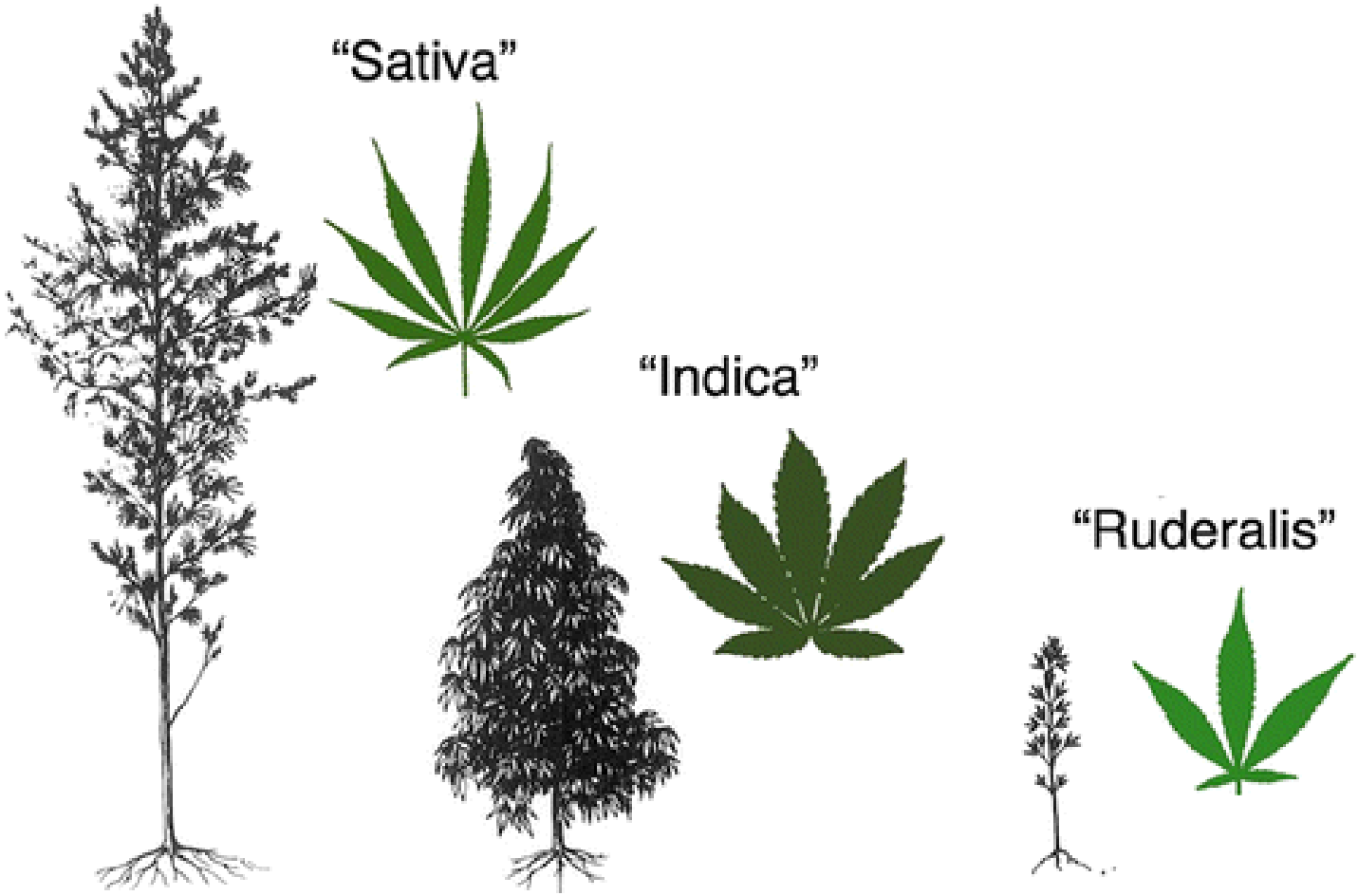
SCIENTIFIC CLASSIFICATION



CANNABIDIOL vs TETRAHYDROCANNABINOL

MEDICAL APPLICATIONS

CBD Cannabidiol	
ANTI-SEIZURE	ANALGESIC
ANTI-TUMOR EFFECTS	ANTI-PSYCHOTIC
ANTI-DEPRESSANT	ALLEVIATES IBS SYMPTOMS
ANTI-INFLAMMATORY	

THC Tetrahydrocannabinol	
SLEEP AID	ANALGESIC
APPETITE STIMULANT	MUSCULAR SPASTICITY
ANTI-ANXIETY	ALLEVIATES GLAUCOMA SYMPTOMS
ANTI-NAUSEANT	

HOW DOES IT WORK?

HOW DOES IT WORK?

The Endocannabinoid System

- The endocannabinoid system (ECS) is a complex, widely distributed regulatory system that provides essential mechanisms for maintaining the biologic balance and feedback throughout the body.
- This essential neuro-modulatory network has been identified in a multitude of species – humans, birds to canines - ECS plays an essential role in health and homeostasis.
- The functions of the ECS have been characterized as "relax, eat, sleep, forget, and protect".
- The classic ECS can be conceptualized as 3 distinct components: cannabinoid receptors (CBRs), endogenous ligands of CBRs known as endocannabinoids (eCBs), and enzymes responsible for the activation, transportation, and breakdown of eCBs.

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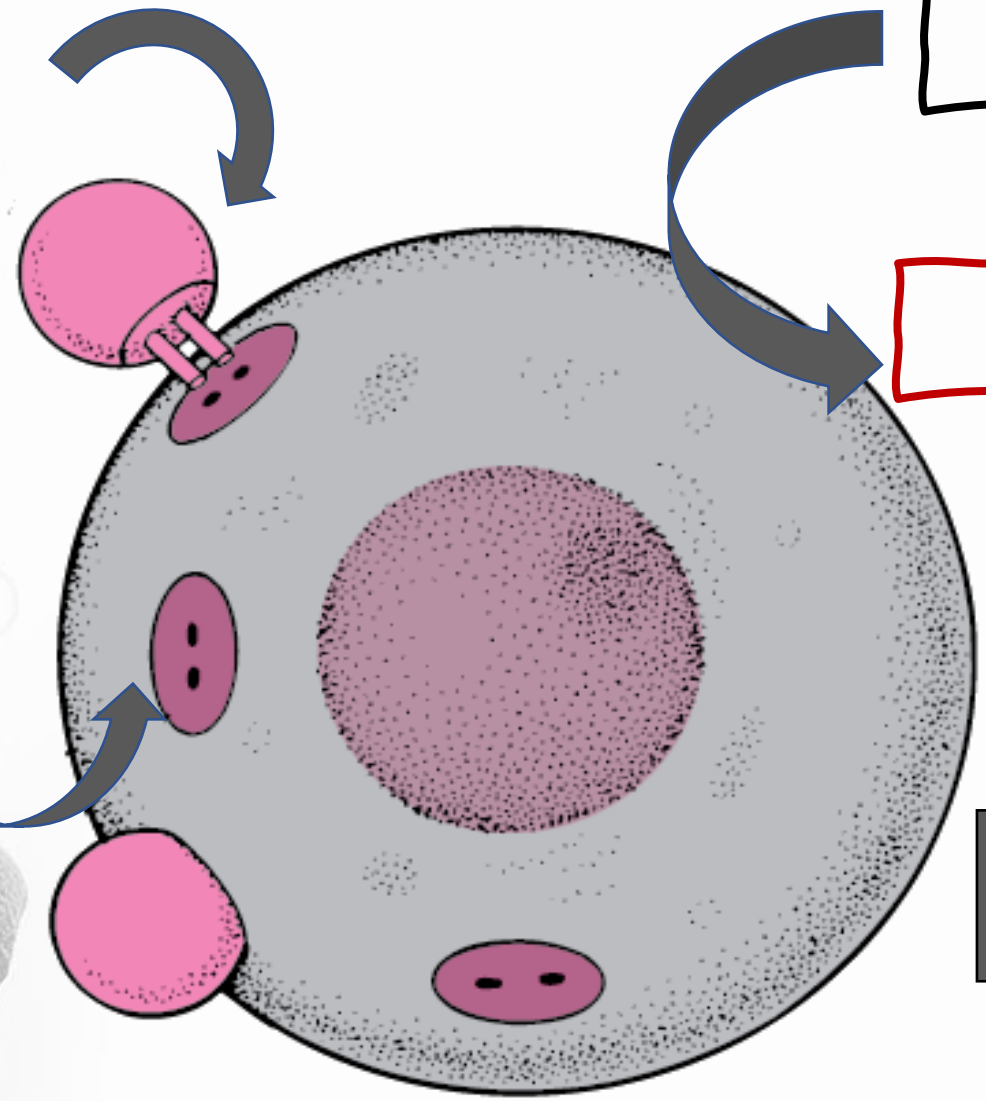
HOW DOES IT WORK?

CANNABINOID PRODUCTS

CANNABINOID RECEPTORS



CANNABINOID ENZYMES

REGULATE THE RESPONSE

RESPONSE

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HOW DOES IT WORK?

The Endocannabinoid System

- Endogenous cannabinoids (eCBs):
  - N-arachidonoylethanolamide, referred to as anandamide or AEA, and
  - 2-arachidonoylglycerol (2-AG).
- eCBs are derived from inactive precursors and are particularly generated in times of stress, disease, or injury.
- Unlike traditional neurotransmitters, such as glutamate and GABA, which are preformed and stored in intracellular vesicles until needed, eCBs are created on demand from inactive phospholipid precursors embedded in the cell membrane.
- Most neurotransmitters are water-soluble and require transmembrane proteins to transport them across the cell membrane - eCBs (AEA and 2-AG) are uncharged lipid molecules that readily diffuse across the cellular membranes.

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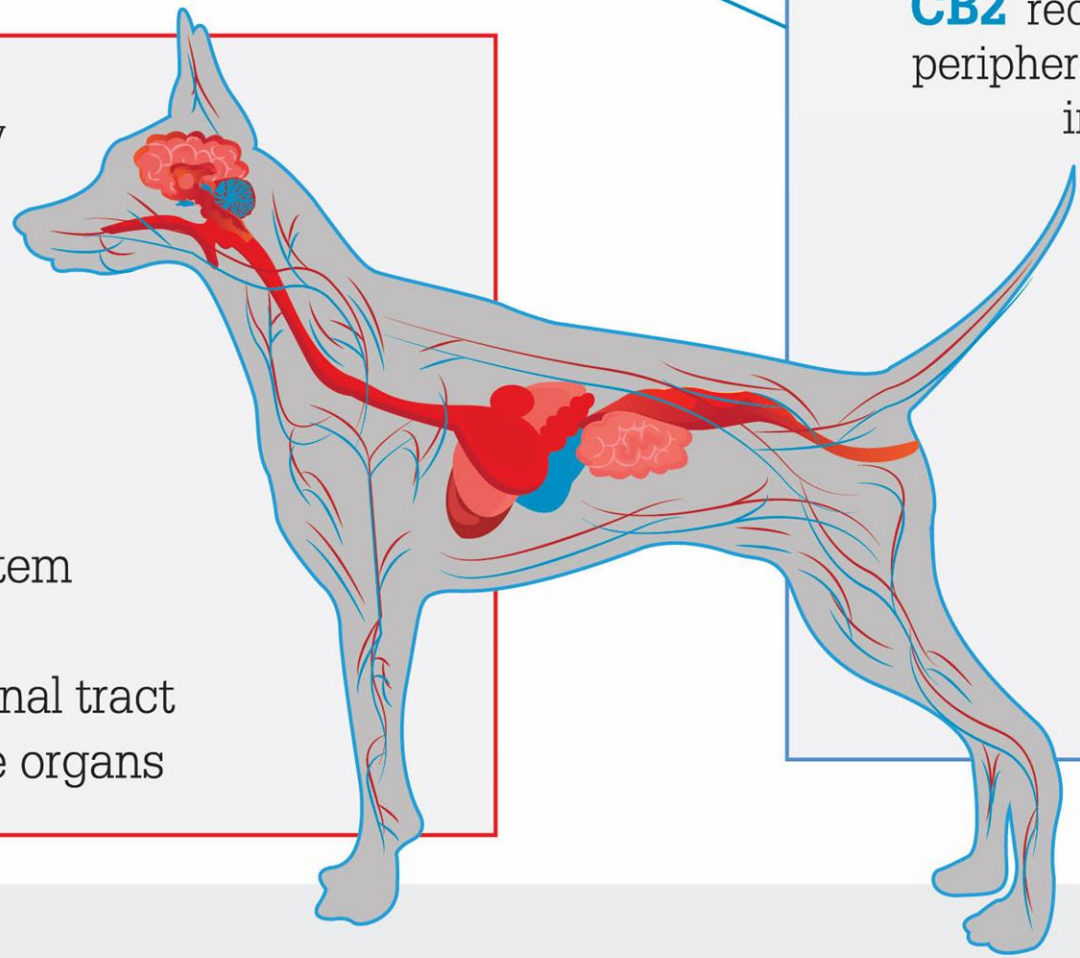
CANNABINOID CB1 & CB2 RECEPTOR LOCATIONS IN DOGS

CB1 receptors are mostly in the brain and central nervous system

CB1

+ Brain
+ Lungs
+ Vascular system
+ Muscles
+ Gastrointestinal tract
+ Reproductive organs



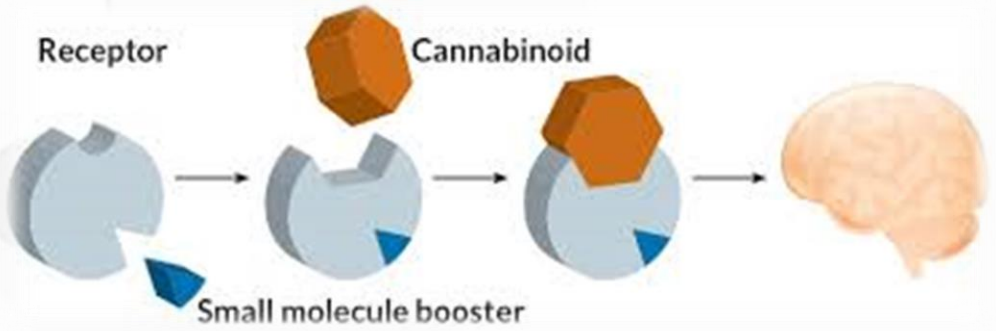
CB2 receptors are mostly in peripheral organs, especially immune cells

CB2

+ Spleen
+ Bones
+ Skin
+ Glial cells (parts of brain)

CB1 + CB2 + Immune system + Liver + Bone marrow + Pancreas + Brainstem

CBD ALSO HAS AN AFFINITY FOR OTHER RECEPTORS:



- Dopamine
  - *Emotion*
  - *Movement*
  - *Sensations of pleasure and pain*
- Serotonin
  - *Mood & happiness*
- Opioid
  - *Pain*

CBD ADMINISTRATION

- Inhalation
  - quickest onset
  - may have a greater bioavailability
- Topical application
  - lotions/creams
- Oral CBD
  - oil based drops / paste
  - oil based capsules
  - oils/tinctures (sublingual or added to food/beverages)
- Edibles
  - gummy bears
- Transdermal skin patch

CBD SIDE EFFECTS

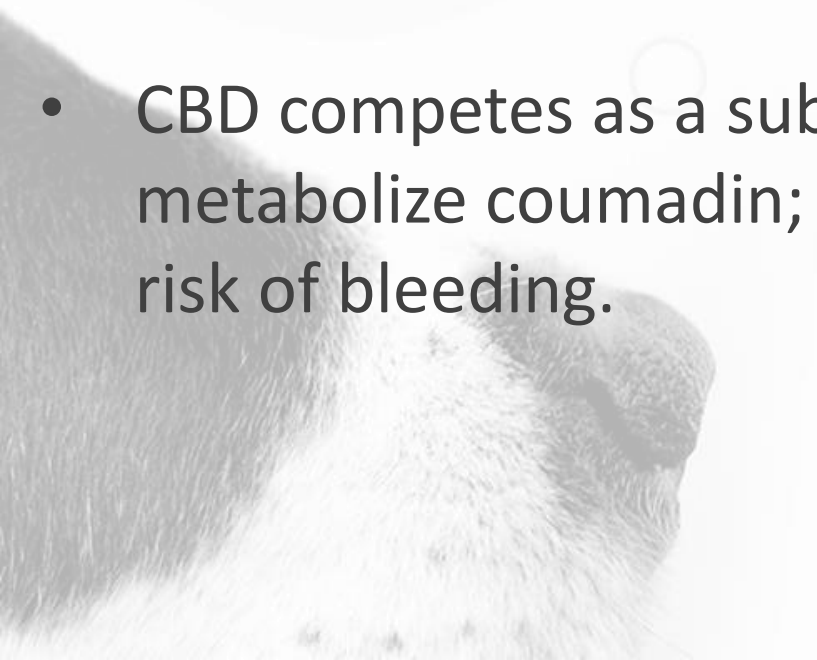
- Sedation/lethargy
- Decreased appetite
- Diarrhea
- Rash
- Sleep disorder
- Psychiatric (depression, anxiety)
- Liver toxicity
    - Long-term consequences??

CBD DRUG INTERACTIONS

- CBD is metabolized by the liver by the Cytochrome (CYP) enzyme system.

- Many drugs either “ramp up” or “ramp down” the CYP metabolic pathway which can affect CBD concentration in the blood.

- CBD competes as a substrate for some of the same CYP enzymes that metabolize coumadin; coumadin blood levels elevate resulting in an increased risk of bleeding.



CBD IN DOGS

Pharmacokinetics, Safety, and Clinical Efficacy of Cannabidiol Treatment in Osteoarthritic Dogs

Lauri-Jo Gamble , Jordyn M Boesch, Christopher W Frye, Wayne S Schwark, Sabine Mann, Lisa Wolfe, Holly Brown, Erin S Berthelsen, Joseph J Wakshlag

Front Vet Sci. 2018 Jul 23;5:165. doi: 10.3389/fvets.2018.00165. eCollection 2018.

- To determine basic oral pharmacokinetics and assess safety and analgesic efficacy of a cannabidiol (CBD) based oil in dogs with osteoarthritis (OA).
- Single-dose pharmacokinetics was performed using two different doses of CBD enriched (2 and 8 mg/kg) oil.
- Thereafter, a randomized placebo-controlled, veterinarian, and owner blinded, cross-over study was conducted.
- Dogs received CBD oil (2 mg/kg) or placebo oil every 12 h - Treatment lasted for 4 weeks with a 2-week washout period.
- Pharmacokinetics revealed an elimination half-life of 4.2 h at both doses and no observable side effects.
- Clinically, canine brief pain inventory and Hudson activity scores showed a significant decrease in pain and increase in activity ($p < 0.01$) with CBD oil.
- Veterinary assessment showed decreased pain during CBD treatment ($p < 0.02$).
- No side effects were reported by owners.
- Serum chemistry showed an increase in alkaline phosphatase during CBD treatment ($p < 0.01$).

CLINICAL SIGNIFICANCE

This pharmacokinetic and clinical study suggests that 2 mg/kg of CBD twice daily can help increase comfort and activity in dogs with OA.

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The Use of Cannabidiol-Rich Hemp Oil Extract to Treat Canine Osteoarthritis-Related Pain: A Pilot Study

Lori Kogan, PhD, Peter Hellyer, DVM, Robin Downing, DVM, MS

AHVMA Journal • Volume 58 Spring 2020

- 90-day pilot clinical trial - assess the impact of a full-spectrum product containing hemp extract and hemp seed oil on dogs with chronic maladaptive pain.
- 37 dogs diagnosed with chronic maladaptive pain primarily as a result of osteoarthritis.
- Biweekly assessment.
- 30 dogs demonstrated improved pain support.
- 10 dogs in the study discontinue the use of gabapentin, and an additional 11 dogs were able to have their daily dose reduced with the addition of the cannabidiol (CBD) oil.
- The reduction in gabapentin dose may be the result of changes in analgesia and/or sedation with the addition of the hemp oil extract.

CLINICAL SIGNIFICANCE

The addition of a hemp derived CBD oil appears to positively affect dogs with chronic maladaptive pain by decreasing their pain, thereby improving their mobility and quality of life.

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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

Stephanie McGrath, Lisa R Bartner, Sangeeta Rao, Rebecca A Packer, Daniel L Gustafson

J Am Vet Med Assoc. 2019 Jun 1;254(11):1301-1308. doi: 10.2460/javma.254.11.1301.

- To assess the effect of oral cannabidiol (CBD) administration in addition to conventional antiepileptic treatment on seizure frequency in dogs with idiopathic epilepsy.
- Dogs were randomly assigned to a CBD (n = 12) or placebo (14) group.
- The CBD group received CBD-infused oil (2.5 mg/kg, PO) twice daily for 12 weeks in addition to existing anti-epileptic treatments, and the placebo group received non-infused oil under the same conditions.
- 2 dogs in the CBD group developed ataxia and were withdrawn from the study.
- Dogs in the CBD group had a significant (median change, 33%) reduction in seizure frequency, compared with the placebo group.
- No adverse behavioral effects were reported by owners.

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CLINICAL SIGNIFICANCE

Significant reduction in seizure frequency was achieved for dogs in the CBD group, the proportion of responders was similar between groups.

Additional research is warranted to determine whether a higher dosage of CBD would be effective in reducing seizure activity by ≥ 50%.

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CBD IN CATS

Single-Dose Pharmacokinetics and Preliminary Safety Assessment with Use of CBD-Rich Hemp Nutraceutical in Cats

Published: 19 October 2019

Kelly A. Deabold, Wayne S. Schwark, Lisa Wolf and Joseph J. Wakshlag.

- Single-dose PK evaluation followed by a 12-week safety assessment in cats.
- 8 healthy research cats - CBD-infused fish oil - 2 mg/kg of the CBD mixed oil orally BID for 84 days.
- 1 cat had a persistently elevated ALT (above the upper limit of the reference range).
- The main adverse events reported were excessive licking and head shaking.
- Cats appear to absorb or eliminate CBD differently than dogs.
- Overall, the absorption kinetics showed maximum serum concentrations are approximately one-fifth of what was observed in the dogs, with a longer retention time and T1/2.
- The delivery method and form can certainly affect absorption and bioavailability.

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Dose (per kg body weight) indications

- Micro (0.1 mg/kg) – anxiety, fear, stress, behavioral issues, mild pain, muscle tension
- Medium (0.2-0.5 mg/kg) – osteoarthritis, moderate pain, muscle spasms
- High (0.5-1.0 mg/kg) – moderate to severe pain, neurogenic pain, degenerative myelopathy, tremors, idiopathic epilepsy, diabetes regulation, IBD
- Ultra (1.0-5.0 mg/kg) – refractory epilepsy, anti-neoplastic, refractory pain, hospice care

Afrigen
Biologics & Vaccines
An Avacare Health & IDC Company

THE TECHNOLOGY BEHIND THE PRODUCTS

WHY IS BIOAVAILABILITY FOR CBD IMPORTANT?

- Oral bioavailability is low (~ 4-6%) as CBD is lipophilic.
- Average pet owner not informed of limited uptake of regular CBD products on the market.

NANOZOMAL™ IMPROVING BIOAVAILABILITY

- Using technology to re-engineer formulation of CBD products.
- Essentially converting a lipophilic compound into a hydrophilic compound.
- Better for uptake in the body with improved bioavailability (up to 75%) – 15 X more bioavailable.
- Improved stability of final products.

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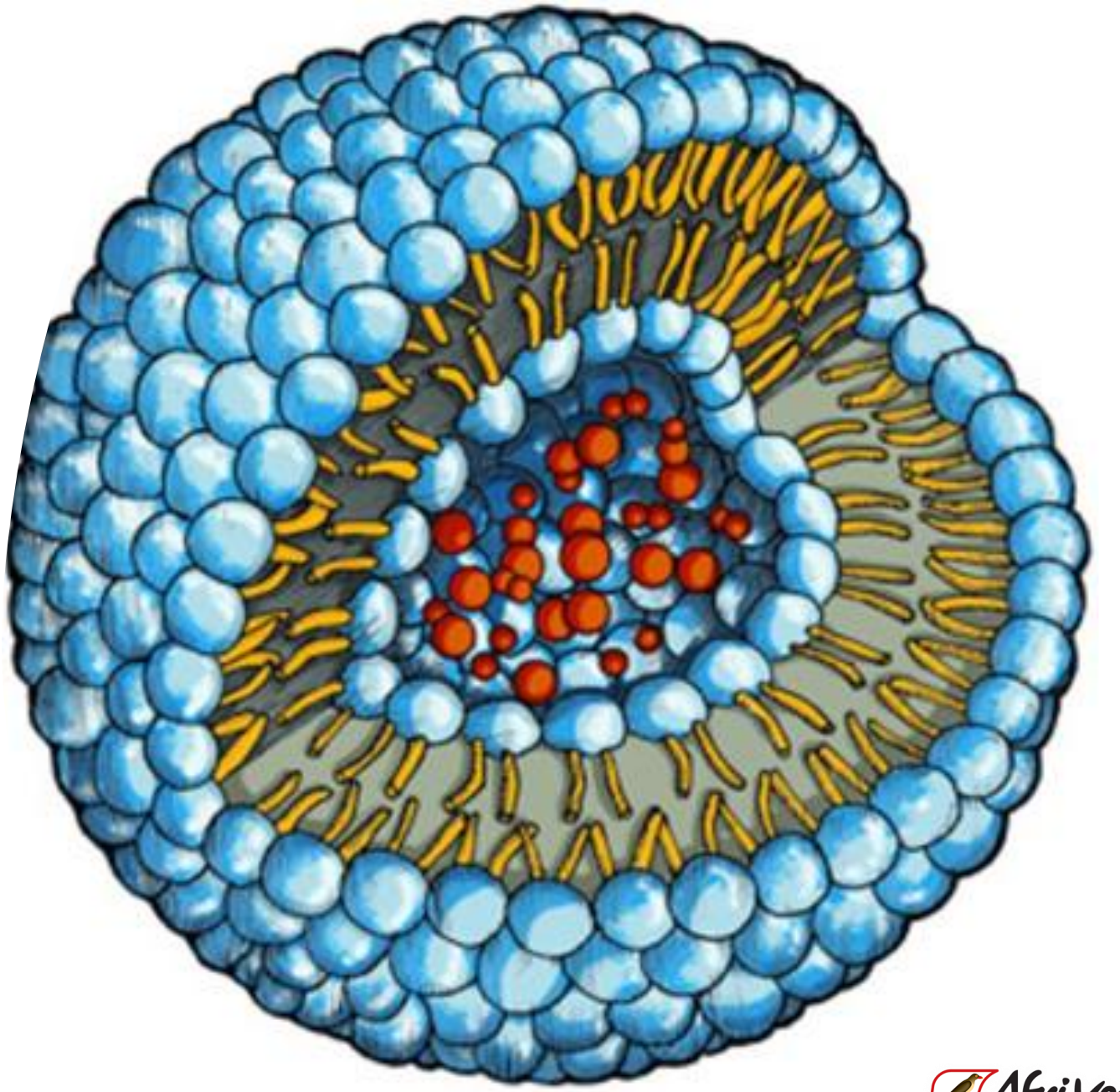
INCREASED BIOAVAILABILITY OF ACTIVES

- Liposomes are ‘nano' sized particles or sphere (vesicle) made from a phospholipid - same material that makes up cell membranes in our body.
- Liposomes can carry either water or fat-soluble active ingredients making them an ideal delivery system for active ingredients.



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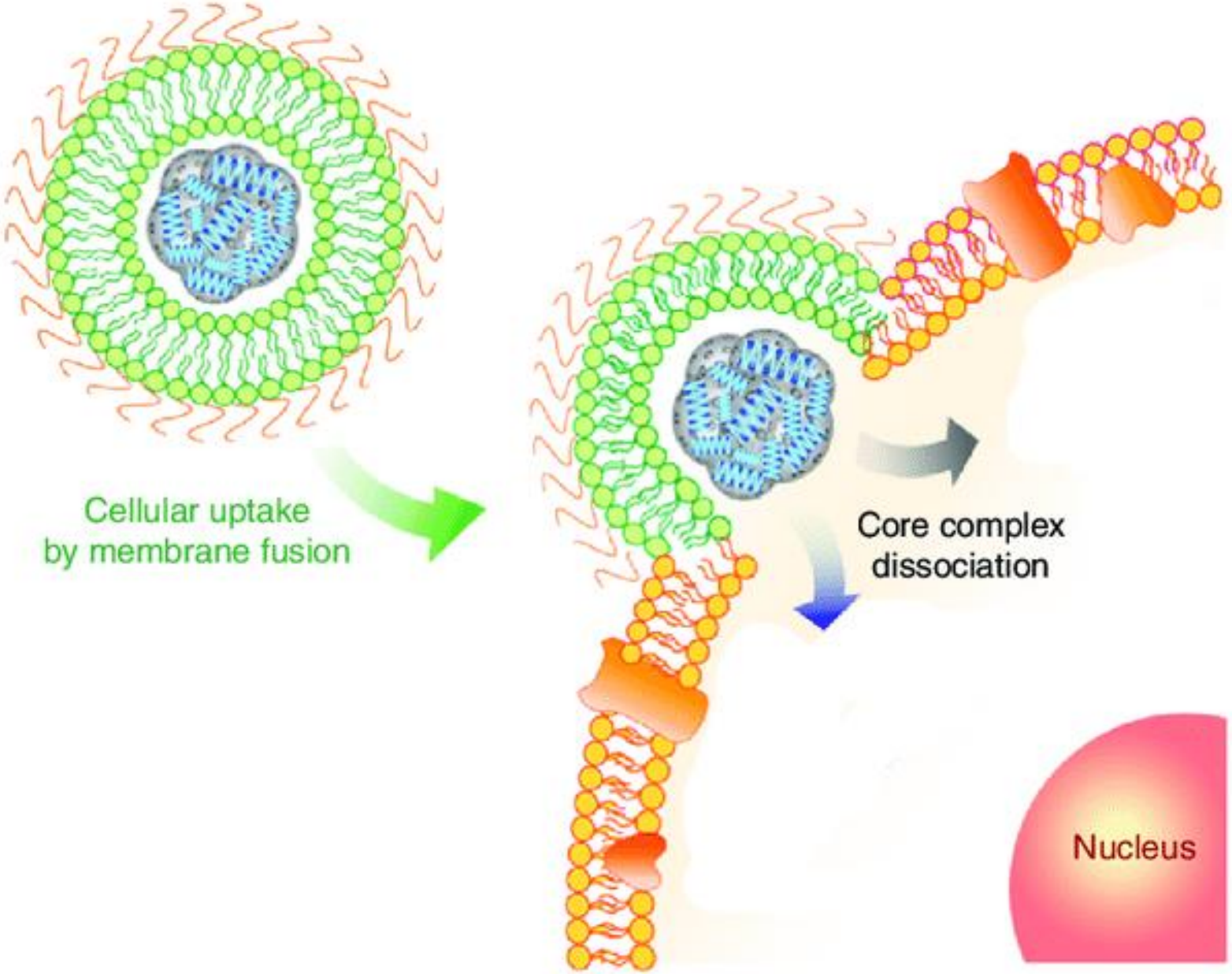
INCREASED BIOAVAILABILITY OF ACTIVES

LIPOSOME WITH
ACTIVE INGREDIENT



Standard Oil

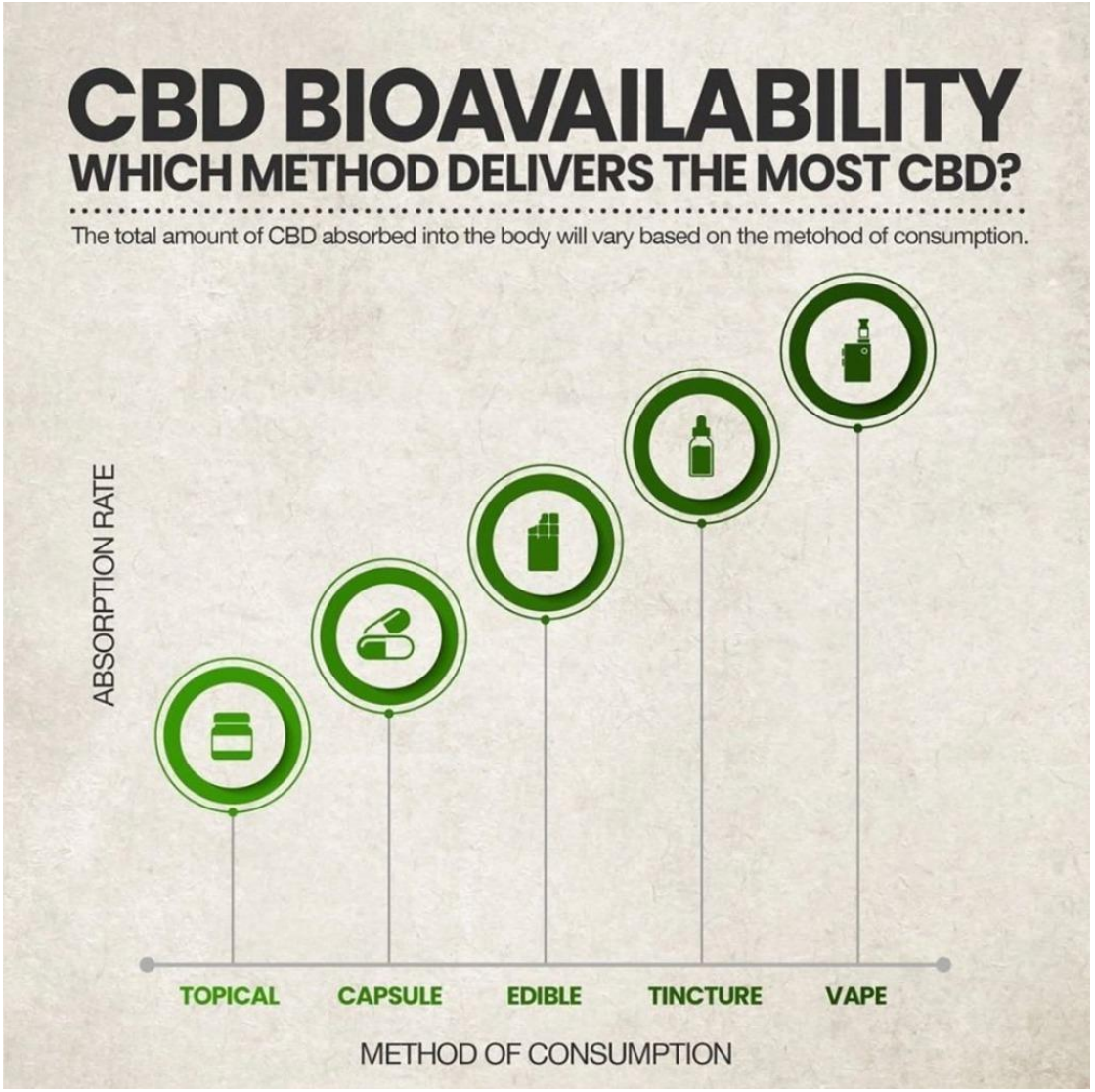
10% or less Absorption

Liposomal Microemulsion

100-1000 Nanometer
<20% Absorption

Nano-Sized Microemulsion

25 Nanometer (AVG)
>50% Absorption
Maximum Bioavailability



A randomized, double-blind, placebo-controlled study of daily cannabidiol for the treatment of canine osteoarthritis pain

Chris D Verrico, Shonda Wesson, Vanaja Konduri, Colby J Hofferek, Jonathan Vazquez-Perez, Emek Blair, Kenneth Dunner Jr, Pedram Salimpour, William K Decker, Matthew M Halpert

PubMed.gov 2020 Sep 1;161(9):2191-2202. doi: 10.1097/j.pain.0000000000001896.

- Therapeutic potential of both naked and liposomally encapsulated CBD was explored in a 4-week, randomized placebo-controlled, double-blinded study in a spontaneous canine model of OA.
- CBD significantly decreased pain and increased mobility in a dose-dependent fashion among animals with an affirmative diagnosis of OA.
- Liposomal CBD (20 mg/day) was as effective as the highest dose of non-liposomal CBD (50 mg/day) in improving clinical outcomes.
- Hematocrit, comprehensive metabolic profile, and clinical chemistry indicated no significant detrimental impact of CBD administration over the 4-week analysis period.

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CLINICAL SIGNIFICANCE

This study supports the safety and therapeutic potential of hemp-derived CBD.

Liposomal CBD (20 mg/day) was as effective as the highest dose of non-liposomal CBD (50 mg/day) in improving clinical outcomes.

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Nanozomal™ CBD+

Powered by Nanotechnology

DELIVERS
15x MORE
CBD COMPARED
TO REGULAR CBD[1]

ASSISTS WITH THE RELIEF OF [2]
- anxiety
- stress
- sleeplessness
- minor pain
- inflammation

NEW CBD RANGE

CBD OIL POWERED BY NANOTECHNOLOGY

WHY CHOOSE NANOZOMAL™ CBD + ?

NANOZOMAL™ CBD + is a premium quality CBD range, powered by nanotechnology. It is highly absorbable, which means faster onset of symptomatic relief.[1] Backed by science and manufactured under stringent conditions.

NANOZOMAL™ CBD + is made using Organic compliant CBD. Our wide range of broad-spectrum, THC-FREE products are suitable to assist with the relief of minor symptoms, including anxiety, stress, sleeplessness, minor pain and inflammation.[2]

References

1. Nakano Y, Tajima M, Sugiyama E, et al. Development of a novel nanoemulsion formulation to improve intestinal absorption of a cannabidiol. Kager 2019; Med Cannabis Cannabinoids 2019;2:35–42.
2. Bruni N, Pepa CD, Oliaro-Bosso S, et al. Cannabinoid delivery systems for pain and inflammation treatment. Molecules 2018;23:2478;doi.org/10.3390/molecules23102478.

Developed by Afrigen

Distributed by biodelta

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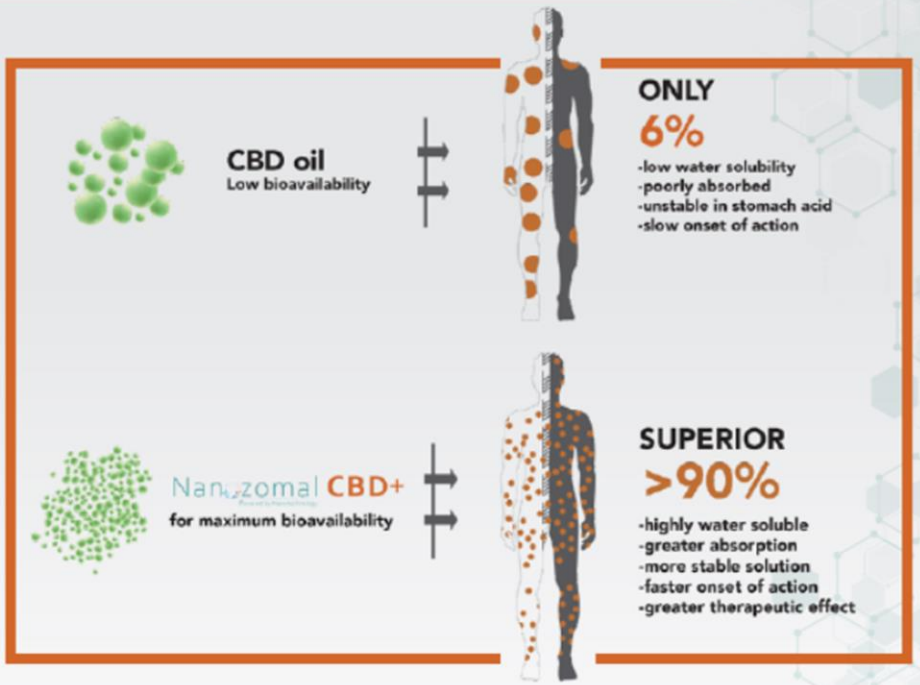
NANOTECHNOLOGY MAXIMISES THE THERAPEUTIC EFFECT OF CBD

CBD NANOEMULSION PROVIDES LEVELS OF BIOAVAILABILITY AND EFFECTIVENESS THAT FAR EXCEED THAT OF CBD OIL



- Delivers 15x more CBD per dose vs. CBD oil
- Therapeutic efficacy
- Quick onset of action
- Contains organic and broad-spectrum CBD (THC free)
- Can be mixed into beverages
- Manufactured in a local laboratory under stringent conditions

Nanozomal™ CBD+

Powered by Nanotechnology

BUYER BEWARE!
(POOR REGULATION)

- Is there THC in the product?
- Advertised amount?
  - *may have more CBD*
  - *may have less CBD*
  - *may have no CBD*

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THANK YOU