

Fundamentals of Hemp (& Cannabis) Chemistry

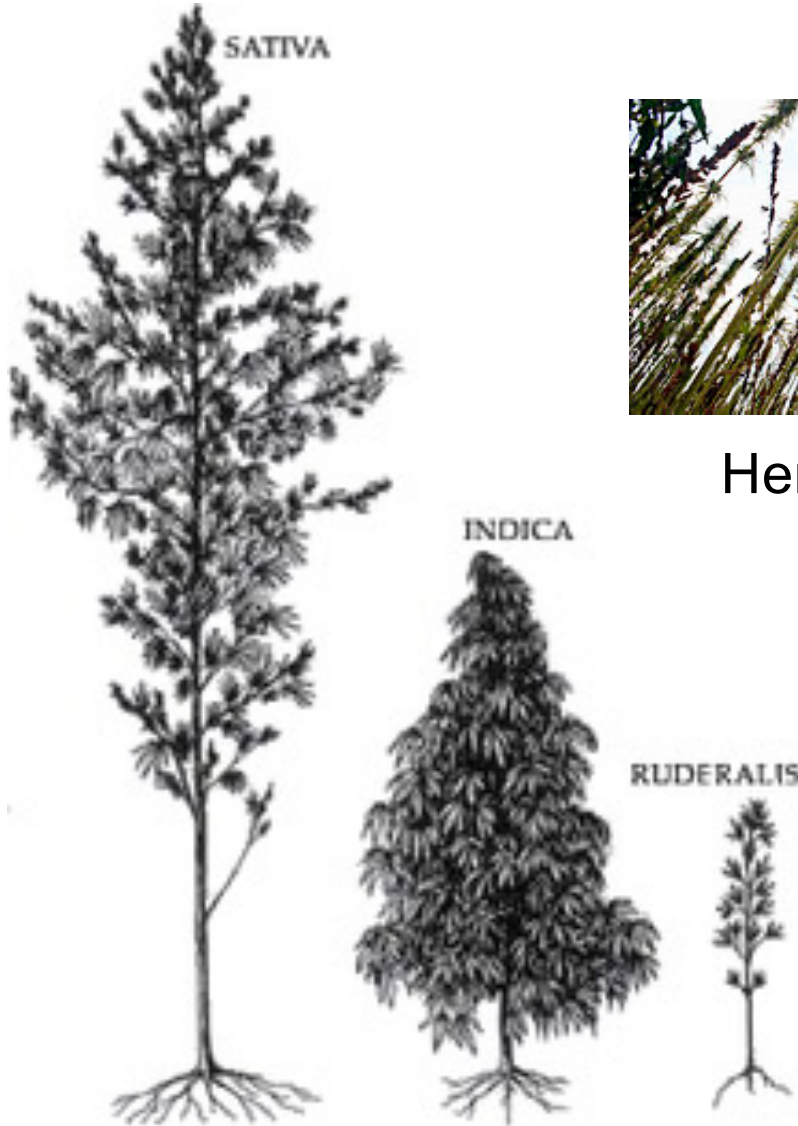
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Colorado State University
Fort Collins, CO 80523 USA

- Discussion of Both Hemp & Cannabis
 - Essentially same plant
 - *cannabis sativa*, *c. indica*, [*c. ruderalis*]
 - Essential difference is THC content
 - Many other differences derive from this
 - Hemp is grown primarily for fiber & CBD
 - Cannabis is grown primarily for THC
 - Interest in other *cannabinoids*
- Chemical Examination into the Plant
- Chemical Examination into Derived Products

- Actually Two Apologies
 - We must discuss organic chemistry (gasp!)
 - So much quality information available
 - Either overstimulation occurs or
 - Some good stuff is overlooked
 - I will endeavor to make this work manageable & useful
 - I encourage (welcome) interruption with questions & commentary

Hemp & Cannabis Similarities

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Hemp Plants



Female



Cannabis Plants



Male

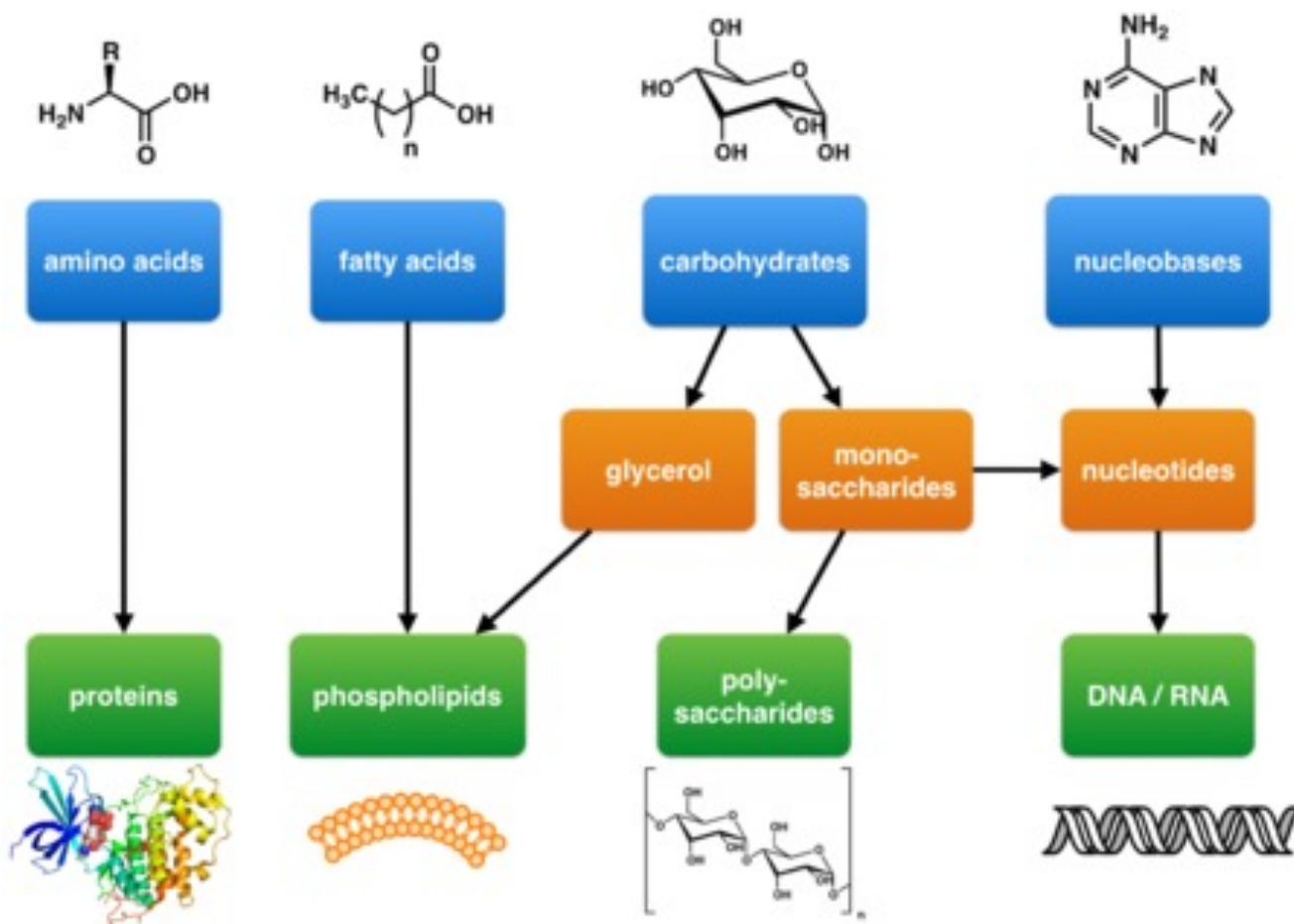
Cultivation Styles

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- Cannabis grown for: THC
 - & other cannabinoids
 - Primarily for euphoria (with or without guilt)
 - Compare market size of wine vs. non-alcoholic wine
 - Secondarily for “therapeutic effects”
- Hemp grown for: fiber, seed, CBD
 - & other cannabinoids
 - Non-trivial market for fiber
 - Competes in favorable growing conditions
 - Source of CBD in neo-pharmaceutical applications
 - Source of other cannabinoids for exploration

- Hemp & Cannabis are Plants
 - Contain Standard & Expected Components
 - cellulose, sugars, amino acids, waxes, *etc.*



- Hemp & Cannabis are Plants
 - Moderately Different in Substantial Concentration of Various Terpenes & Terpenoids
 - Classically thought of as defensive strategy
 - Against herbivores (insect and vertebrate)
 - Not unique among plants
 - The
 - Substantially Different in Containing Cannabinoids
 - Rare elsewhere in the Plant kingdom

- Terpenes & Terpenoids
 - myrcene, α -pinene, β -pinene, limonene, linalool, β -caryophyllene, terpeninene
- Cannabinoids
 - THC, CBD, CBD, CBV, CBG, THCV, *etc.*
-
- “Full Spectrum”, Isolate, Concentrate, Oil, Tincture

Three FDA Approved Medicines

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- dronabinol (Marinol, Syndros)
 - Synthetic racemic (S, S)-(+)- (S, S)-(-)- *trans*- Δ^9 -tetrahydrocannabinol
 - Sesame oil mixture in capsules
 - Used to stimulate appetite, treat sleep apnea & treat chemotherapy-induced nausea
- nabilone (Cesamet)
- Synthetic (-)-*trans*- Δ^9 -tetrahydrocannabinol
- Used to treat chemotherapy-induced nausea
- Modest efficacy in treatment of fibromyalgia, parkinsonism, chronic pain and dystonia

Three FDA Approved Medicines

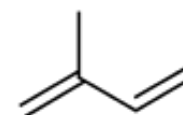
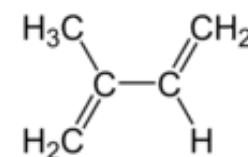
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- cannabidiol (Epidiolex)
 - Synthetic (-)-*trans*-cannabidiol
 - Orally administered ethanol & sesame oil solution
 - Used to treat of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS) in patients 2 years of age and older.

Let's Talk Terpenes

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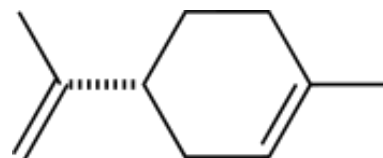
- Terpenes are a class of molecules:
 - Biosynthesized by plants
 - Consisting of multiples of the isoprene unit
 - Isoprene (C_5H_{10}) 2-methyl-1,3-butadiene
 - Consisting of only hydrogen and carbon
 - Thus they are hydrocarbons
 - Present in the sap of many different trees
 - First isolated from turpentine



isoprene

- For example:

- Limonene ($C_{10}H_{16}$)



limonene

- Two isoprene units combined
- Referred to as a monoterpene (go figure)
- The fragrance of citrus fruit peels

So Many Terpenes

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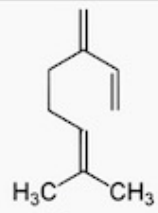
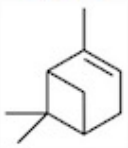
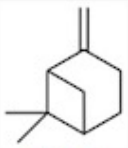

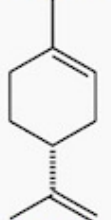
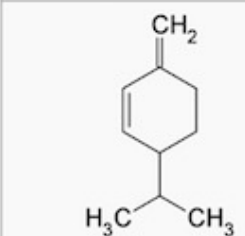
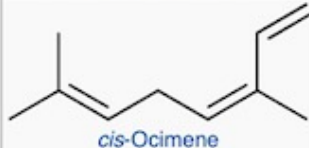
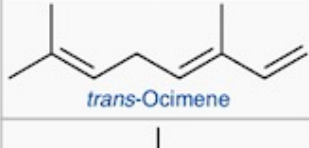
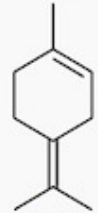

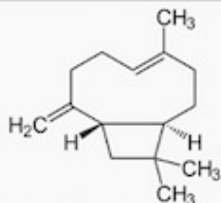
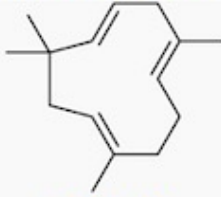
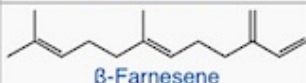



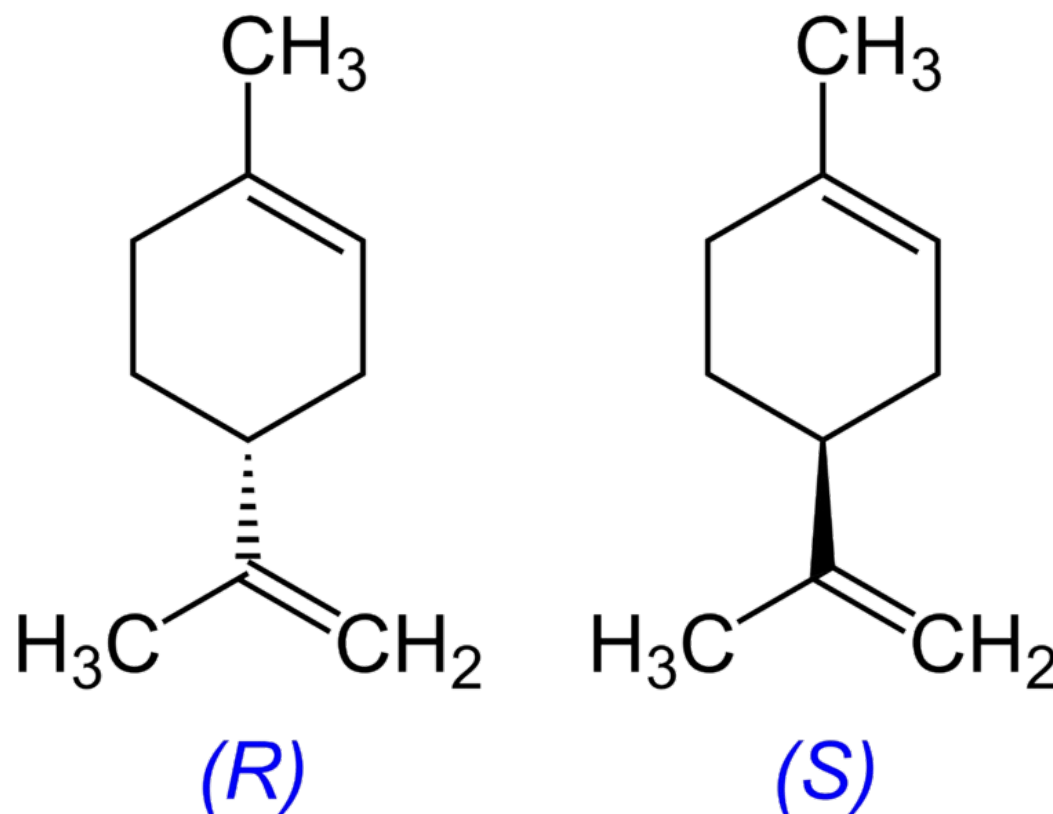
Compound	% of total
 Myrcene	29.4–65.8
 α-Pinene	2.3–31.0
 β-Pinene	0.9–7.8
 delta-3-Carene	trace–3.5
 Limonene	0.2–6.9
 β-phellandrene	0.2–0.6
 cis-Ocimene	trace–0.3
 trans-Ocimene	0.3–10.2
 α-Terpinolene	trace–23.8
 α-Bergamotene	trace–0.8
 trans-Caryophyllene	3.8–37.5
 α-Humulene	0.7–7.4
 β-Farnesene	trace–1.4
 β-Selinene	trace–0.5
 Selina-3,7(11)-diene	trace–0.7
 Caryophyllene oxide	trace–11.3
Total monoterpenes	47.9–92.1
Total sesquiterpenes	4.0–47.5

Table includes prevalence in cannabis (& hemp)
There are many more ...

Chirality – Limonene Example

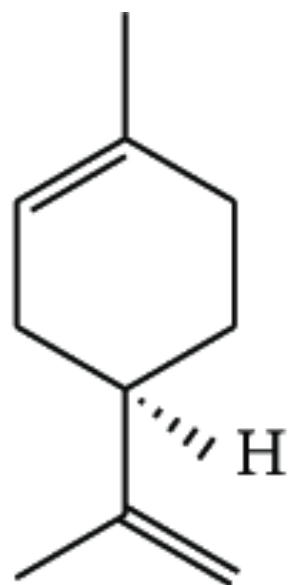
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The number and kind of atoms in a molecule are central to the chemistry of that molecule including its olfactory perception (fragrance). However, the arrangement of those atoms *in space* is also key.

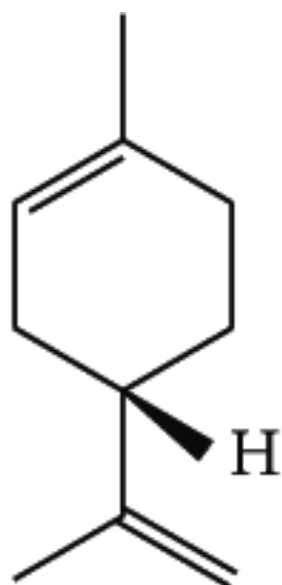


Chirality & Fragrance

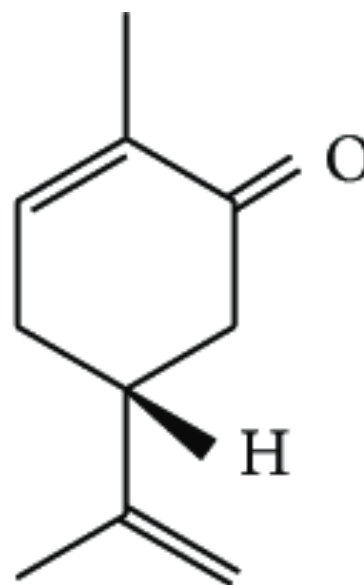
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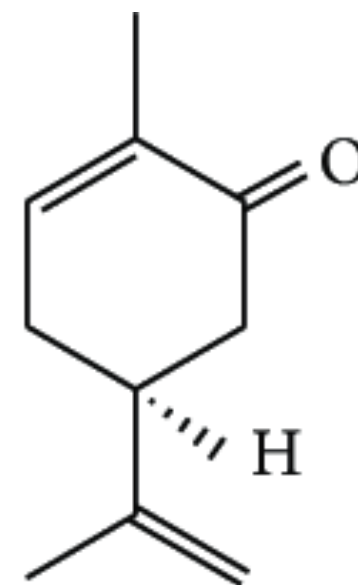
R-(+)-limonene
soft, sweet,
orangey odor



S-(-)-limonene
hard, acrid,
lemony odor



R-(-)-carvone
spearmint
odor [13, 26]



S-(+)-carvone
caraway
odor [13, 26]

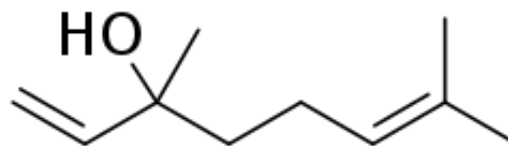
Let's Talk Terpenoids

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- Terpenoids are modified terpenes
 - Replace one or more methyl groups with oxygen atoms
 - Thousands have been discovered

- For example:

- linalool ($C_{10}H_{18}O$)

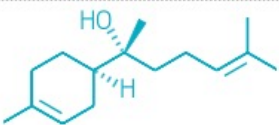

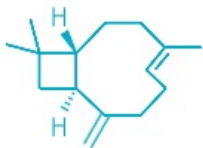

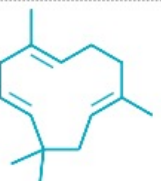

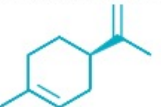









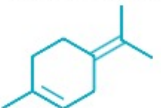



- Two isoprene units combined
 - Referred to as a monoterpene (again)
 - The fragrance of lavender
 - Also found in hundreds of plant species

- In Popular Usage:
 - Terpenes and terpenoids are mixed up freely
 - Any molecule with an aroma is often mis-called a terpene or terpenoid
 - Not all odor molecules are terpenes/terpenoids
 - Not all terpenes and terpenoids have aromas
 - Since terpenes and terpenoids have differing (chemical) functional groups on them they do have differing chemistry
 - For example, solubility in different solvents
 - Just have to commit them to memory

A Few More Examples

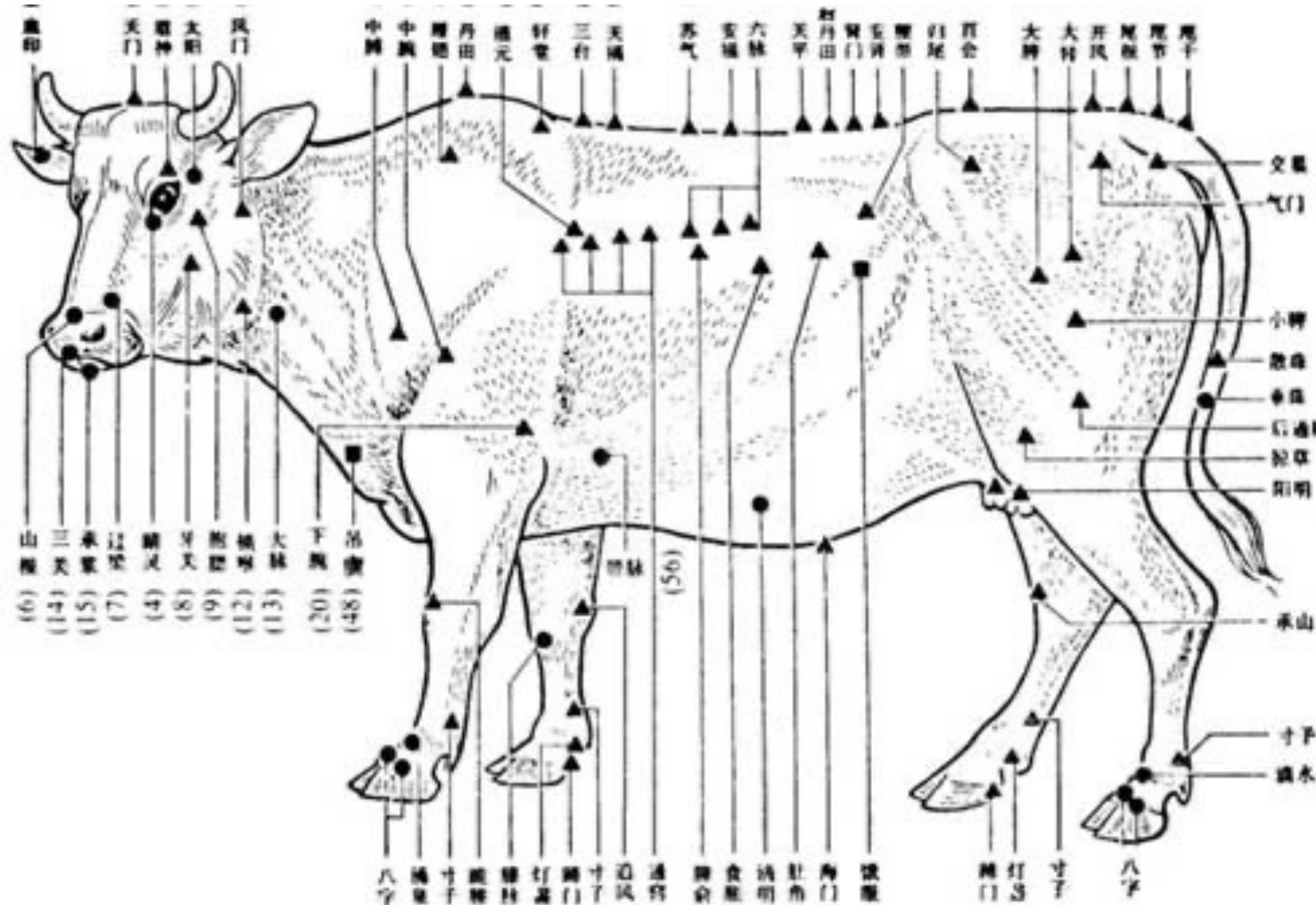
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TERPENE	STRUCTURE	ALSO FOUND IN	AROMAS AND FLAVORS
α -Bisabolol			Coconut, fruity, nutty
β -Caryophyllene			Clove, dry, spicy, woody
α -Humulene			Bitter, floral, peppery, woody
(+)-Limonene			Citrusy, sweet
Linalool			Floral, rose, woody
Myrcene			Celery-like, herbaceous, turpentine-like, woody
α -Pinene			Cool, fresh, herbal, piney, turpentine-like
β -Pinene			Green hay, piney, spicy, woody
Terpinolene			Fresh, lemon peel, sweet

- Both terpenes and terpenoids have been used as aromas in common products
 - Cleaners, colognes, perfumes, fresheners
- In recent times (and older ones) fragrant molecules have been ascribed medicinal characteristics because of their fragrance
 - Aromatherapy
 - Pseudoscience - consists of statements or practices that are claimed to be both scientific and factual but are incompatible with the scientific method
 - This stuff is contentious

Acupuncture in Cattle

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Did a cow prepare this chart?

- A proposed mechanism (1999) by which other compounds act synergistically to modulate the psychoactive effects of THC
- CBD has been evaluated critically (as of 2018) and a small signal has been observed
- In the reverse, the psychoactive effects of THC overwhelm those of CBD
- The idea of an entourage effect has taken root in the hemp and cannabis industries and among consumers

- The term “full spectrum” traditionally refers to a product that contains a range of cannabinoids from the plant as contrasted to one which contains (typically) CBD only and to a high purity
- Unfortunately, the analytic chemistry and product labeling in this industry are far below common expectations of FDA-approved pharmaceuticals
- Hope is strong; data is lean

CBD ISOLATE



96%-99.9% pure isolated
cannabidiol (CBD). Always 3rd party
lab tested.

1 gram - \$24.95



Hemp Extract Oil

CLASSIC



250+ mg cannabinoids per ounce.
Hemp CBD oil extract & organic
hemp seed oil.

1oz - \$24.95

COMPLETE



250+ mg raw & heated cannabinoids
per ounce, plus hemp terpenes.

1oz - \$29.95

SIGNATURE



250+ mg cannabinoids per ounce.
Classic blend plus frankincense &
black seed oil.

1oz - \$29.95

Concentrated CBD Oil

CLASSIC 6X



1,500+ mg cannabinoids per ounce.
Hemp extract & organic hemp seed
oil.

1oz - \$109.95



COMPLETE 6X



1,500+ mg raw & heated
cannabinoids per ounce, plus hemp
terpenes.

1oz - \$119.95



CBD VAPE JUICE



CBD Vape Juice. 1,000+ mg
cannabidiol (CBD) per ounce of vape
juice.

333mg - \$19.95

COMPANION OIL



250+ mg cannabinoids per ounce.
CBD hemp oil & organic virgin hemp
seed oil.

1oz - \$24.95



COMPANION CAPSULES



CBD hemp extract & organic virgin
hemp seed oil. 5+ mg cannabinoids
per capsule.

60 count - \$24.95





Steroid transdermal recipe

It is developed for base steroid hormones, testosterone base, etc.

The absorption is estimated to be around 40%.

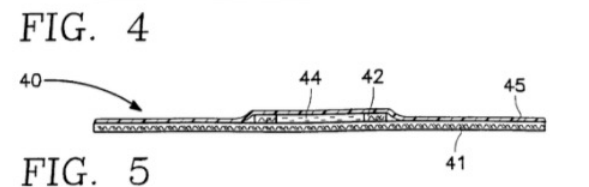
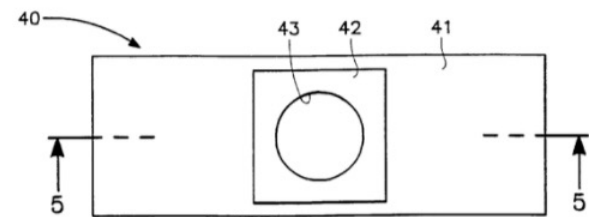
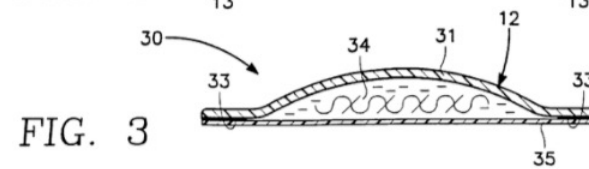
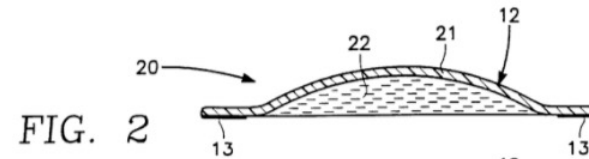
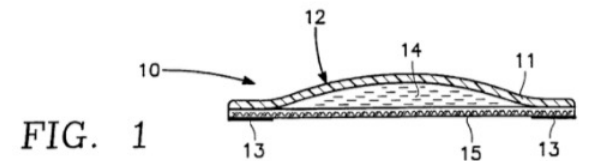
The final product is a liquid.

40% isopropyl alcohol	- solvent
15% isopropyl myristate	- lubricates and softens the skin
15% isopropyl palmitate	- lubricates and softens the skin
10% oleic acid	- disrupts the lipid layer of the skin
10% propylene glycol	- seals moisture in skin
10% DMSO	- penetrant

U.S. Patent


Dec. 11, 2001

US 6,328,992 B1

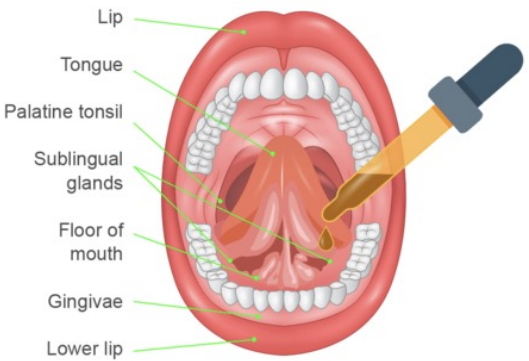




A tincture is a medical solution made from dissolving cannabis in alcohol. Most cannabis tincture products usually come in a half ounce bottle along with a dropper for easy dosing. Most cannabidiol tinctures contain **10% to 25% CBD**, a much stronger concentration than you'll find in any marijuana strain (with a few exceptions).


ENDOCA

HOW TO USE CBD OIL



Lip

Tongue

Palatine tonsil

Sublingual glands

Floor of mouth

Gingivae

Lower lip

It's best not to drink, eat or smoke approximately 5 minutes before and after using CBD.

Go and stand in front of a mirror, so you can see how many drops you drop under your tongue.

Put your personal amount of drops right under your tongue.

Let it sit there for at least 1-2 minutes.

After 1-2 minutes swallow what is left of the CBD oil.

Repeat this twice a day.

www.endoca.com



FLUID EXTRACT
Cannabis Americana

AS ACTIVE AS INDIAN CANNABIS

We are marketing a reliable fluid extract of *Cannabis Sativa* from American-grown drug. It has been thoroughly tested by experienced clinicians and pronounced fully equal to the fluid extract obtained from the best Indian Cannabis.

Fluid Extract Cannabis Americana (P. D. & Co.) is physiologically standardized. Practitioners may specify it with perfect assurance of its activity and uniformity. We market it at a price considerably lower than that asked for fluid extract Cannabis Indica.

Supplied in pint, 1/4-pint and 5-pint bottles.

PARKE, DAVIS & COMPANY
HOME OFFICES AND LABORATORIES, DETROIT, MICH.

FLUID EXTRACT
NO. 508
CANNABIS AMERICANA
P. D. & CO.
Contains active principle of the plant
in a palatable form
ALCOHOL, WATER
When administered in moderate quantities
it produces a mild
stimulant effect
Manufactured by Parke, Davis & Co., Detroit, Mich.
TRADE MARK U. S. A.

- THC (tetrahydrocannabinol)
- THCA (tetrahydrocannabinolic acid)
- CBD (cannabidiol)
- CBDA (cannabidiolic acid)
- CBN (cannabinol)
- CBG (cannabigerol)
- CBC (cannabichromene)
- CBL (cannabicyclol)
- CBV (cannabivarin)
- THCV (tetrahydrocannabivarin)
- CBDV (cannabidivarin)
- CBCV (cannabichromevarin)
- CBGV (cannabigerovarin)
- CBGM (cannabigerol monomethyl ether)
- CBE (cannabielsoin)
- CBT (cannabicitran)

Type	Skeleton	Cyclization
Cannabigerol-type CBG		
Cannabichromene-type CBC		
Cannabidiol-type CBD		
Tetrahydrocannabinol- and Cannabinol-type THC, CBN		
Cannabielsoin-type CBE		
<i>iso</i> - Tetrahydrocannabinol- type <i>iso</i>-THC		
Cannabicyclol-type CBL		
Cannabicitran-type CBT		

From the 1920s

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**RADIUM
EMANATION WATER**
Drives Out Uric Acid

Suffering from too much uric acid and diseases caused by faulty elimination—**Rheumatism, Gout, Periodical Headaches, Neuralgia, Constipation, Neurasthenia, Auto-Intoxication and Lack of Bodily Vigor**—quickly relieved in a natural way without drugs or chemicals by our new discovery

**THE WAY TO MAKE
RADIUM WATER
IN YOUR OWN HOME**

with our Rayode. A little device containing Radium enough to supply 2,700 Mache Units of Radio-activity, in two quarts of water every twenty-four hours, for less than 10c a day. The Rayode will last a lifetime.

SEND FOR FREE LITERATURE

Tells how you can buy or rent a Rayode to make Radium Water in your own home, with your own ordinary drinking water. Address:

THE COLORADO RADIUM PRODUCTS COMPANY
635 First National Bank Building Denver, Colo



From the 2010s

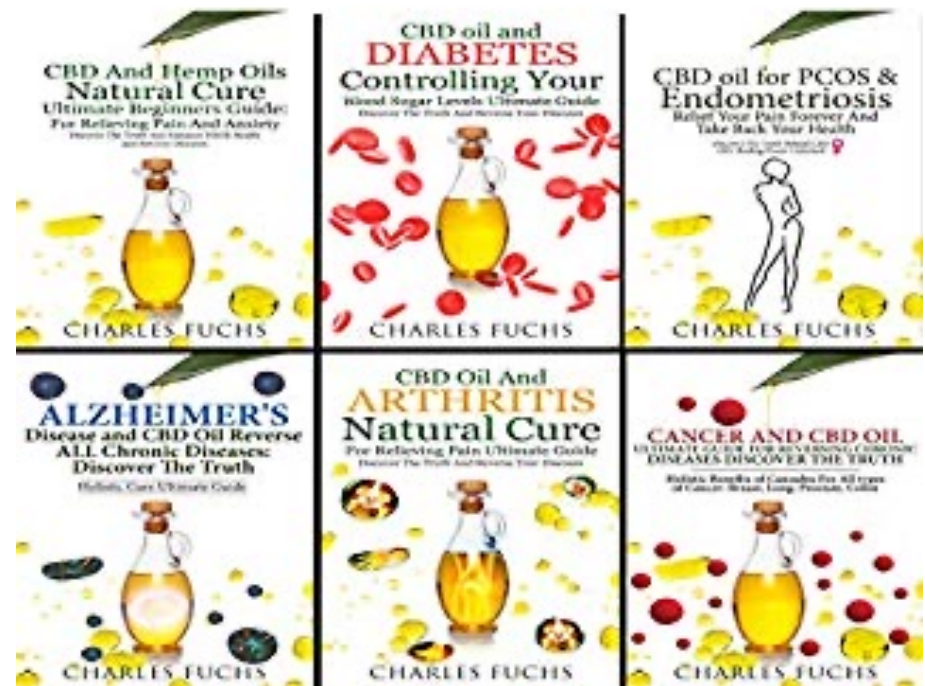
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CBD OIL
Cannabidiol

Perfect Curative Approach on How CBD Oil Relieves
Severe Pain, Anxiety, Arthritis, Erectile Dysfunction,
Stress, Depression etc., Without Adverse Effect

Cannab Pearl

**CBD OIL AND HEMP OIL FOR CANCER, DIABETES,
ALZHEIMER'S DISEASE, ARTHRITIS, PCOS & ENDOMETRIOSIS
ULTIMATE STARTER PACK GUIDE**



Hemp Industry Daily

FDA cracks down on three CBD companies making COVID-19 claims

The U.S. Food and Drug Administration has sent warning letters to three more CBD retailers for making COVID-19 claims.

Letters were sent to [Indigo Naturals](#) and [Native Roots Hemp](#) on Monday, and to [CBD Online Store](#) on Wednesday. The FDA warned them to stop making claims linked to the coronavirus or else risk legal action, including seizure and injunction.

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HEMP
PRODUCTION ▶

HYDR FARM®

The FDA said all three companies sold CBD products that were unapproved and misbranded drugs and violated the Federal Food, Drug and Cosmetic Act. The claims made on their websites, the FDA said, “misleadingly represent them as safe and/or effective for the treatment or prevention of COVID-19.”

Last month, U.S. Attorney General William Barr [directed](#) all U.S. Attorneys to prioritize the investigation and prosecution of coronavirus-related fraud, particularly individuals and businesses selling fake cures for COVID-19

online.

In the letter to Indigo Naturals, the FDA cited company statements suggesting that CBD has “both antibacterial and antiviral effects” and could be an “Anti-Viral Agent For Coronavirus.”

The letter to Wisconsin-based Native Roots Hemp cited company statements claiming that a strain of cannabis “speeds up” coronavirus recovery and that its soaps and “immune boosting oils” could help fight COVID-19.

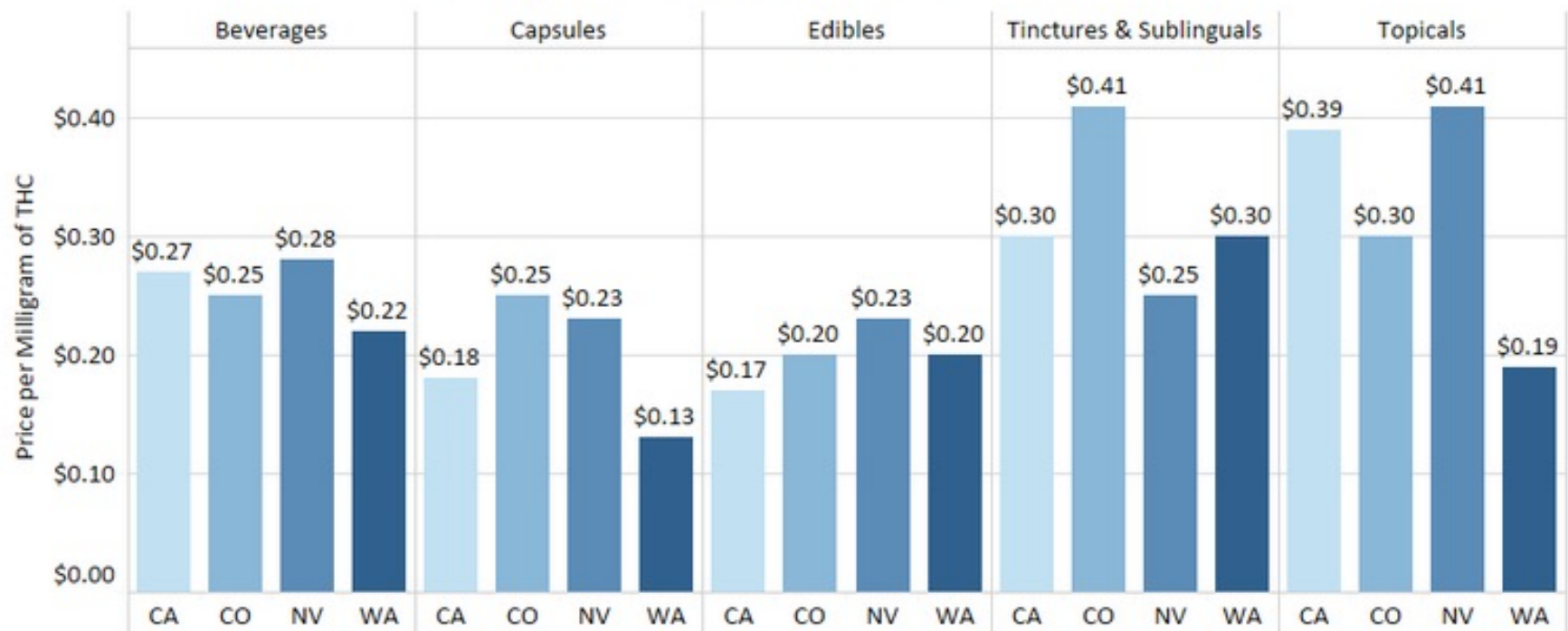
The FDA said CBD Online Store, located in Laguna Hills, Calif., made statements that suggested inflammation in the lungs caused by COVID-19 could be combatted by the “powerful anti-inflammatory effects of CBD.”

The Real Thing

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Price per Milligram of THC in Non-Inhalable Cannabis Products in California, Colorado, Nevada & Washington state



Source: Headset

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Popular CBD Tinctures

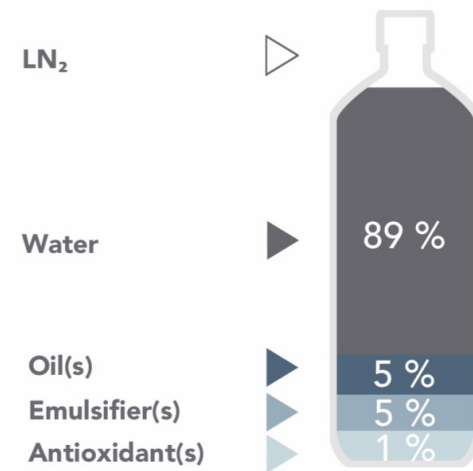
Lazarus Naturals \$0.05/mg Free shipping after \$50	Green Mountain CBD \$0.06/mg \$3.48 shipping under \$81 or \$6.10 above \$81
CBDistillery \$0.08/mg Free shipping after \$75	Bluebird Botanicals \$0.09/mg Free shipping after \$49
Koi CBD \$0.10/mg Free shipping after \$35	Kat's Naturals \$0.14/mg \$4 flat rate plus \$1 per product
Charlotte's Web \$0.14/mg Free shipping after \$74.99	Medical Mary \$0.16/mg \$6.95 flat rate shipping
Green Roads \$0.16/mg Free shipping after \$125	4 Corners Cannabis \$0.21/mg \$5 flat rate shipping

Full Spectrum Tinctures

Lazarus Naturals \$0.05/mg Free shipping after \$50	Green Mountain CBD \$0.06/mg \$3.48 shipping under \$81 or \$6.10 above \$81
CBDistillery \$0.08/mg Free shipping after \$75	Bluebird Botanicals \$0.09/mg Free shipping after \$49
Koi CBD \$0.10/mg Free shipping after \$35	NuLeaf Naturals \$0.14/mg Free shipping in the U.S.
Charlotte's Web \$0.14/mg Free shipping after \$74.99	Medical Mary \$0.16/mg \$6.95 flat rate shipping
4 Corners Cannabis \$0.21/mg \$5 flat rate shipping	Populum \$0.24/mg Free shipping




General Composition



THC CONTENT PER DOSE	WHAT TO EXPECT	WHO'S IT FOR?
● 1 - 2.5 mg THC	<ul style="list-style-type: none"> Mild relief of pain, stress, anxiety, and other symptoms Improved focus and creativity 	<ul style="list-style-type: none"> First-time consumers Microdosers
● 2.5 - 15 mg THC	<ul style="list-style-type: none"> Stronger symptom relief Euphoria May impair coordination and alter perception 	<ul style="list-style-type: none"> Patients with persistent problems Restless sleepers Social butterflies
● 15 - 30 mg THC	<ul style="list-style-type: none"> Strong euphoria or unwanted effects in unaccustomed consumers May impair coordination and alter perception 	<ul style="list-style-type: none"> Well-seasoned consumers Medical patients with developed tolerances Experienced consumers seeking to sustain sleep
● 30 - 50 mg THC	<ul style="list-style-type: none"> Very strong euphoria in unaccustomed consumers Likely to impair coordination and alter perception 	<ul style="list-style-type: none"> Consumers who have poor GI absorption of cannabinoids People with significant tolerance to THC
● 50 - 100 mg THC	<ul style="list-style-type: none"> Can cause extreme side effects such as rapid heart rate, nausea, and pain Highly likely to impair coordination and alter perception 	<ul style="list-style-type: none"> For experienced THC individuals only Patients with cancer, inflammatory disorders, or conditions that necessitate high doses

Seizures

Indicated for seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS)

2.5 mg/kg PO BID initially; after 1 week, dose may be increased to maintenance dose of 5 mg/kg BID 

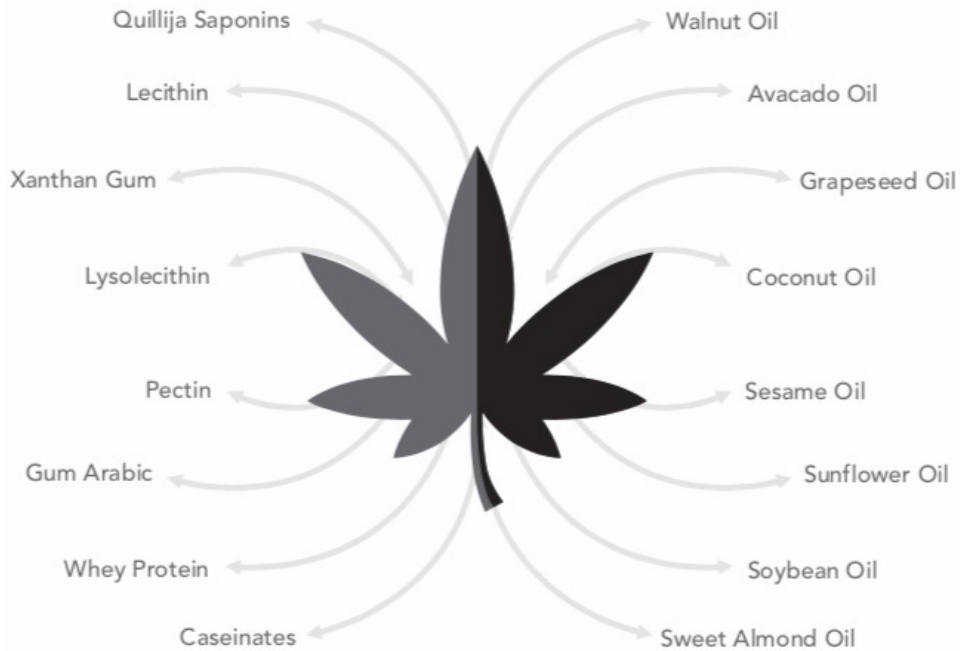
If 5 mg/kg BID tolerated and further seizure reduction required, patient may benefit from a dosage increase up to a maximum recommended maintenance dosage of 10 mg/kg BID (ie, 20 mg/kg/day)

Increasing to 10 mg/kg BID may be achieved by increased weekly increments of 2.5 mg/kg BID, as tolerated

If a more rapid titration from 10 mg/kg/day to 20 mg/kg/day is warranted, the dosage may be increased no more frequently than every other day

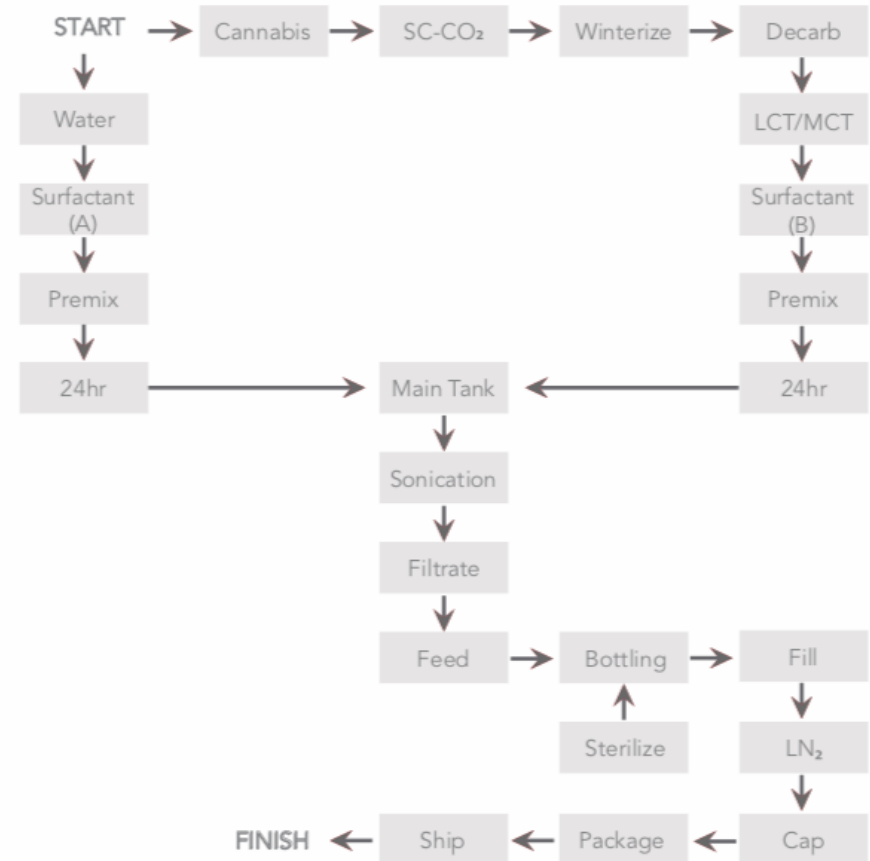
Administration of the 20-mg/kg/day dosage resulted in somewhat greater reductions in seizure rates than the recommended maintenance dosage of 10 mg/kg/day, but with an increase in adverse reactions

General Formula



Emulsifier + **Cannabis Oil** + **Carrier Oil**

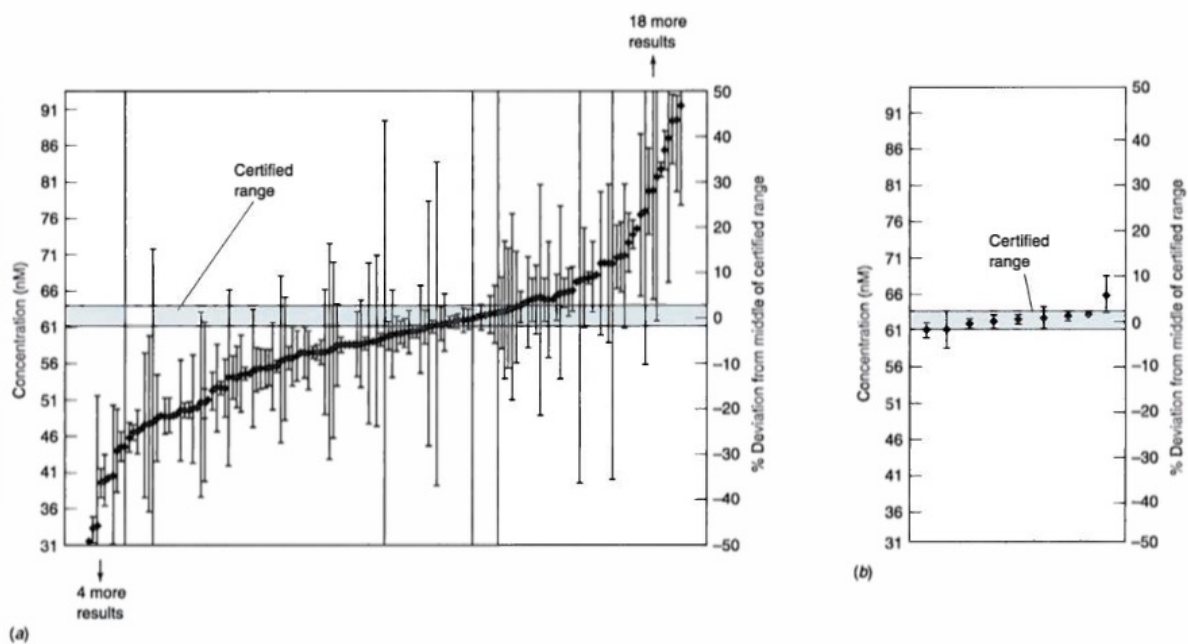
General Workflow



Sobering Study

CSU CHEM 442
Spring 2024 – Fort Collins, CO

THE NEED FOR QUALITY ASSURANCE



(a) Scattered measurements of lead in river water by different laboratories, each of which employed a recognized quality management system. (b) Reproducible results from national measurement institutes. [From P. De Bièvre and P. D. P. Taylor, "Demonstration' vs. 'Designation' of Measurement Competence: The Need to Link Accreditation to Metrology," *Fresenius J. Anal. Chem.* 2000, 368, 567.]

Quantitative Chemical Analysis
Daniel C. Harris, 8th edition (2010)

The Institute for Reference Materials and Measurements in Belgium conducts an International Measurement Evaluation Program to allow laboratories to assess the reliability of their analyses. Panel *a* shows results for lead in river water. Of 181 labs, 18 reported results more than 50% above and 4 reported results more than 50% below the certified level of 62.3 ± 1.3 nM. Even though most labs in the study employed recognized quality management procedures, a large fraction of results did not include the certified range. Panel *b* shows that when this same river water was analyzed by nine different national measurement institutes, where the most care is taken, all results were close to the certified range.

This example illustrates that there is no guarantee that results are reliable, even if they are obtained by "accredited" laboratories using accepted procedures. A good way to assess the reliability of a lab working for you is to provide the lab with "blind" samples—similar to your unknowns—for which you know the "right" answer but the analyst does not. If the lab does not find the known result, there is a problem. Periodic blind check samples are required to demonstrate continuing reliability.

Our Own Examination

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