

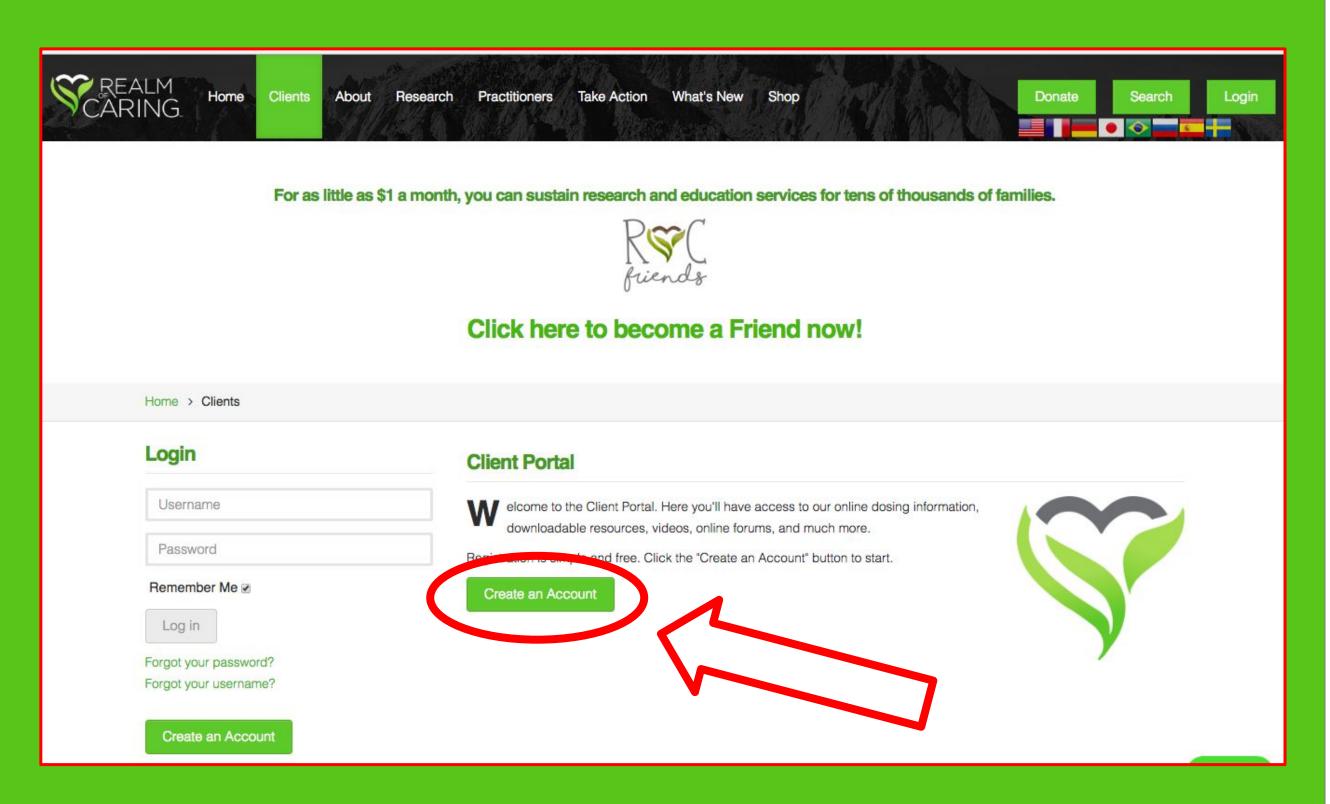
THE REALM OF CARING FOUNDATION SPECIFICALLY INVOKES THE FIRST AMENDMENT RIGHTS OF FREEDOM OF SPEECH AND OF THE PRESS WITHOUT PREJUDICE. THESE STATEMENTS HAVE NOT BEEN EVALUATED BY THE FOOD AND DRUG ADMINISTRATION. THE PRODUCTS DISCUSSED ARE NOT INTENDED TO DIAGNOSE, CURE, PREVENT OR TREAT ANY DISEASE. ROC ALWAYS RECOMMENDS WHEN AND WHEREVER POSSIBLE THAT LICENSED LOCAL HEALTHCARE PROFESSIONALS BE CONSULTED.

THE REALM OF CARING FOUNDATION IS AN INDEPENDENT NONPROFIT WITH ITS OWN GOVERNING BOARD. WE DO NOT PRODUCE OR SELL CANNABINOID PRODUCTS, NOR DO WE RECEIVE FUNDS FROM THE SALE OF OTHER COMPANY'S PRODUCTS.

Getting Started: What Are We Covering Today?

- Realm of Caring Overview
 - History, What We Do, Who We Serve,
 Mission/Vision, Our Demographics,
 Research, Resources
- Quality of Life Guide at RoC
- Research Initiatives & Research Library
- CBD & THC & Terpenes
- CBD from Hemp vs CBD from Marijuana
- The Endocannabinoid System
- Administration & Half Llfe
- The Entourage Effect
- Quality Products
- Side Effects, Potential Interactions, Safety
- How to talk with your healthcare provider
- Donate, Volunteer, Register

Be Sure to Register: theroc.us/clients



Create An Account















Because quality of life matters

The Realm of Caring (RoC) is an independent 501(c)3 high impact nonprofit that is re-defining the way we talk about cannabis.

- * Collaborating on innovative research.
- * Providing revolutionary education.
- * Empowering people to lead better lives.

Research · Education · Advocacy · improving Lives · Measurable results













Services

For members, physicians, community

MEMBERS/CLIENTS (over 58,000)

- Detailed Guide to CBD
- How to talk with your doctor
- Guide to using cannabinoid oils
- Research library
- IRB-Approved Research Study (ORR)
- Administration resources and calculators
- Drug interaction information
- Helpful Videos
- Orientation (webinar and in-person)
- Online Client Forums
- Monthly support groups
- Connect to others with your diagnosis
- Discounts on approved CBD products
- Realm Cares[™] Family assistance grants
- Joy Fund Relocation grants
- And more

PHYSICIANS (Over 1,400)

- Provider resources
- Referrals
- Use of ORR for approved physicians
- Monthly provider education
- Research logistics
- Funding for research
- And more

COMMUNITY

- School education
- Hospital education
- Nursing agency education
- Grassroots political efforts
- Legislative testimony
- Family support
- Continuing Education Units
- And more





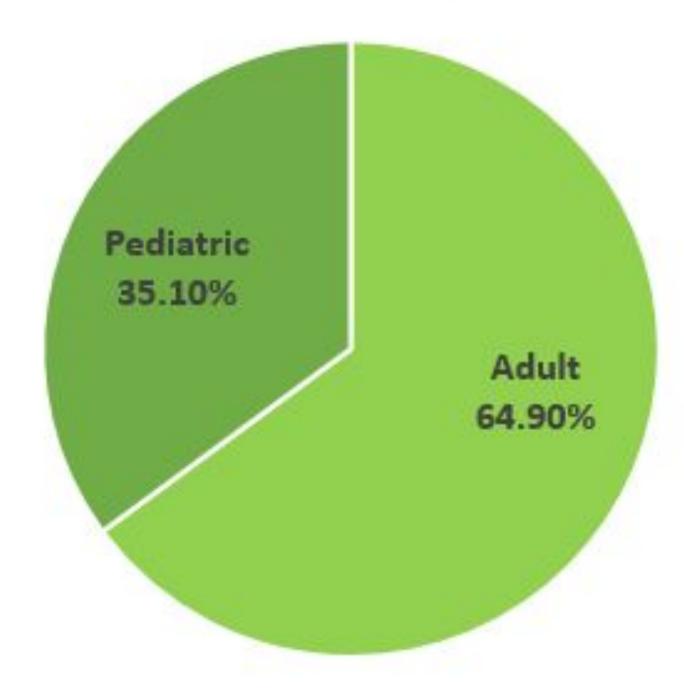






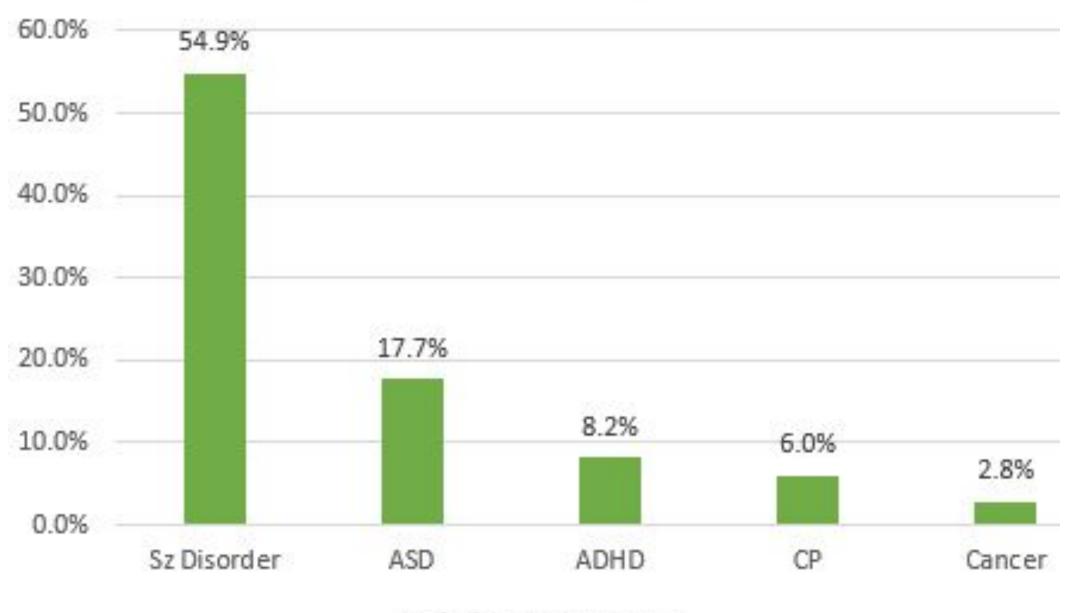
Realm Demographics



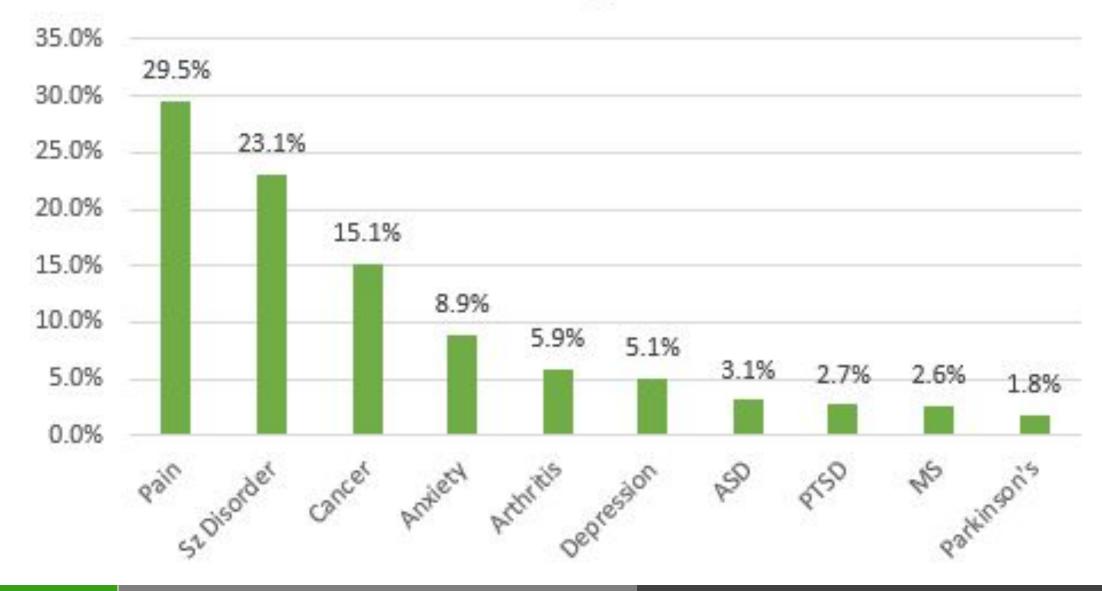


- Over 58,000 clients worldwide
- Demographics have changed significantly in 5 years

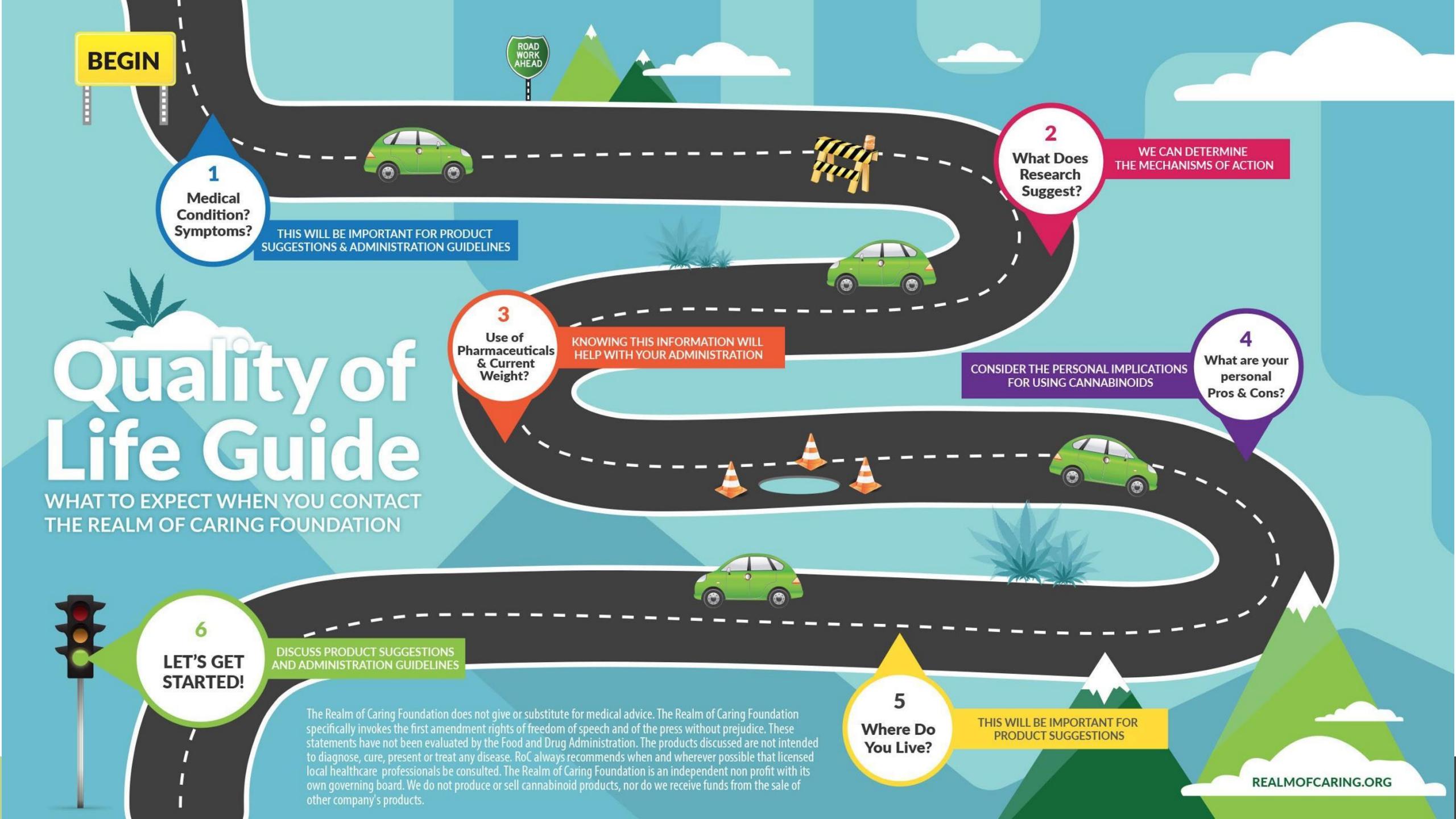
Pediatric Diagnoses



Adult Diagnoses









Current Research Initiatives

Enrolling in 5 studies











Other Research Projects

- Metabolite Study
- Current NFL Player Study
- Former Professional Athlete Study
- Adult Epilepsy Study
- PTSD at Harvard

Observational Research Registry (ORR)

- Institutional Review Board (IRB) approved
- In collaboration with Johns Hopkins University,
 University of Pennsylvania, VA Palo Alto and others
- Launched April 2016
- Open to anyone with any condition, whether using cannabis or not
- Largest cannabis observational study in the USA













Research Resources

USE THE SEARCH FIELDS TO FIND INFORMATION

Conditions	
Pain (35) ×	δ-Ctenitoxin-Pn1a, a Peptide from Phoneutria nigriventer
	Spider Venom, Shows Antinociceptive Effect Involving Opioid
Research Keywords	and Cannabinoid Systems, in Rats
All Research Keywords	PnTx4(6-1), henceforth renamed δ-Ctenitoxin-Pn1a (δ-CNTX-Pn1a), a peptide
100	from Phoneutria nigriventer spider venom, initially described as an insect toxin,
Search Text	binds to site 3 of sodium channels in nerve cord synaptosomes and slows down
ocurent text	sodium current inactivation in isolated axons in cockroaches (Periplaneta
	americana). δ-CNTX-Pn1a does not cause any apparent toxicity to mice, when
	intracerebroventricularly injected (30 []
ournal	
All Items	Use of Prescription Pain Medications Among Medical Cannabis
All Items	
All Items Publication Years	Patients: Comparisons of Pain Levels, Functioning, and
Publication Years	그는 사람들이 얼마나 되었다면 하는 것이 되었다면 하는 것이 되었다면 하는 것이 없는 것이었다면 없는 것이었다면 없는 것이 없는 것이었다면 없는 없는 것이었다면 없었다면 없는 것이었다면 없는 것이었다면 없는 것이었다면 없었다면 없는 것이었다면 없는 것이었다면 없었다면 없었다면 없었다면 없었다면 없었다면 없었다면 없었다면 없
Publication Years	Patients: Comparisons of Pain Levels, Functioning, and Patterns of Alcohol and Other Drug Use
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Publication Years 1972 - 2022 Human or Animal	Patients: Comparisons of Pain Levels, Functioning, and Patterns of Alcohol and Other Drug Use Objective: Management of chronic pain is one of the most common reasons give by individuals seeking medical cannabis. However, very little information exists about the concurrent use of cannabis and prescription pain medication (PPM).
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Realm of Caring Research Library https://www.theroc.us/research-library

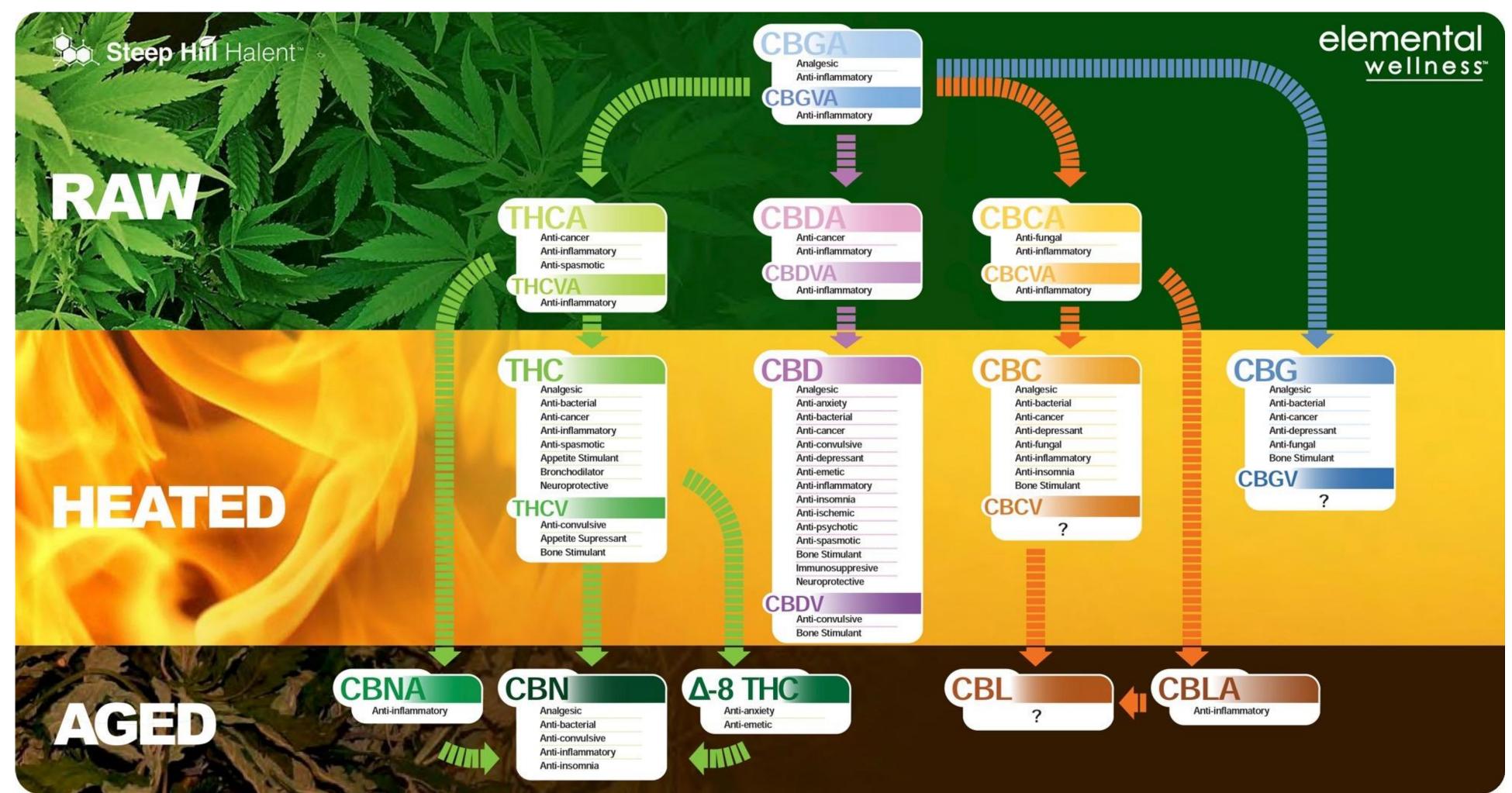
International Research http://www.cannabis-med.org/

Domestic Research (NIH) https://www.pubmed.gov



What Is Cannabis?

- Over 400 chemical compounds identified
- 65+ of these compounds are specific to the cannabis plant, known as cannabinoids or phytocannabinoids (for example, they are delta -9- tetrahydrocannabinol (THC), tetrahydrocannabivarin (THCV), cannabidiol (CBD), cannabichromene (CBC), and cannabigerol (CBG).



5









What is CBD? What is THC?

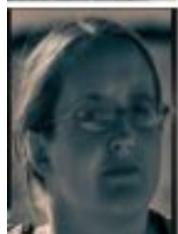
CBD is a major phytocannabinoid from the Cannabis plant which is non-addictive and research has shown that it has more than 52 mechanisms of action (therapeutic benefits).

THC is phytocannabinoid uniquely found on the cannabis plant. THC works by binding to cannabinoid receptors concentrated in the brain and central nervous system to produce psychoactive effects.

Hemp Derived CBD vs "Cannabis" Derived CBD

- Cannabis and Hemp are biologically the same plant!
- CBD derived from hemp contains less than 0.3%THC.
- Cannabis also known as "marijuana" contains more than 0.3% THC.
- Hemp derived CBD products are not designed to get people or animals high or inebriated.
- It is possible to produce a positive drug test when using whole plant hemp products because the trace amounts of THC consumed is stored in the fatty tissues in the body.
- Hemp can be purchased and used in all 50 states and even some countries like Canada and the EU.
- Access to Medical or Recreational Cannabis requires your state to establish cannabis dispensaries or licensed caregivers to dispense products with higher THC amounts.











What Is The "Entourage Effect"?

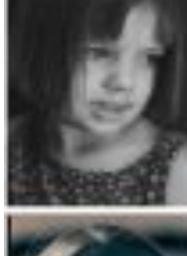


- Whole plant extractions typically include CBD, THC, and more than 400 trace compounds.
- Synergy amongst compounds: **Entourage Effect**
- The combined action magnifies the therapeutic benefits of the plant's individual components.
- **CBD Isolates** (CBD only products) uses one out of the hundreds of compounds that are meant to work together to produce homeostasis (balance) in the body.
- Broad Spectrum products retain a whole plant profile but contain 0% THC.
- If THC is prohibitive due to drug tests Broad
 Spectrum or CBD Isolates may reduce the chances of THC detection.
- Please note: NO guarantees that these particular extractions will not produce a positive test result!





How Does Cannabis Work?









The Human Endocannabinoid System

CBD, CBN and THC fit like a lock and key into existing human receptors. These receptors are part of the endocannabinoid system which impact physiological processes affecting pain modulation, memory, and appetite plus anti-inflammatory effects and other immune system responses. The endocannabinoid system comprises two types of receptors, CB1 and CB2, which serve distinct functions in human health and well-being

THC

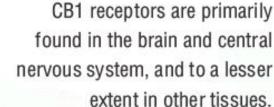
CBD

CBN

Tetrahydrocannabinol

Cannabidiol

Cannabinol



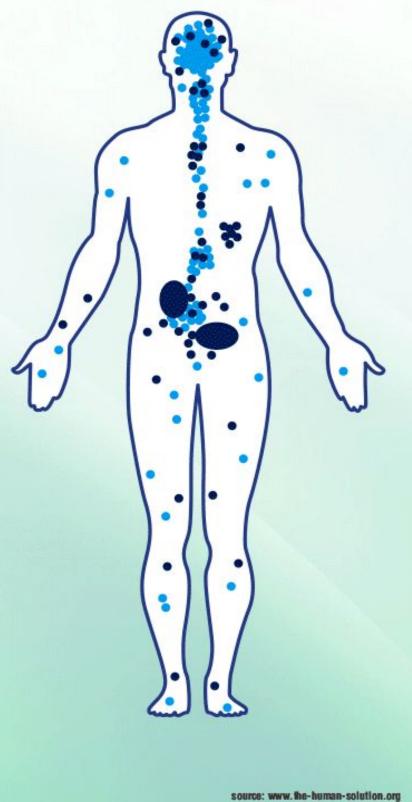
Receptors are found on cell surfaces



CBD does not directly "fit" CB1 or CB2 receptors but has powerful indirect effects still being studied



CB2 receptors are mostly in the perepheral organs especially cells associated with the immune system.



Cannabis works directly with the Endocannabinoid System.

The Endocannabinoid System (ECS) is a network of receptors located in the brain and throughout the nervous system; it is the body's way of maintaining and regulating the homeostasis of crucial body functions.



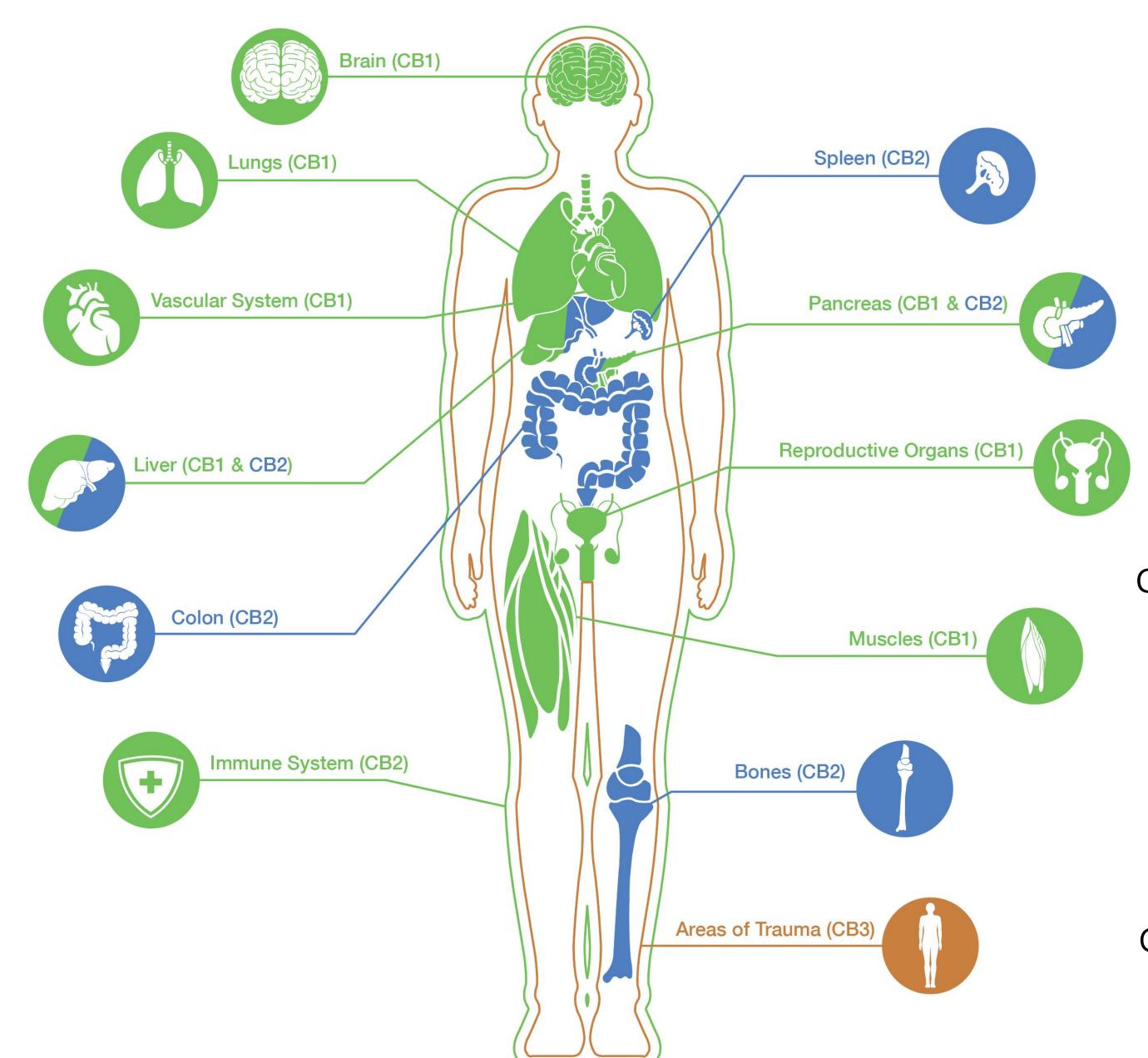












Endocannabinoid System interacts with these other regulatory systems in our body.

<u>CB1</u>

Central Nervous System Sleep

Pain

Memory

Mood

Smell

Appetite

Liver Activity
Cardiovascular Activity

Gastrointestinal Activity

<u>CB2</u>

Peripheral Nervous
System
Immune System
Gastrointestinal Activity
Brain Activity











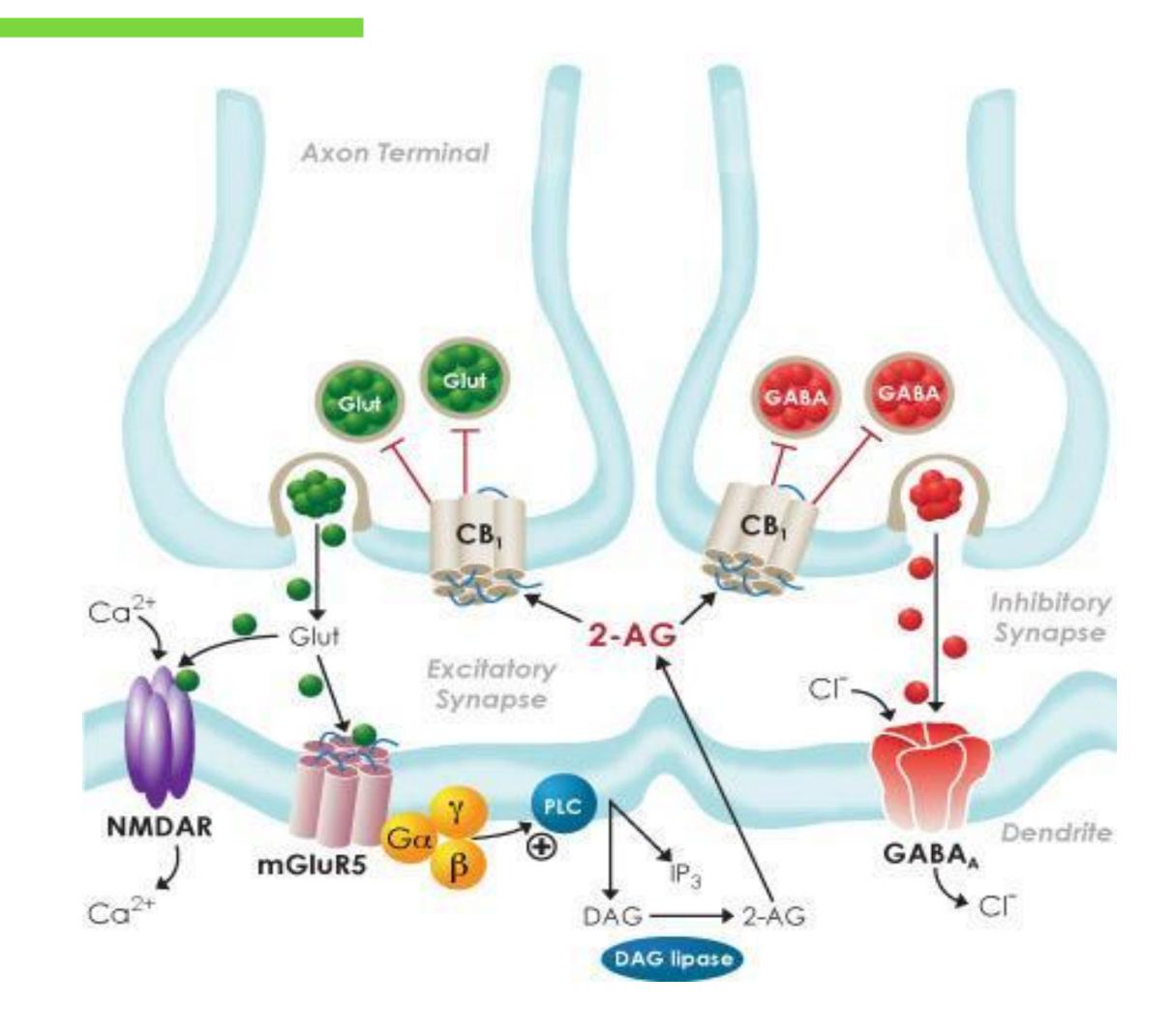
Mechanisms Of Action

CBD interacts with many other non-endocannabinoid receptors

Summary: Neurological and Immune modulation.

Evidence that CBD works on the following brain receptors:

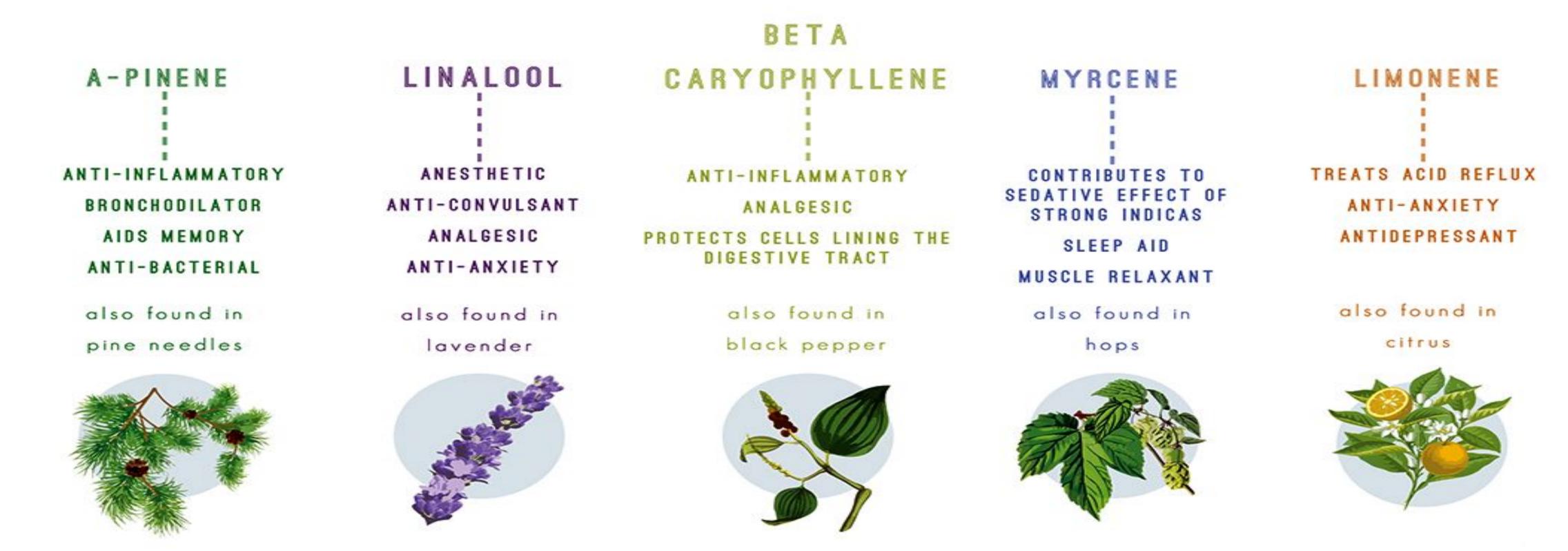
- CB1 neuromodulation
- CB2 neuro/immune modulation
- 5-HT1A receptors, antidepressant, anti-anxiety
- Endogenous Opioid Receptors (mechanism for pain "analgesic" effects).
- GABA (Gamma-aminobutyric acid is an amino acid in the body that acts as a neurotransmitter in the central nervous system).
- Decrease glutamate (excitatory neurotransmitter that is released by nerve cells in the brain).
- Regulate Ca2 Channels (calcium channel)
- Modulate ion channels
- Enhancing adenosine an endogenous anti-inflammatory
- It also acts upon other receptors with neuroprotective effects



How Do Terpenes Affect the ECS, THC, & CBD?

What are Terpenes?

- Aromatic components, plant's smell/odor
- Made in the flower bud
- Found in many plants and foods (i.e. black pepper, cinnamon, citrus fruits)
- Effect modulation ECS, especially the uptake of THC, CBD and other phytocannabinoids.



How Might Cannabis Alleviate CRPS? Peer-Reviewed Journal Articles

Burns Trauma. 2017; 5: 2.

Published online 2017 Jan 19. doi: 10.1186/s41038-016-0066-4

Complex regional pain syndrome: a recent update

En Lin Goh, "Swathikan Chidambaram," and Daging Ma

Neuroscience. 2005;135(1):235-45.

Peripheral nerve injury induces cannabinoid receptor 2 protein expression in rat sensory neurons.

Wotherspoon G1, Fox A, McIntyre P, Colley S, Bevan S, Winter J.

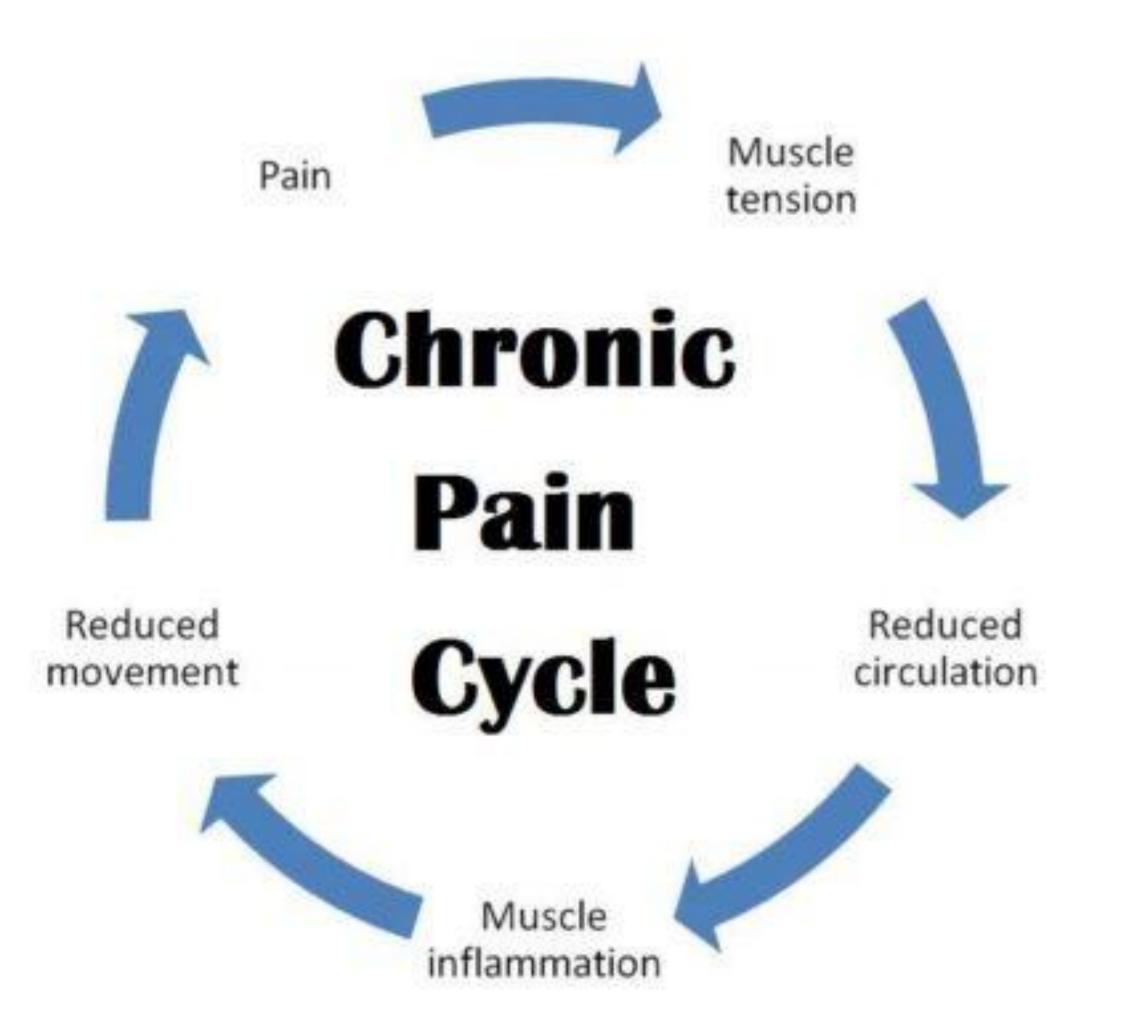
Eur J Neurosci. 2016 Dec;44(12):3046-3055. doi: 10.1111/ejn.13414. Epub 2016 Oct 13.

Activation of cannabinoid receptor 2 attenuates mechanical allodynia and neuroinflammatory responses in a chronic postischemic pain model of complex regional pain syndrome type I in rats.

Xu J^{1,2}, Tang Y^{3,4}, Xie M¹, Bie B⁴, Wu J⁴, Yang H⁴, Foss JF⁴, Yang B⁵, Rosenquist RW¹, Naguib M^{4,6}.

- CB2 receptors play a significant role in neuroinflammation.
- Potentially reduce pain and inflammation by regulating the CB2 receptors.
- Rat models with CRPS prove this hypothesis to be true.
- Next steps: human studies.
 Though plenty of anecdotal accounts.

How Might Cannabis Alleviate CRPS?



- Heightened pain perception can be rooted in a malfunctioning neurological system or a structural problem (including peripheral nerve abnormalities), but it can also arise from chronic inflammation, of which pain is a primary symptom. This may indicate a compromised immune system which regulates inflammation in the body. Research suggests CBD is a strong anti-inflammatory that can regulate pain on a cellular level.
- Cannabinoids like CBD may also help alleviate pain by targeting and activating *glycine receptors* the central nervous system.
- Glycine receptors are located in in various regions of the brain and spinal cord and play an important role in reducing chronic inflammatory pain and neuropathic pain.
- When inflammatory factors such as *prostaglandins* are present, they often shut down these receptors, which increases the sensation of pain, but CBD can reactivate these receptors and decrease pain hypersensitivity.



What Is a Quality Product?

Because Quality of Product Matters

Quality of Product Matters



What about other products?

Here are some great questions to ask manufacturers and suppliers to better understand the quality and consistency of their products.

Sourcing

- 1. In what country is the product grown?
- 2. Is it certified as hemp? By whom?
- 3. Is it grown naturally using organic processes?
- 4. Can you track production of the product from seed to delivery?
- 5. Is there a consistent supply? Is it possible I'll run out?

Quality

- How many milligrams of active cannabinoids (CBD, THC, THC-A, etc.) does the product contain? What is the total volume (milliliters) of the product?
 - Active cannabinoids are typically described in terms of milligrams per milliliter (mg/ml).
- Is the product third party tested for the following:
 - a. Identity
 - Potency (Cannabinoid Profile)
 - c. Heavy Metals:
 - i. Inorganic Arsenic
 - ii Cadmium
 - iii. Lead
 - Methylmercury

- d. Residual Solvents
- e. Aflatoxins
- f. Microbial Contaminants:
 - Aerobic Plate Count
 - Yeast and Molds
 - iii. Coliforms
 - iv. Salmonella spp.
 - v. Escherichia coli

- 3. Is it produced in an FDA registered lab?
 - a. Are they following the FDA's CGMP standards?
 - b. Do they adhere to the American Herbal Products Association (AHPA) guidelines?

Cost and Customer Service

- 1. What is the cost per milligram? Is there financial assistance?
- Is there a refund policy?
- 3. Is customer service readily available?
- 4. Who will help me with questions regarding use of the product?

- The only way to prove efficacy is to measure, and repeat with consistent products
- FACT: Cannabis is safe. Very safe. Not ensuring consistency, proper labeling and testing can cause an inadvertent event.
- American Herbal Products Association (AHPA) guidelines
- Current Good Manufacturing Practices (cGMP) labs
- Self Regulation, Third Party Testing
- *As a consumer it is your right to have access to certificates of analysis also known as batch reports for the products you purchase.
- *To check out quality products we have personally vetted and to download this consumer checklist please visit theroc.us/quality-matters



Are CBD Products Regulated?

Labeling Accuracy of Cannabidiol Extracts Sold Online

Marcel O. Bonn-Miller, PhD Mallory J. E. Loflin, PhD Brian F. Thomas, PhD Jahan P. Marcu, PhD, Travis Hyke, MS Ryan Vandrey, PhD

JAMA November 7, 2017 Volume 318, Number 17

Problem: Inadequate regulation and oversight of products, inaccurate labeling

Purchased 84 products:

69% mislabeled, more or less CBD content 31% were accurately labeled.

New York City plans to start fining restaurants that use CBD in food and drinks













What are the Side Effects of Cannabis?

Although not everyone's experience comes with a side of adverse reactions, it's worth knowing potential side effects, especially if you're a new user.

"Chronic use and high doses up to 1,500 mg/day of CBD are reportedly well tolerated in humans."

CBD is not toxic and reported side effects when first starting CBD have been:

- -an increase in sleep and/or lethargy.
- -an increase/decrease in appetite

Nausea, upset stomach, diarrhea, and vomiting may be indications that the CBD dose is too high.

This is referred to as oversaturation. Oftentimes it is due to too much carrier oil being ingested at one time.

THC does have intoxicating effects and can potentially increase anxiety

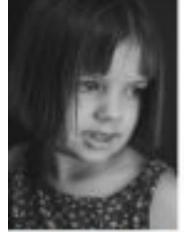
- -an increase in sleep and/or lethargy.
- -an increase in appetite
- -an increase in dry mouth or red eyes

Rashes or anything medically significant may indicate drug interactions.



Source: Beramaschi, et al. Safety and Side Effects of Cannabidiol, a Cannabis sativa Constituent. Current Drug Safety, 2011 6:4;237-249













Are There Potential Drug Interactions?

Potential Drug-Drug Interaction: CBD is metabolized in the liver by Cytochrome P450 (CYP) system and can interfere with metabolism of other medications that use the same system for metabolism, which can result in altered levels especially CYP2C9, CYP2C19, CYP3A4



Space CBD 2-4 hours before or after pharmaceutical medication to reduce the likelihood of drug interactions!

- Ask a pharmacist or doctor if and how medications could potentially interact.
- You can also use <u>www.drugbank.ca</u> to find medication pathways.
- Blood Serum testing can determine medication levels in the body. You can repeat this test every 6-8 weeks until a pattern is formed. This test can be a catalyst for medication weaning schedules with help from your attending physician(s).





www.theroc.us





What CBD does not do:

- Get you high
- Become addictive
- Cause withdrawals or dependency issues

Typical misconceptions about CBD:

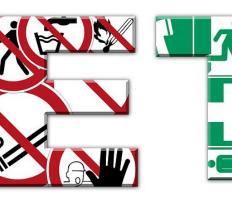
- You do not need to wean CBD. If you stop CBD it typically metabolizes out of the body within 72 hours
- You cannot overdose
- CBD is not Toxic in ANY amount even less toxic than caffeine.

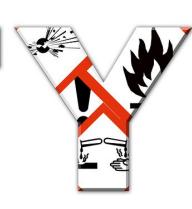
Special Considerations: Pregnancy/Nursing, Adolescents, Psychiatric Illnesses like Schizophrenia



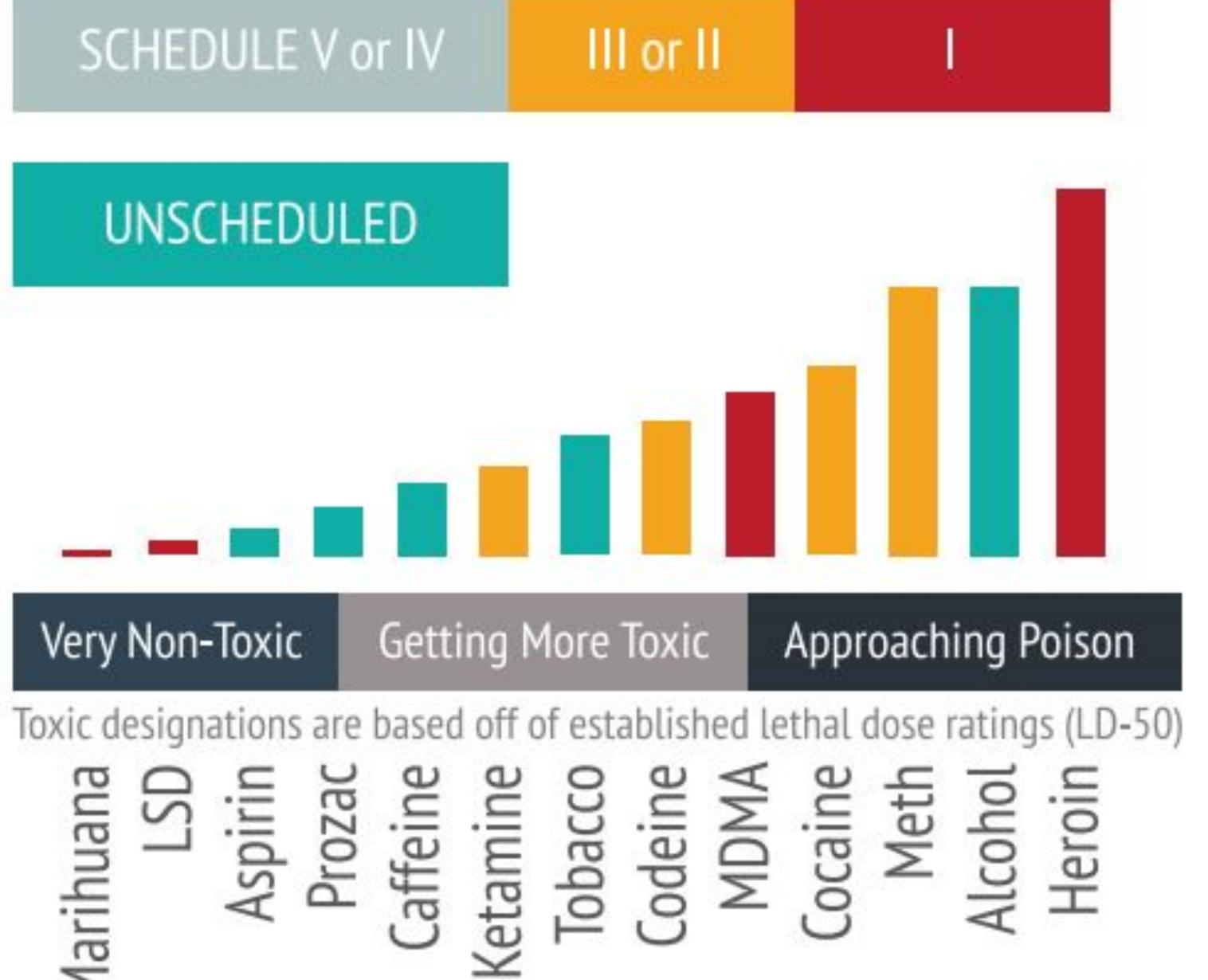












- Graph compares the toxicity levels of Schedule 1, 2, 3, and 4 substances.
- Toxic designations of the substances are based off of established lethal dose ratings (LD-50).
- LD stands for "Lethal Dose"
- LD50 is the amount of a material, **given all at once**, which causes the death of 50% (one half) of a group of test animals.
- It is one way to measure the short-term poisoning potential of a material.

You can't consume enough cannabis to die!





Sublingual

TIP: Hold under tongue for 30-60 sec before swallowing to increase absorption in the body.



TIP: Take with good fatty foods like almond milk, cheese, peanut butter, avocado, etc to increase absorption in the body.



Applied to the skin absorbed into your bloodstream. This means it can not only work as a localized effect, but also throughout your whole body.

Topical

Vapor

NO evidence of long term effects of PG/VG in vape products!

Suppositories

Bioavailability through rectal absorption is about twice that of oral absorption.

•GT/GJ

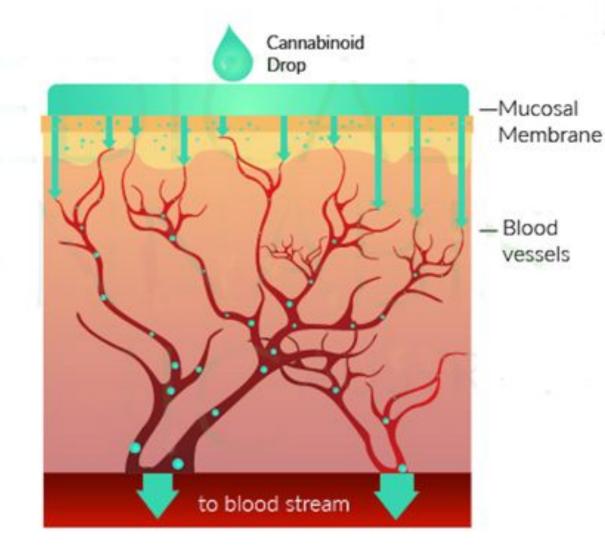
Sometimes a combination of administration methods is needed for lasting results. For pain management consider using a quality sublingual tincture 2-3 times a day everyday complimented with a transdermal or topical product applied to pain points as needed.



Administration Methods; How Do I Take This?







Sublingual Drops



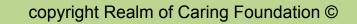














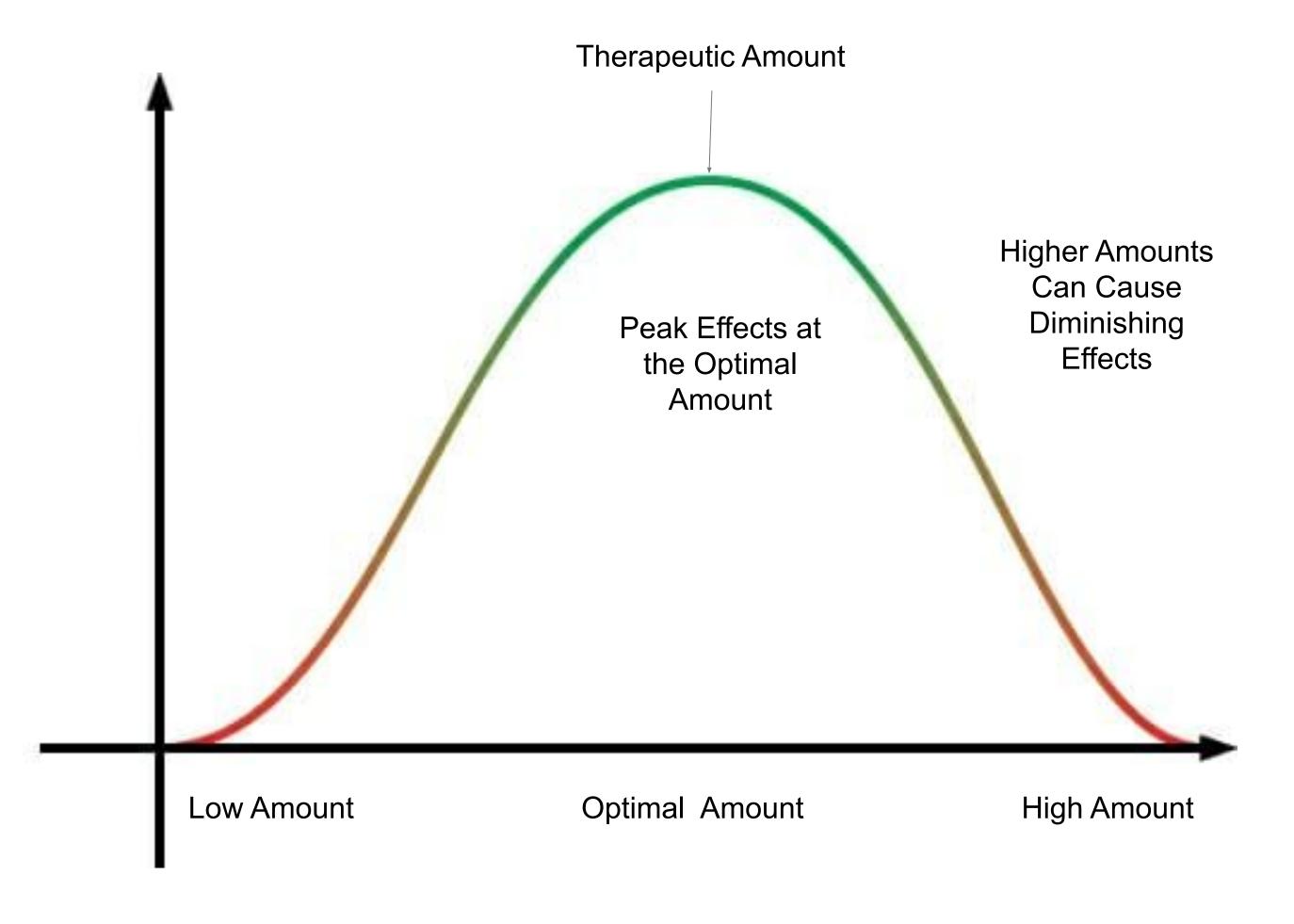








What is a Therapeutic Amount & Half Life BIPHASIC RESPONSE?



When first starting out on CBD, its average half-life (The half-life of a given medication is how long it takes for the body to get rid of half of the amount) is about 9 hours. With continual use, that half-life can build up to about 72 hours.

Because of this, occasional short breaks and skipping your daily serving *may* not affect symptom relief in someone who has been using it for several weeks.

This also makes it easy for someone wishing to stop taking CBD completely, as it will work its way very gradually out of the system without any abrupt disruption or dependency.













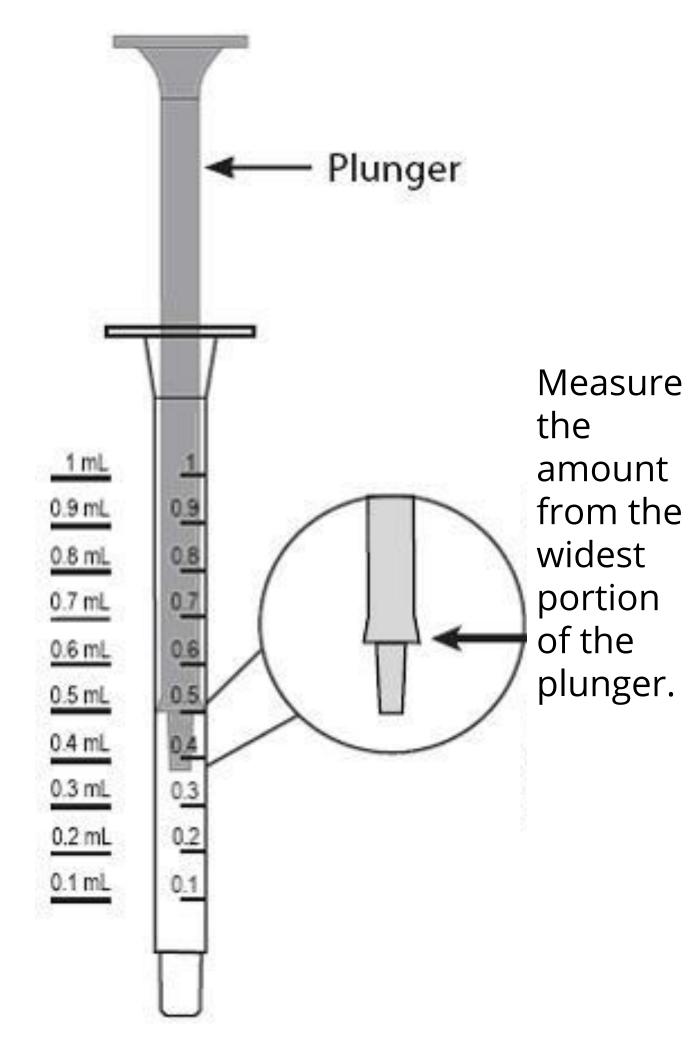
Administration - How Much Do I Take?

For Example: High CBD >26:1(CBD:THC)

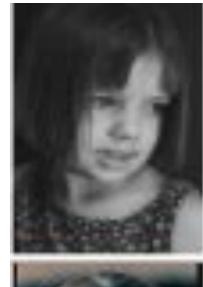
- Log in to your client account to access <u>Administration Guidelines Calculators</u>
- We suggest taking cannabis 2-3 times per day everyday.
- Space 2-4 hours from pharmaceuticals
- Potential interactions (ask doctor/pharmacist)
- Frequent monitoring. We suggest journaling on a daily/weekly basis.
- Your notes and observations will help the Care Team with troubleshooting.
- Baseline medication levels, including desmethyl levels.
- Transition to a new bottle for sensitive clients-<u>Dilution Calculator</u>.

Based on our investigations and research the mean amount is 2mg per kilogram, there is a wide range from our database amongst those with epilepsy, 7mg to 600mg!

There's a huge range of amounts that clients take, everyone has their own therapeutic amount. **CBD works by accumulation and saturation into the system**, where it is stored in fat cells and acts on specific cannabinoid receptors within the brain and body. We all have different genetic and biochemical makeups, and individual health issues that can take days or sometimes months to address.









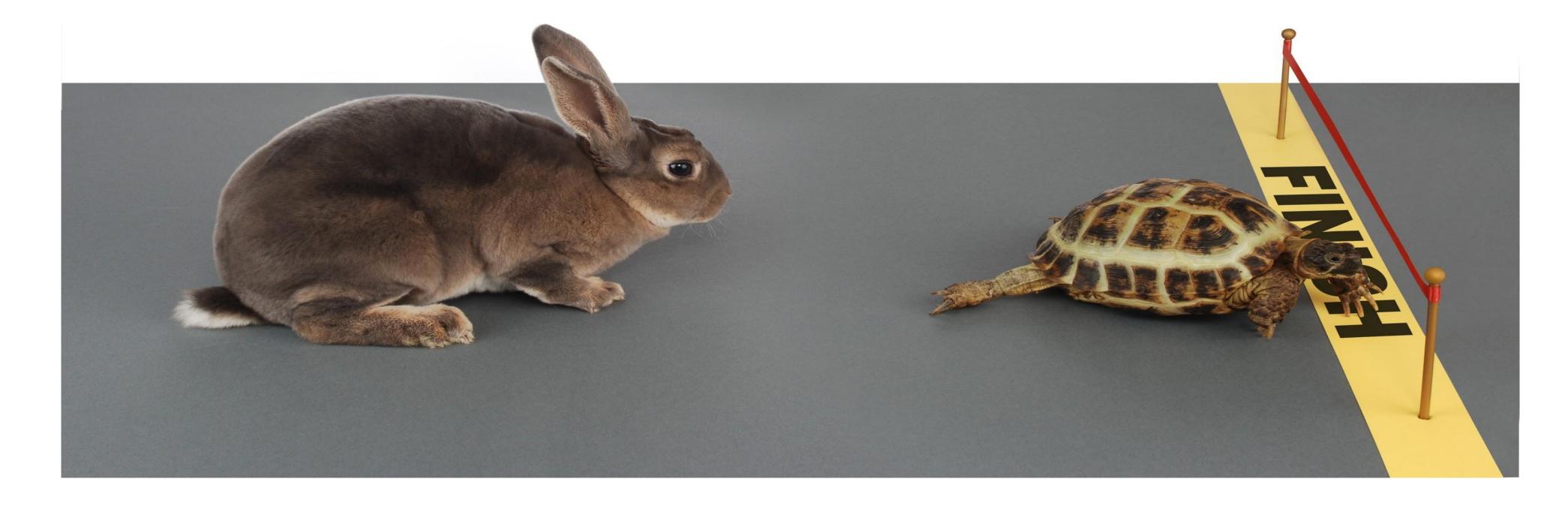






Why Slow & Steady?

- Sensitivities
- Bell Curve/Biphasic Effect
- Herxheimer Reactions (mainly in regards to Lyme Disease)















Reasonable Expectations

What will I measure, how will I measure, how often?

How long will this take anyway?

- Can take a couple of weeks to several months
- allow up to 6 months
- Not overnight
- tweaking
- labs
- titrating slowly up
- Try different administration methods

What does success mean to me?

- Decide what will be success for your family
- Pain rating
- Measurable labs
- Scans
- Sleep
- Mood
- Cognition
- Quality of Life

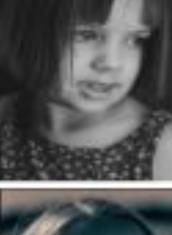
Measure

- Consistency
- Daily (or as often as you exhibit symptoms)
- Be Objective
- Symptom Tracker
- Online Tools
- Phone Apps like Releaf and GoFire
- Good old fashion notebook
- RoC Research Registry





Communicating With Your Physician











Health Care Practitioner Portal



Welcome to the Health Care Practitioner Portal. We hope this portal will be a beneficial resource to you, the health care practitioner, in treating your patients more effectively.

Concerned with legality?

Don't know where to start with dosing?

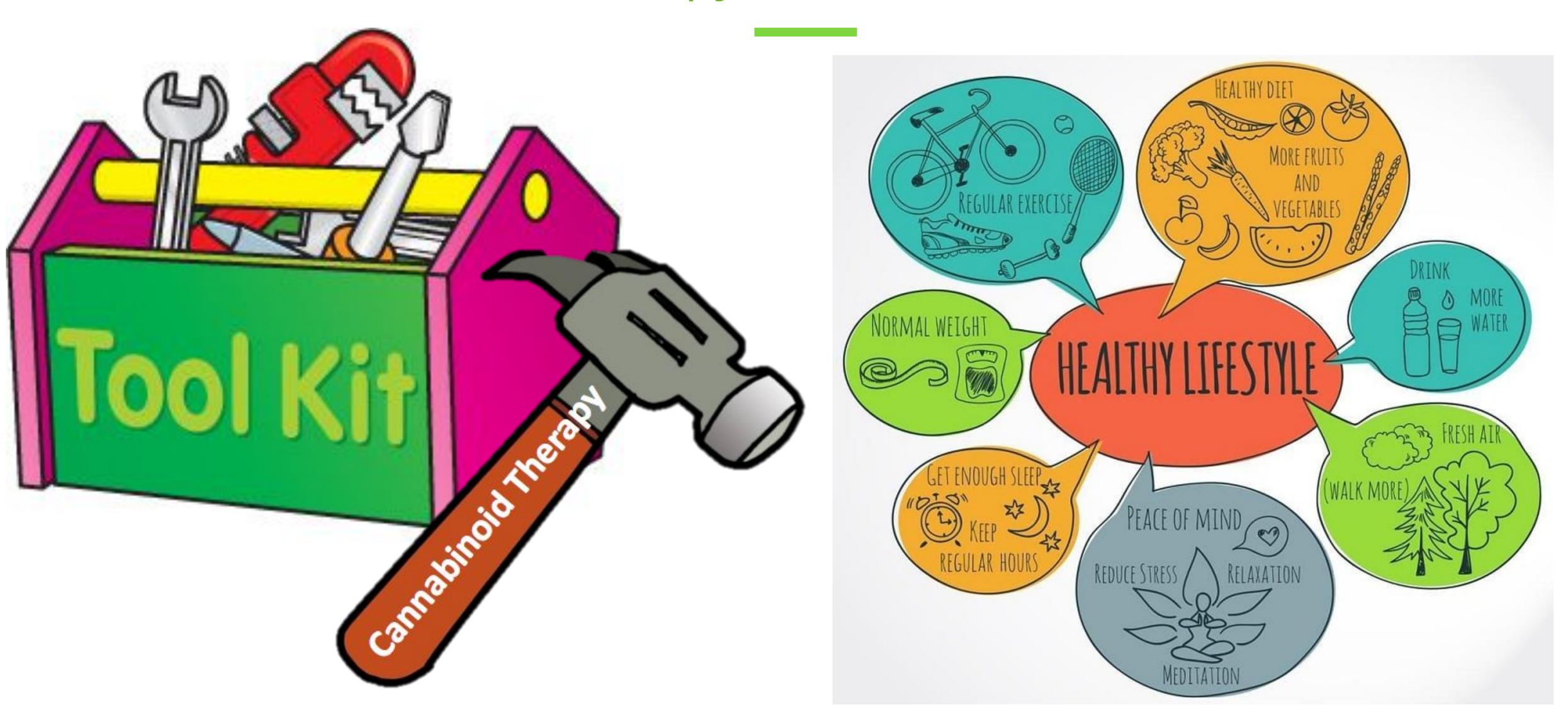
Click the button below to register and gain access to these answers and more.

https://www.theroc.us/practitioner-portal

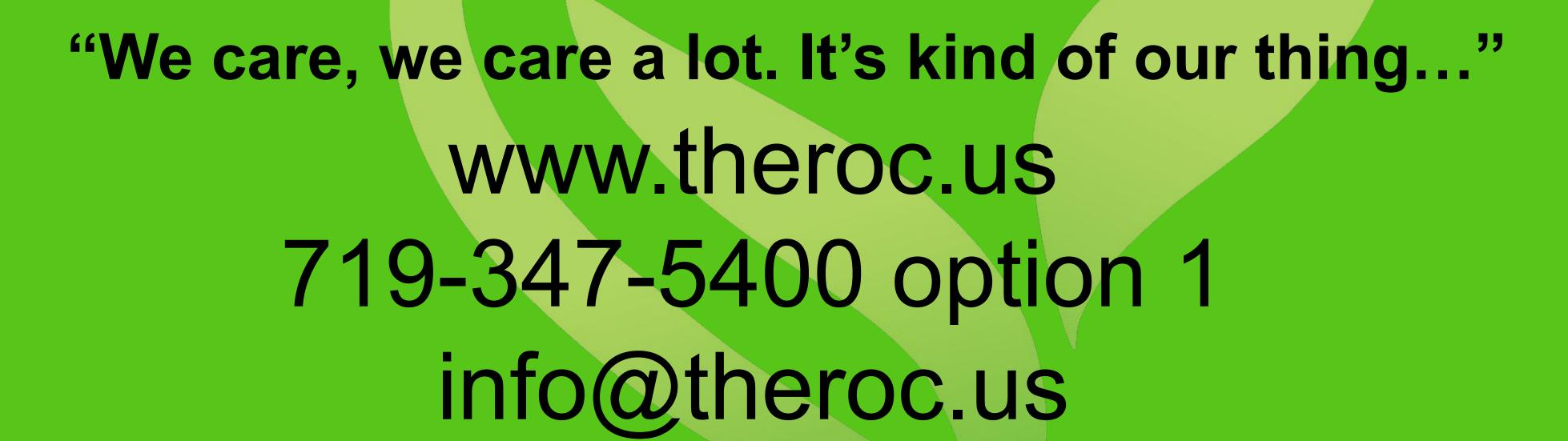


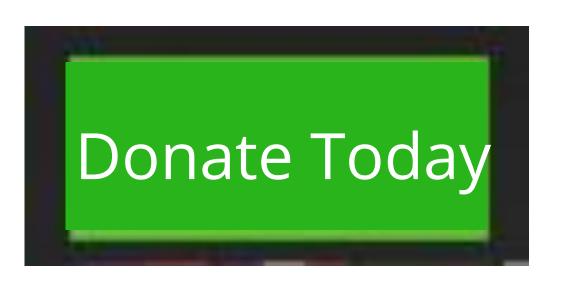


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