Cannabis and Botanical Formulations:

Does the Queen herb play well with other herbs?

Glen Nagel, ND
Traditional Roots
May 19, 2019

Glen Nagel, ND

- Herbalist since 1984
- Graduate of NUNM in 1993
- Licensed Naturopathic Doctor since 1993 and currently with the State of Oregon
- Former Associate Professor in Botanical medicine with National University of Natural Medicine in Portland, Oregon, Former Assistant Professor at Bastyr University, in Kenmore, Washington
- Current Adjunct Faculty at NUNM
- Conflict of Interest: Consultant to the Botanical and Cannabis industry
- Protanicals™: Co-owner and formulator

How to become the best botanical focused Naturopathic Physician

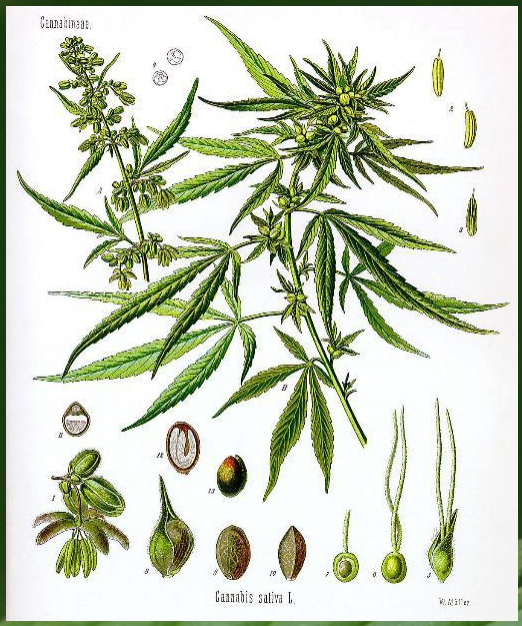
My Path……..


Ed, Sara and Herbal Interns Spring 1982
If I have glasses like Ed maybe I'm an herbalist


Of course the plants !!!

Right Names

- Marijuana is spanish word that was used during prohibition to associate uses with immigrants from Mexico.
- It is considered offensive. Use *Cannabis*, which is the plant's genus.
- Common names are regional nicknames.
- Weed, Mary Jane, Pot, herb, smoke, etc.
- New attitude, new research , new language!



Family: Cannabaceae
related to Hops

- *Cannabis sativa*
- *Cannabis indica*
- *Cannabis ruderalis*

"An additional nonsensical nomenclature controversy pertains in common parlance to *Cannabis* "strains," an appellation that is appropriate to bacteria and viruses but not plants, especially so with *Cannabis,* where the chemical variety, abbreviated 'chemovar.' is the most appropriate appellation."

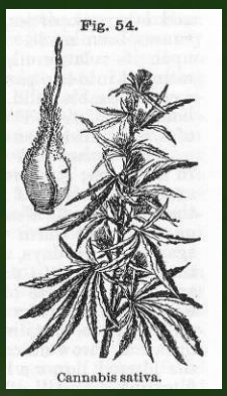
— Ethan Russo

Historical Use: Cannabis from Kings Dispensary, 1898

- **Action**.—
- "The principal seat of action of cannabis is upon the ***intellectual part of the cerebrum"***
- "In many respects its ***effects parallel those of opium*** and its chief alkaloid. Without doubt it is the most perfect psychic stimulant known to medicine".
- It produces an "***agreeable semi-delirium taking on the character of a sense of well-being and exhilaration-a state highly coveted by its devotees"***
- Who call it loftily "***the increaser of pleasure***, ***the laughter mover***, the ***cementer of friendship***,"

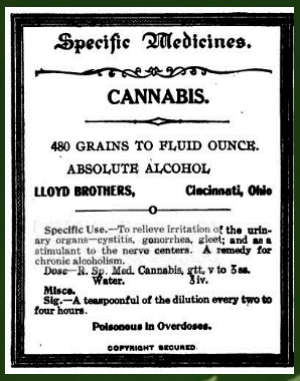
Cannabis from Kings Dispensary, 1898

- **Therapy**.—
- A peculiarity in many individuals taking cannabis is the voracious appetite induced. The effects of cannabis are far less powerful and less disturbing to the general system than those of opium, and it does not, like the latter, restrain the secretions nor produce itching. If anything the urine is increased by cannabis and constipation does not occur.
- The keynote indication for cannabis is marked depression of the nervous system usually with insomnia. Secondly, it allays irritation of the urino-genital tract and relieves pain.



- *Source: King's American Dispensatory, 1898, was written by Harvey Wickes Felter, M.D., and John Uri Lloyd, Phr. M., Ph. D.*

Lloyd Brothers: Cannabis Specific Medicine 1907



Specific Medicines.

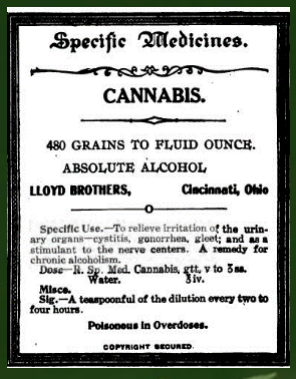
CANNABIS.

480 GRAINS TO FLUID OUNCE.
ABSOLUTE ALCOHOL
LLOYD BROTHERS, Cincinnati, Ohio

Specific Use.—To relieve irritation of the urinary organs—cystitis, gonorrhea, gleet; and as a stimulant to the nerve centers. A remedy for chronic alcoholism.
Dose—R. Sp. Med. Cannabis, gtt. v to 3ss.
Water. 3iv.
Misce.
Sig.—A teaspoonful of the dilution every two to four hours.
Poisonous in Overdoses.
COPYRIGHT SECURED.

Indications from Label:
To relieve irritation of the urinary organs, cystitis, gonorrhea, gleet and as a stimulant to the nerve centers. A remedy for chronic alcoholism.

Lloyd Brothers: Cannabis Specific Medicine 1907



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Suggested Dosing from 1907 label:

- 5 drops to 1 dram (3.75 mls)
- Large Range in Dosing
- 480 grains = 30 grams of Cannabis / oz
- 1 to 1 strength tincture: One ml has 1000 mg of cannabis x.05= 50 mg
- Absolute alcohol = ~95-99%
- 5% Cannabinoids (Guess?)
- Dose Range 4-187 mg of Cannabinoids?

Historical Cannabis and Botanical Formulas

Neuralgia:

Periodic Trifacial:

℞ Sp. Med. Cannabis gtt. xx.
Sp. Med. Piscidia
Sp. Med. Cinchona āā. ʒj.
Glyconda q.s. ʒiv. M.

Sig: A teaspoonful every three hours.

Rudolph Wagner, M.D.

Cannabis

Neurasthenia:

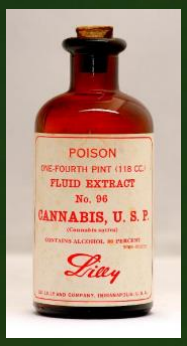
℞ Sp. Med. Cannabis gtt. xx.
Sp. Med. Pulsatilla ʒss.
Sp. Med. Matricaria ʒj.
Sp. Med. Passiflora ʒiij.
Sp. Med. Avena ʒiv.
Aq. Dest. q.s. ʒiv. M.

Sig: A teaspoonful every three hours.

Rudolph Wagner, M.D.

Source: Useful Prescriptions by Cloyce Wilson, MD 1935

Historical Cannabis Tinctures



Cannabis Strains

- All Cannabis comes from the same plants
  - *Cannabis indica*
  - *Cannabis sativa*
- Various names are chemotypes or chemovars
- Similar to types of apples: Granny Smith, Opal, gala, honeycrisp

Traditional thoughts:

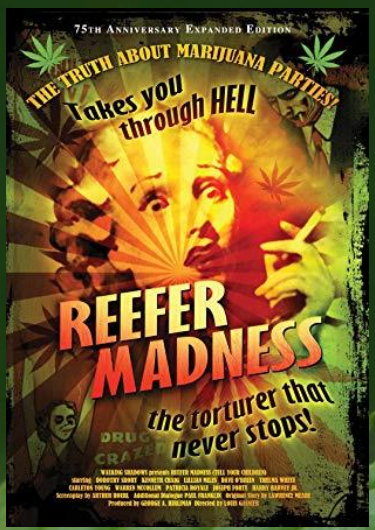
- *Cannabis sativa*
  - Stimulating, invigorating
- *Cannabis indica*
  - Calming, relaxing
- Most are now hybrids
- What counts is content of actives, not name.

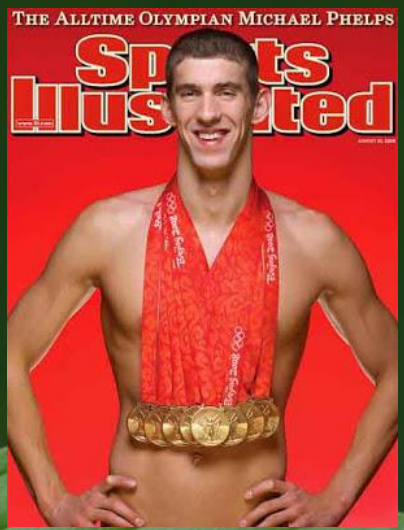
Cannabis: Myth or Medicine?

- Cannabis and Hops (*Humulus*) separated 27 million years ago
- Found in Japanese archeological sites 8000BC
- 2737 BC in famous prescription Chinese Emperor Shen Neng
- Historical Medical texts
  - China, India, Central Asia, Middle East and Africa
- US Pharmacopeia listing in 1854
- US Federal law banned 1937
- Removed from US Pharmacopeia 1943
- 1978 US Government supplies Cannabis to medically necessitated patients
- Schedule 1: No accepted medical use, high potential for abuse
- 1996 first medical law in California
- 2019 …….
- Source: Pharmacy therapeutics. 2017 Mar; 42(3): 180–188.

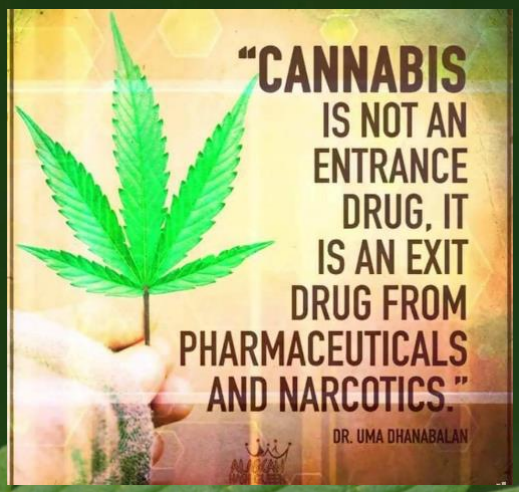
Cannabis Legalization 2018

This is your brain on Drugs: Cannabis





Cannabis the New Exit Drug



Cannabis as a Super food

Hundreds of compounds in *Cannabis*

- Terpenes
- Cannabinoids
- Antioxidants
- Minerals, protein
- Alkaloids

Hundreds of types of *Cannabis*

- Hemp (low in both CBD and THC)
- High THC
- High CBD

Important with Cannabis:
Set and Setting

- Create a supportive environment
- Positive belief and attitude
- Dispel negativity
- Good People you work with
  - Dispensary
  - Friends
  - Family
  - Doctors

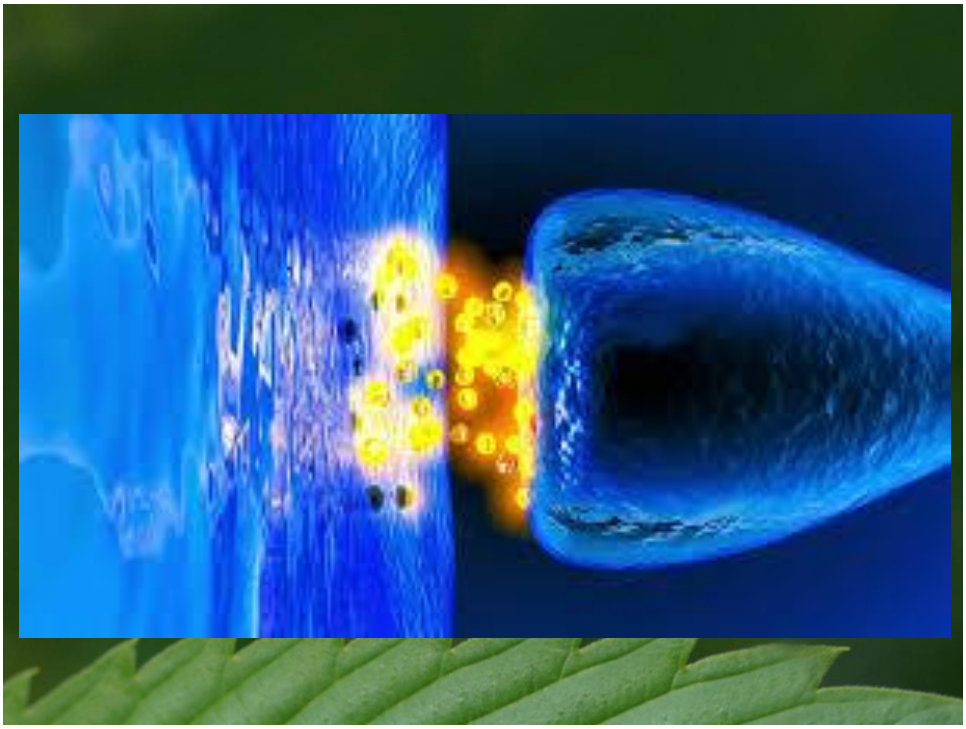
Realistic Expectations:
if it sounds to good to be true

- Can help with moods, energy, sleep, pain, etc.
- But is part of a lifestyle modification system including diet, stress management sleep and supplements
- Not a cure for everything like cancer, MS and other deep-seated disease.
- Talk to your doctor (ND or MD) about working together.

Herbs need your help to work ! Paradigm of healing: Intent

Starting Cannabis conversations

- If you are cannabis user they people will ask you for help
- Know the facts and research the studies
- Overcome resistance by being specific
  - Research show it can help with….
- Check state by state legality, Alaska has recreational law
- Start low and go slow with a newbie
- Don't bug people, some folks like their problems….
- Do not medicate anyone without their consent!



The Endocannabinoid System

- The purpose of the ECS is to serve as a master conductor, sending chemical messages and triggering biological actions throughout the body that are critical to health and well-being.
- The role of the ECS is to create homeostasis/ balance

- www.researchgate.net/publication/302979785_Beyond_Cannabis_Plants_and_the_Endocannabinoid_System, Russo

The Endocannabinoid System

- Appetite, digestion, and hunger
- Cellular energy
- Emotions
- Memory
- Metabolism
- Mood
- Motivation, pleasure, and reward
- Motor control
- Immune function
- Inflammation/ Pain
- Reproduction and fertility
- Sleep
- Stress response
- Temperature regulation

www.researchgate.net/publication/302979785_Beyond_Cannabis_Plants_and_the_Endocannabinoid_System, Russo

ENDOCANNABINOIDS

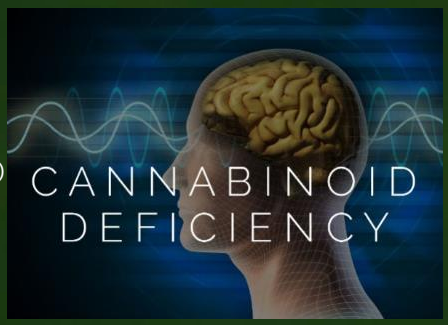
Endocannabinoids:

- –Anandamide(AEA) –Sanskrit for bliss important in pain
- –2-AG (2-arachydonoyl glycerol) •important in
  - brain injury
  - –Made from EFAs •manufactured in gut
  - Enzymes
  - –DAGL (diacylglycerol lipase) –synthesis –FAAH (fatty acid amide hydrolase) –degradation –MAGL (monoacylglycerollipase) –degradation
  - •CB1 &CB2 Receptors

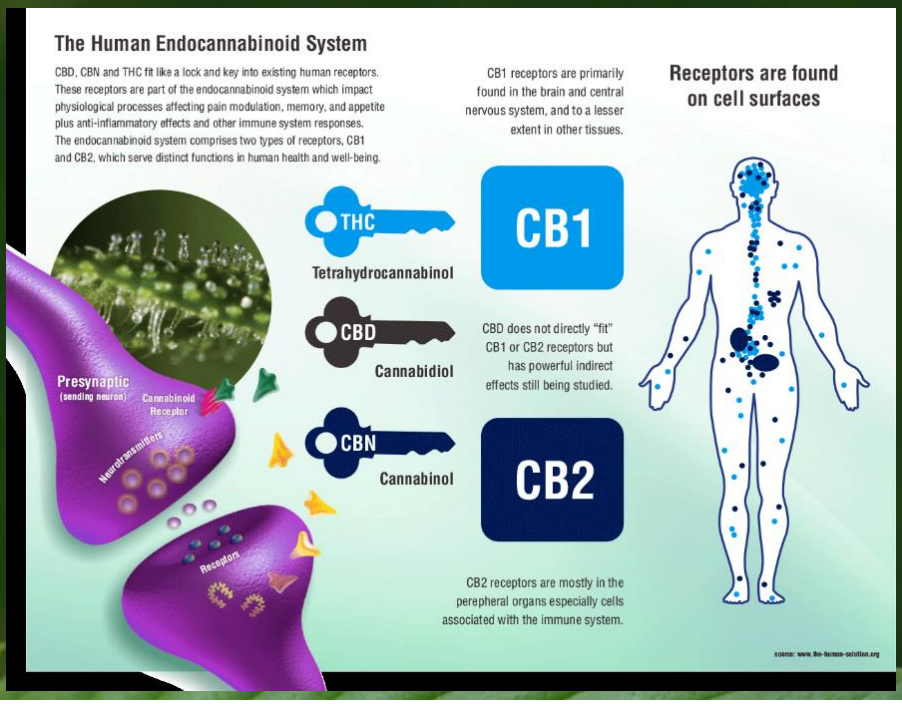
www.researchgate.net/publication/302979785_Beyond_Cannabis_Plants_and_the_Endocannabinoid_System, Russo

Endocannabinoid Deficiency Syndrome

- **Migraine, dysmenorrhea**
- **Fibromyalgia**
- **Irritable bowel syndrome (IBS)**
- Post-traumatic stress disorder (PTSD)
- Bipolar disease
- The Theory:

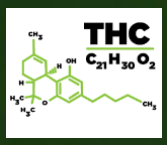


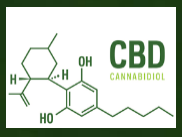
Russo, EB. Clinical endocannabinoid deficiency (CECD): Can this concept explain the therapeutic benefits in cannabis in migraine, fibromyalgia, irritable bowel syndrome and other treatments resistant conditions? Neuroendocrinolgoy Letters 2004.25(1-2):31-9.



The Great Triad of Activity

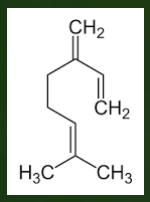
THC: The Queen Bee





CBD: The Smarty pants

Terpenes: Directors, influencers, Gate keepers



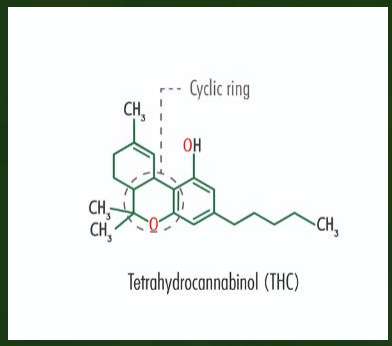
Cannabis Actives: Like Driving a Bus

- THC is the Gas
  - Let's Go CB1 team, where's the party?
- CBD is the brake
  - Whoa, slow down a bit team, let's use our head!
- Terpenes (essential oils) are the steering wheel
  - Which way are we going?
  - A little turn and you're on a new road!

THC: delta-9-tetrahydrocannabinol

Mimics Endogenous Agonists of CB Receptors
- –CB1 &CB2 agonist
- –high affinity for CB1receptors

- Euphoric
- Analgesic
  - –acute pain
  - –chemical, mechanical, thermal
  - –muscular and neuropathic pain
- Anti-emetic, esp. with chemo
- Appetite stimulant
- Anti Inflammatory
- Anti Spasmodic: with MS and ALS
- Anti Cancer: increase autophagy

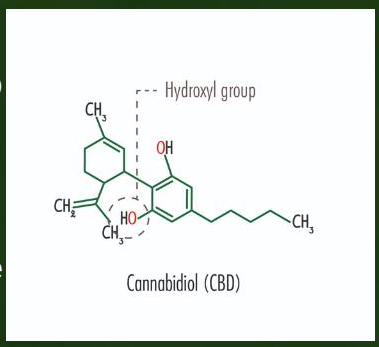


Tetrahydrocannabinol (THC)

Source: NATIONALACADEMIES.ORG/CANNABISHEALTHEFFECTS

CBD: Cannabidiol

- Low affinity for CB receptors – CB2 partial agonist –Attaches to TRPV1 (Vallinoid), GRP55, PPARs –Independent
- Suppresses FAAH enzyme, which breaks down anandamide (CB1 affinity)
- Found in Hemp and Cannabis



Cannabidiol (CBD)

www.researchgate.net/publication/315802003_Cannabidiol_Claims_and_Misconceptions_Trends_in_Pharmacological_Sciences_38_198-201_2017

CBD: Cannabidiol

- Anxiolytic
- Anti-Convulsant
- Anti-Emetic
- Anti-Inflammatory
- Antioxidant
- Anti-Psychotic –attenuates psychoactivity of THC – blocks THC conversion to >psychoactive derivative 11hydroxy-THC
- Blood Pressure Regulation
- Pain Perception
  - modulates neuropathic pain
- Neuroprotective/Neuro-regenerative
  - stimulates synaptic plasticity
  - increases adenosine levels
- Serotonin Balancing Agent
  - anti-depressant •reduces addiction •appetite
  - facilitates bone resorption
- Inhibits Cancer Cell Growth
  - increased production ROS inducing cytotoxicity, apoptosis &autophagy
  - reduces angiogenesis
  - inhibits EGF, NFkB, mTOR pathways

www.researchgate.net/publication/315802003_Cannabidiol_Claims_and_Misconceptions_Trends_in_Pharmacological_Sciences_38_198-201_2017

Prescription Cannabinoids

- Nabilone–Cesamet
  - THC Derivative
  - Sleep Disorders
- Dronabinol–Marinol
  - THC Derivative
  - Cachexia
  - AIDS
- Epidiolex: Cannabidiol
  - Epilepsy
- •Nabiximols–Sativex
  - THC:CBD –1:1
  - MS
  - Spasticity

Minor Cannabinoids

Potentially 70-100 know Cannabinoids

- CBG: Cannabigerol
- CBN: Cannabinol
- CBC: Cannabichromene
- THCV: tetrahydrocannabivarin
- ACIDS: raw , not decarboxylated
  - THCA, won't make you high, supports immunity and anti inflammatory
  - CBDA

The Entourage Effect

- The sum is greater than the parts
- 1+1+1=10
- Coined in 1998 by Ben-Shabat and by Raphael Mechoulam
- Isolated components will not work as well
- Same understanding that herbalist have
- Use whole plant for best results

- *Russo EB (August 2011). "Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects"*
- *British Journal of Pharmacology.* ***163*** *(7): 1344–64.*

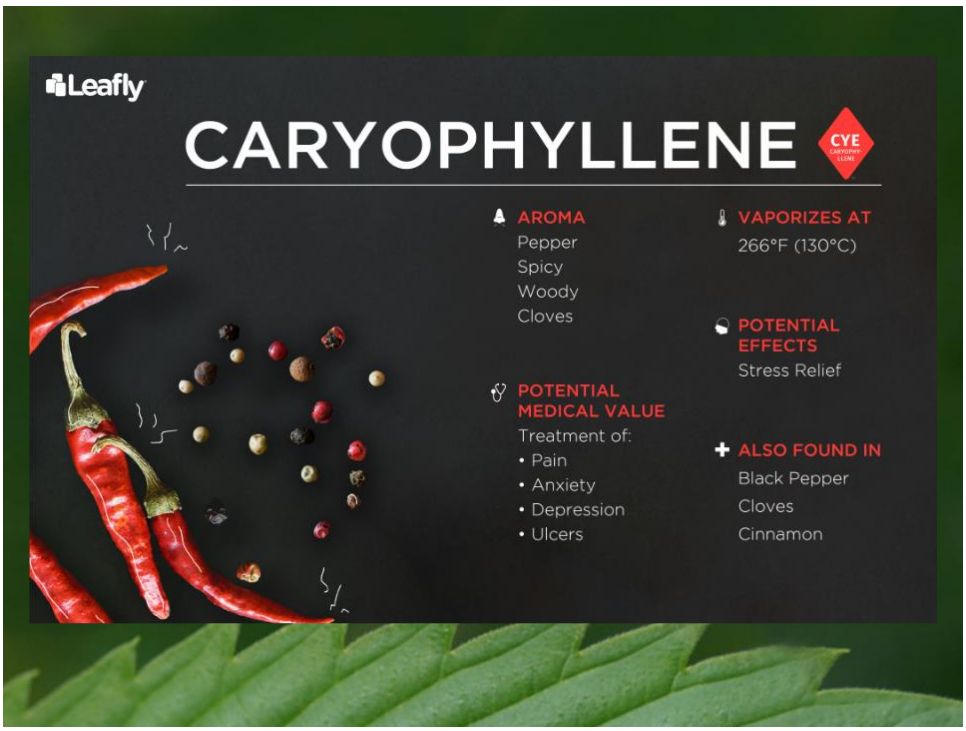
The Terpenes

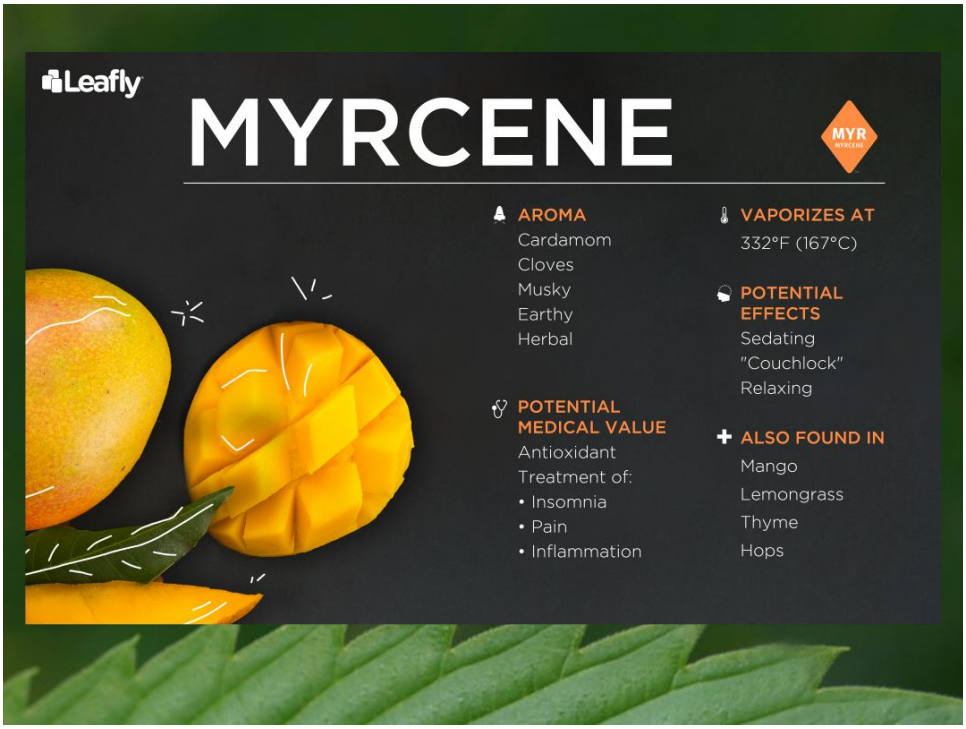
- Chemical components of essential oils •Terpene content strongly determines therapeutic effect
- •Entourage Effect thought to work synergistically with plant cannabinoids – reduce
  - THC anxiety
  - reduce cholinergic deficits –memory loss

  –enhances anti-inflammatory benefits –boosts anti-microbial activity –suppresses overactive immune systems

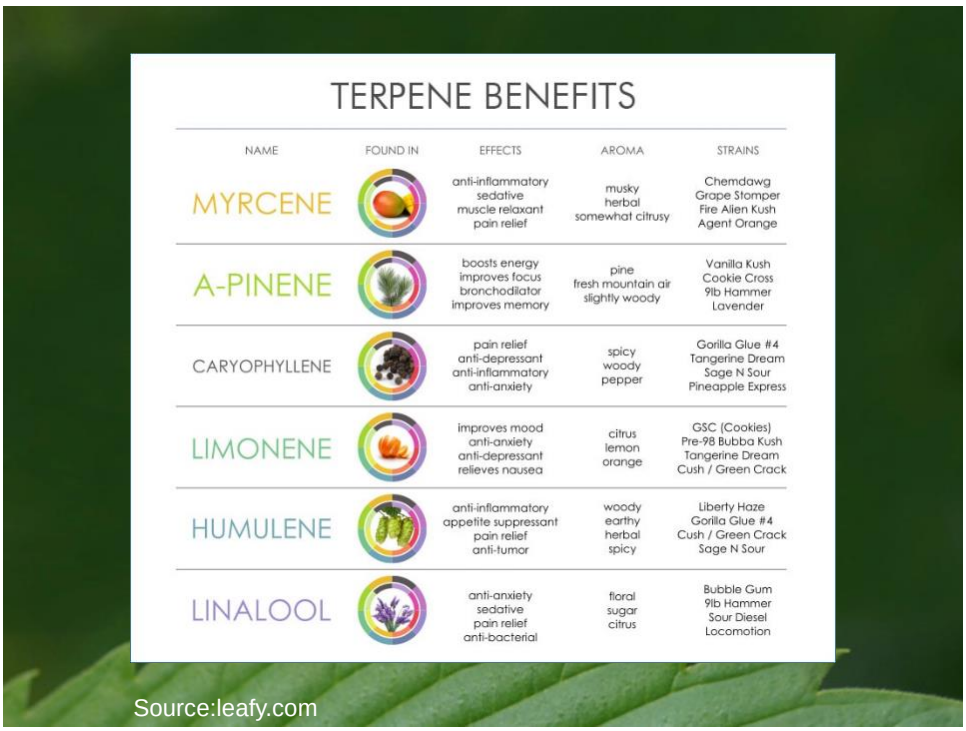
Trichomes: close up


Leafly
α-PINENE
PNE
AROMA
Pine
VAPORIZES AT
311°F (155°C)
POTENTIAL MEDICAL VALUE
Treatment of:
• Asthma
• Pain
• Ulcers
• Anxiety
• Cancer
POTENTIAL EFFECTS
Alertness
Memory Retention
Counteracts some THC effects
ALSO FOUND IN
Pine Needles
Rosemary
Basil
Parsley
Dill


Leafly
CARYOPHYLLENE
CYE
AROMA
Pepper
Spicy
Woody
Cloves
VAPORIZES AT
266°F (130°C)
POTENTIAL EFFECTS
Stress Relief
POTENTIAL MEDICAL VALUE
Treatment of:
• Pain
• Anxiety
• Depression
• Ulcers
ALSO FOUND IN
Black Pepper
Cloves
Cinnamon


Leafly
MYRCENE
MYR
AROMA
Cardamom
Cloves
Musky
Earthy
Herbal
VAPORIZES AT
332°F (167°C)
POTENTIAL EFFECTS
Sedating
"Couchlock"
Relaxing
POTENTIAL MEDICAL VALUE
Antioxidant
Treatment of:
• Insomnia
• Pain
• Inflammation
ALSO FOUND IN
Mango
Lemongrass
Thyme
Hops


Leafly
LIMONENE
LME
AROMA
Citrus
VAPORIZES AT
348°F (176°C)
POTENTIAL MEDICAL VALUE
Treatment of:
• Anxiety
• Depression
• Inflammation
• Pain
• Cancer
POTENTIAL EFFECTS
Elevated Mood
Stress Relief
ALSO FOUND IN
Fruit Rinds
Rosemary
Juniper
Peppermint



Source:leafy.com

Cannabis Safety

- Effective oral dosing range 0.05- 25 mg/kg /day
- No deaths occurred in moneys treated acutely with THC 9,000 mg a day
- Acute fatal cases in humans have not been substantiated
- Alcohol and benzodiazepines: can increase sedation
- Cannabis and opioids: no enhancement of cardiorespiratory suppression because of low number of CB receptors in brain stem
- Source: Healer.com

Cannabis Safety

- Cannabis flavones and CBD inhibit Cyp3A4 and 3A11. Can raise drug levels
- CBD inhibits Cyp 2C19.
- THC and CBN inhibit Cyp 3A4 and 2C9.
- Potential to interact with hundreds of medical drugs and natural agents.
- Practically very safe, but in serious illness work with physician

Source: NATIONAL ACADEMIES.ORG

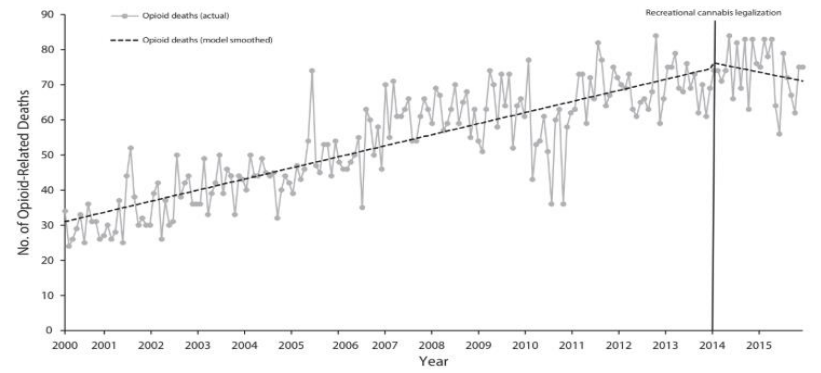
Cannabis: Psychosis and Violence

- Recent interest because of new book by author Alex Berenson
- He says states with increase rec — Oregon, Washington, Colorado and Alaska — have increase rates of violence
- Correlation or causal?
- Caution with mental psychosis?
- Avoid high-THC strains

AJPH RESEARCH

Recreational Cannabis Legalization and Opioid-Related Deaths in Colorado, 2000–2015

Melvin D. Livingston, PhD, Tracey E. Barnett, PhD, Chris Delcher, PhD, and Alexander C. Wagenaar, PhD



Note. Change in opioid-related deaths per month following legalization = −0.68 (95% confidence interval = −1.34, −0.03; $P = .043$). Change in model-estimated opioid-related deaths was robust to covariate control of opioid-related deaths in all comparison states. Change in model-estimated opioid-related deaths was robust to whether the prescription drug monitoring program (PDMP) covariate was modeled at the beginning of implementation or at full implementation of the 2014 PDMP change.

FIGURE 1—Changes in Monthly Opioid-Related Deaths Following Recreational Cannabis Legalization in Colorado, 2000–2015

CONCLUSIONS FOR: MENTAL HEALTH

There is substantial evidence of a statistical association between cannabis use and:
- The development of schizophrenia or other psychoses, with the highest risk among the most frequent users (12-1)

There is moderate evidence of a statistical association between cannabis use and:
- Better cognitive performance among individuals with psychotic disorders and a history of cannabis use (12-2a)
- Increased symptoms of mania and hypomania in individuals diagnosed with bipolar disorders (regular cannabis use) (12-4)
- A small increased risk for the development of depressive disorders (12-5)
- Increased incidence of suicidal ideation and suicide attempts with a higher incidence among heavier users (12-7a)
- Increased incidence of suicide completion (12-7b)
- Increased incidence of social anxiety disorder (regular cannabis use) (12-8b)

There is moderate evidence of *no* statistical association between cannabis use and:
- Worsening of negative symptoms of schizophrenia (e.g., blunted affect) among individuals with psychotic disorders (12-2c)

There is limited evidence of a statistical association between cannabis use and:
- An increase in positive symptoms of schizophrenia (e.g., hallucinations) among individuals with psychotic disorders (12-2b)
- The likelihood of developing bipolar disorder, particularly among regular or daily users (12-3)
- The development of any type of anxiety disorder, except social anxiety disorder (12-8a)
- Increased symptoms of anxiety (near daily cannabis use) (12-9)
- Increased severity of posttraumatic stress disorder symptoms among individuals with posttraumatic stress disorder (12-11)

There is no evidence to support or refute a statistical association between cannabis use and:
- Changes in the course or symptoms of depressive disorders (12-6)
- The development of posttraumatic stress disorder (12-10)

TO READ THE FULL REPORT AND VIEW RELATED RESOURCES, PLEASE VISIT NATIONALACADEMIES.ORG/CANNABISHEALTHEFFECTS

medicines MDPI

Review

Medicinal Cannabis—Potential Drug Interactions

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Abstract: The endocannabinoids system (ECS) has garnered considerable interest as a potential therapeutic target in various carcinomas and cancer-related conditions alongside neurodegenerative diseases. Cannabinoids are implemented in several physiological processes such as appetite stimulation, energy balance, pain modulation and the control of chemotherapy-induced nausea and vomiting (CINV). However, pharmacokinetics and pharmacodynamics interactions could be perceived in d
drug interactio
practitioners al
In general, can
concomitant ac
resistance prote
and UDP-gluc
of cannabis use
chronic disease

Keywords: can
P450; UDP-glu

"Cannabinoids are usually well tolerated, but bidirectional effects may be expected with concomitant administered agents via affected membrane transporters (Glycoprotein p, breast cancer resistance proteins, and multidrug resistance proteins) and metabolizing enzymes (Cytochrome P450 and UDP,glucuronosyltransferases)"

Medicines 2019, 6, 3; doi:10.3390/medicines6010003

Drug/ Herb Interactions Flow Chart: Five Points to determine potential interaction risk Start at point one and go right to left and check the box if it applies. Add up all point to determine risk.	Minimal Risk Potential No/ low risk	Moderate Risk Potential	Higher Risk Potential Higher Risk
Point #1 Read the Label. What type or form of herb is used? Native extracts, simplified fractions or isolated constituents.	Native Extract: Using Teas, whole plant extracts(liquids) Whole herb capsules or tablets, Powders Give 1 point ☐	Using Standardized extracts, or concentrates for marker(s) compounds. Non-natural chemical ratios Give 3 points ☐	Using Isolated concentrates or purified compounds Give 6 points ☐
Point #2: Dose of Herb Is it a low to high dose given?	Giving Low Dose of Herb Give 1 point ☐	Giving Moderate Dose of Herb Give 2 points ☐	Giving High dose of Herb Give 3 points ☐
Point # 3: Duration of Herb Is the herb given for short to long duration?	Herb duration under 4 weeks Give 1 point ☐	Herb Duration 4 to 12 weeks Give 2 points ☐	Herb Duration Three months or more Give 3 points ☐
Point #4: Detox Pathways Is the Herb a known Inducer or Inhibitor of Detox pathways (P 450), based on literature research or detox databases? (See Resource list)	No known effects on detox pathways or Neutral on detox pathways or "in vitro only interactions Give 1 point ☐	Moderate potential on detox pathways, Inducer or Inhibitor in Animal Studies mostly Give 3 points ☐	Well known inhibition or induction of detox pathways in human clinical trials Give 8 points ☐

5 Point
Drug / Interaction
Flow chart
by Glen Nagel, ND

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This is a useful handout and another class …

Point #5: Herb Increases or Decreases Drug Absorption: High fiber, High Tannins, Laxative, Inhibiting or Inducing P-Glycoprotein (See resource list)	No Known effects on drug absorption Give zero points		Know effect increasing or decreasing drug absorption Give 2 points ☐
Total Risk Potential Add up all the points from above to determine if the drug / herb combination has a Minimal, Moderate or Significant risk of interaction.	**Total 7or less points** Minimal Risk. Most whole, broad-based herbs, given at a reasonable dose are at a minimal risk.	**Total 8 to 14 points** Moderate Risk of potential drug / herb interactions	**Total 15-22 points** Significant Risk of potential drug /herb interaction Advise patient or monitor situation

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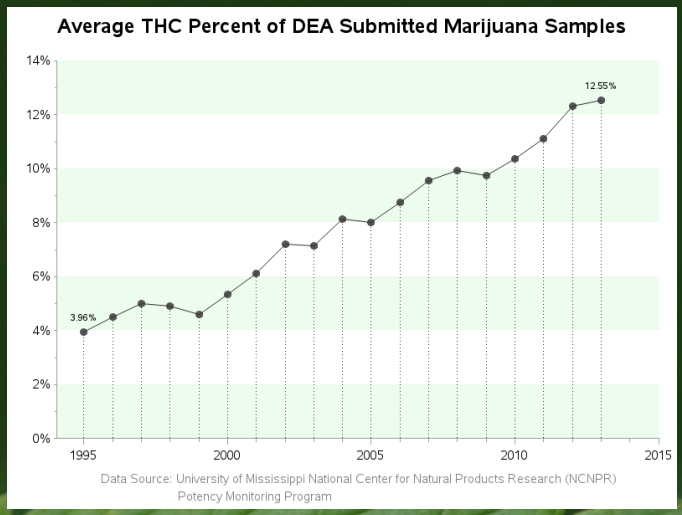
Potency of Cannabis



Potency of Cannabis

Levels of feeling High

- Very High: High THC, low CBD
- Moderate High: Balanced THC and low CBD
- Mild High: Low THC, High CBD

Potency Numbers

- Very High: 15-30% THC, low CBD 0-2 %
- Moderate High: 5-15% THC, 5-15% CBD
- Low to No High: THC 1-5%, CBD 5-30%

Intoxication Strategies

Historical Antidotes:
Terpenes can lower potency

- Lemon juice/lemonade
- Orange juice
- Pistachios
- Pine Nuts/Pine Oil

- Citicholine or Choline CDP
  - Mitigates psychoactivity
  - 5x mg of THC Ingested

Tolerance to Cannabinoids

- Everyone has their own unique chemistry
- Your natural endocannabinoid production
  - Stress will reduce natural ananamide amounts
  - Large daily dose will lead to large doses to keep same effect
  - Best to take breaks, days off, of use smaller doses
- Body size, and body fat content
  - Low size and body fat = smaller dose

Increase Sensitization

- Finding the right minimum dose
- Encourage increasing natural Endocannabinoid receptors
  - Taking 48 hour breaks frequently
  - Increase enjoyable mild to moderate exercise
  - Omega 3 oils
  - Breathing
  - Dark Chocolate, organic food
  - Source: Dr Sulaks info at healer.com

Phyto Cannabinoids

- Other plants besides Cannabis have effects on the Endocannabinoid system
  - Beta-caryophyllene is a terpene found in black pepper, oregano, cinnamon, clove
  - Echinacea spp.
  - Turmeric raises EC levels
  - Green tea
  - Kava
  - Peony, Magnolia, Ginger

British Journal of Pharmacology 163(7):1344-64 · August 2011

CANNABINOIDS IN THE PLANT KINGDOM

www.cbdoil.life

Cannabinoids, as a naturally occurring chemical compound, exist in many plants - not just cannabis (or non-psychoactive hemp). How cannabinoids interact with humans' Endocannabinoid System (or ECS for short) has been known for decades - their pain-relieving, immune-boosting, and 'feel-good' properties are a part of our experience with many other plants. Here are six of the most well-known species from the plant kingdom that have cannabinoids in them!

CONEFLOWER (ECHINACEA)

Some species of echinacea contain cannabinoids - specifically, cannabimemetics - and it is no surprise that they engage the Endocannabinoid System. These compounds interact mostly with the CB2 receptor, which is responsible for regulating pain, the immune system, and inflammatory responses. Echinacea is known for fighting the common cold and relieving symptoms of fatigue, arthritis, anxiety, and migraines - now we have another reason to love this plant!

ELECTRIC DAISY (ACMELLA OLERACEA)

This plant contains cannabinoid-like compounds that are called "N-isobutylamides" which interact with the CB2 receptor in the ECS. It works as a powerful pain killer that also has anti-inflammatory properties.

HELICHRYSUM UMBRACULIGERUM

This is a daisy that contains a large amount of the cannabinoid CBG (cannabigerol). CBG has anti-inflammatory properties, as well as antidepressant and mood stabilizing properties.

LIVERWORT (RADULA MARGINATA)

This lichen plant has been used historically to treat liver, gallbladder and bladder problems, as well as bronchitis. However, the New Zealand liverwort has a large amount of perrottetinenic acid, which is similar to the psychoactive cannabinoid THC, and is thought to act upon the CB1 receptor.

BLACK PEPPER (PIPER NIGRUM)

Black peppers contain a large amount of the terpene called beta-caryophyllene. This particular terpene functions much like a cannabinoid - it has an affinity to bind to the CB2 receptor. Initial research is showing that beta-caryophyllene has therapeutic potential as an anti-inflammatory compound and enhances the effects of anti-cancer drugs.

CHOCOLATE (THEOBROMA CACAO)

As if we needed another reason to love chocolate, it turns out that this plant (and tasty products made from such) has multiple compounds that interact with our ECS. Similar to CBD, the enzyme FAAH (Fatty acid amide hydrolase), is deactivated by compounds in chocolate - this increases the amount of anandamide in the body and can make us feel good - more happy and relaxed.

That's Natural!

Protecting Food & Medicine Freedom Since 2005... That's Natural!

Source: www.cbdoil.life

OPEN ACCESS Freely available online

PLOS ONE

Care and Feeding of the Endocannabinoid System: A Systematic Review of Potential Clinical Interventions that Upregulate the Endocannabinoid System

John M. McPartland[1,2]*, Geoffrey W. Guy[1], Vincenzo Di Marzo[3]

1 GW Pharmaceuticals, Porton Down Science Park, Salisbury, Wiltshire, United Kingdom, 2 Department of Family Medicine, University of Vermont, Burlington, Vermont, United States of America, 3 Endocannabinoid Research Group, Istituto di Chimica Biomoleculare, CNR, Via Campi Flegrei, Pozzuoli, Napoli, Italy

Abstract

Backgroun anandamid "eCB deficie other cond upregulate

Methodolo Data synth human stu (acetamino anxiolytics, upregulate

Clinical interventions characterized as "complementary and alternative medicine" also upregulate the eCB system: massage and manipulation, acupuncture, dietary supplements, and herbal medicines. Lifestyle modification (diet, weight control, exercise, and the use of psychoactive substances—alcohol, tobacco, coffee, cannabis) also modulate the eCB system.

Conclusions/Significance: Few clinical trials have assessed interventions that upregulate the eCB system. Many preclinical studies point to other potential approaches; human trials are needed to explore these promising interventions.

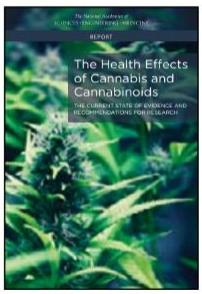
McPartland JM, Guy GW, Di Marzo V (2014) Care and Feeding of the Endocannabinoid System: A Systematic Review of Potential Clinical Interventions that Upregulate the Endocannabinoid System. PLoS ONE 9(3): e89566. https://doi.org/10.1371/journal.pone.0089566

Cannabis Therapeutics

THE HEALTH EFFECTS OF CANNABIS AND CANNABINOIDS

COMMITTEE'S CONCLUSIONS

January 2017



In the report *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research,* an expert, ad hoc committee of the National Academies of Sciences, Engineering, and Medicine presents nearly 100 conclusions related to the health effects of cannabis and cannabinoid use.

The committee developed standard language to categorize the weight of the evidence regarding whether cannabis or cannabinoids used for *therapeutic* purposes are an effective or ineffective treatment for certain prioritized health conditions, or whether cannabis or cannabinoids used primarily for *recreational* purposes are statistically associated with certain prioritized health conditions. The box on the next page describes these categories and the general parameters for the types of evidence supporting each category.

The numbers in parentheses after each conclusion correspond to chapter conclusion numbers. Each blue header below links to the corresponding chapter in the report, providing much more detail regarding the committee's findings and conclusions. To read the full report, please visit **nationalacademies.org/CannabisHealthEffects.**

CONCLUSIONS FOR: THERAPEUTIC EFFECTS

There is conclusive or substantial evidence that cannabis or cannabinoids are effective:
- For the treatment for chronic pain in adults (cannabis) (4-1)
- Antiemetics in the treatment of chemotherapy-induced nausea and vomiting (oral cannabinoids) (4-3)
- For improving patient-reported multiple sclerosis spasticity symptoms (oral cannabinoids) (4-7a)

There is moderate evidence that cannabis or cannabinoids are effective for:
- Improving short-term sleep outcomes in individuals with sleep disturbance associated with obstructive sleep apnea syndrome, fibromyalgia, chronic pain, and multiple sclerosis (cannabinoids, primarily nabiximols) (4-19)

There is limited evidence that cannabis or cannabinoids are effective for:
- Increasing appetite and decreasing weight loss associated with HIV/AIDS (cannabis and oral cannabinoids) (4-4a)
- Improving clinician-measured multiple sclerosis spasticity symptoms (oral cannabinoids) (4-7a)
- Improving symptoms of Tourette syndrome (THC capsules) (4-8)
- Improving anxiety symptoms, as assessed by a public speaking test, in individuals with social anxiety disorders (cannabidiol) (4-17)
- Improving symptoms of posttraumatic stress disorder (nabilone; one single, small fair-quality trial) (4-20)

There is limited evidence of a statistical association between cannabinoids and:
- Better outcomes (i.e., mortality, disability) after a traumatic brain injury or intracranial hemorrhage (4-15)

There is limited evidence that cannabis or cannabinoids are *ineffective* for:
- Improving symptoms associated with dementia (cannabinoids) (4-13)
- Improving intraocular pressure associated with glaucoma (cannabinoids) (4-14)
- Reducing depressive symptoms in individuals with chronic pain or multiple sclerosis (nabiximols, dronabinol, and nabilone) (4-18)

TO READ THE FULL REPORT AND VIEW RELATED RESOURCES, PLEASE VISIT
NATIONAL ACADEMIES.ORG/CANNABISHEALTHEFFECTS

CONCLUSIONS FOR: PROBLEM CANNABIS USE

There is substantial evidence that:
- Stimulant treatment of attention deficit hyperactivity disorder (ADHD) during adolescence is *not* a risk factor for the development of problem cannabis use (13-2e)
- Being male and smoking cigarettes are risk factors for the progression of cannabis use to problem cannabis use (13-2i)
- Initiating cannabis use at an earlier age is a risk factor for the development of problem cannabis use (13-2j)

There is substantial evidence of a statistical association between:
- Increases in cannabis use frequency and the progression to developing problem cannabis use (13-1)
- Being male and the severity of problem cannabis use, but the recurrence of problem cannabis use does not differ between males and females (13-3b)

There is moderate evidence that:
- Anxiety, personality disorders, and bipolar disorders are *not* risk factors for the development of problem cannabis use (13-2b)
- Major depressive disorder is a risk factor for the development of problem cannabis use (13-2c)
- Adolescent ADHD is *not* a risk factor for the development of problem cannabis use (13-2d)
- Being male is a risk factor for the development of problem cannabis use (13-2f)
- Exposure to the combined use of abused drugs is a risk factor for the development of problem cannabis use (13-2g)
- Neither alcohol nor nicotine dependence alone are risk factors for the progression from cannabis use to problem cannabis use (13-2h)
- During adolescence the frequency of cannabis use, oppositional behaviors, a younger age of first alcohol use, nicotine use, parental substance use, poor school performance, antisocial behaviors, and childhood sexual abuse are risk factors for the development of problem cannabis use (13-2k)

There is moderate evidence of a statistical association between:
- A persistence of problem cannabis use and a history of psychiatric treatment (13-3a)
- Problem cannabis use and increased severity of posttraumatic stress disorder symptoms (13-3c)

There is limited evidence that:
- Childhood anxiety and childhood depression are risk factors for the development of problem cannabis use (13-2a)

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European Journal of Internal Medicine 49 (2018) 12–19

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Review Article

Practical considerations in medical cannabis administration and dosing

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[b] International Cannabis and Cannabinoids Institute, Prague, Czech Republic

ARTICLE INFO

Keywords:
Cannabis
Cannabinoids
Marijuana
Drug abuse
Psychopharmacology
Adverse events

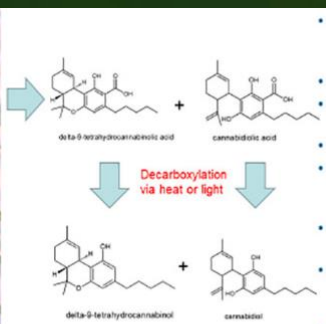
ABSTRACT

Cannabis has been employed medicinally throughout history, but its recent legal prohibition, biochemical complexity and variability, quality control issues, previous dearth of appropriately powered randomised controlled trials, and lack of pertinent education have conspired to leave clinicians in the dark as to how to advise patients pursuing such treatment. With the advent of pharmaceutical cannabis-based medicines (Sativex/nabiximols and Epidiolex), and liberalisation of access in certain nations, this ignorance of cannabis pharmacology and therapeutics has become untenable. In this article, the authors endeavour to present concise data on cannabis pharmacology related to tetrahydrocannabinol (THC), cannabidiol (CBD) et al., methods of administration (smoking, vaporisation, oral), and dosing recommendations. Adverse events of cannabis medicine pertain primarily to THC, whose total daily dose-equivalent should generally be limited to 30 mg/day or less, preferably in conjunction with CBD, to avoid psychoactive sequelae and development of tolerance. CBD, in contrast to THC, is less potent, and may require much higher doses for its adjunctive benefits on pain, inflammation, and attenuation of THC-associated anxiety and tachycardia. Dose initiation should commence at modest levels, and titration of any cannabis preparation should be undertaken slowly over a period of as much as two weeks. Suggestions are offered on cannabis-drug interactions, patient monitoring, and standards of care, while special cases for cannabis therapeutics are addressed: epilepsy, cancer palliation and primary treatment, chronic pain, use in the elderly, Parkinson disease, paediatrics, with concomitant opioids, and in relation to driving and hazardous activities.

Practical considerations in medical cannabis administration and dosing.

Caroline A. MacCallum, Ethan B. Russo

Cannabis sativa



- Dosing need and tolerance depends on prior patient experience with cannabinoids and underlying endocannabinoid tone
- "Start low and go slow!"
- 2.5 mg of THC is a threshold dose for most patients
- 5 mg of THC is usually efficacious and tolerated
- 10 mg of THC produces a strong effect in all except those with tolerance, and may be too much for some
- Doses greater than 20-30 mg/day before tolerance risk psychoactive and other AEs
- Presence of CBD and certain terpenoids in significant amounts may extend therapeutic index.
- Patients should never confuse psychoactivity with efficacy.
- Rather, the correct dose is the lowest that produces a therapeutic benefit without associated adverse events.

European Journal of Internal Medicine: 49(2018) 12-19

Level of Evidence

Table 3
Levels of evidence for cannabis-based medicines in various conditions.

Cannabis and nabiximols supporting evidence	
Level of evidence	**Benefits**
Conclusive or substantial evidence of efficacy	• Adult chronic pain treatment • Multiple sclerosis spasticity symptoms • Chemotherapy-induced nausea and vomiting • Treatment of intractable seizures in Dravet and Lennox-Gastaut syndromes (CBD)
Moderate evidence of efficacy	• Improving outcomes in individuals with sleep disturbances associated with chronic pain, multiple sclerosis, fibromyalgia, obstructive sleep apnea syndrome • Decreasing intraocular pressure in glaucoma
Limited evidence of efficacy	• Symptoms of dementia • Symptoms of Parkinson disease • Positive and negative symptoms of schizophrenia • Symptoms of posttraumatic stress disorder • Appetite and decreasing weight loss associated with HIV/AIDS • Multiple sclerosis spasticity (clinician-measured) • Traumatic brain injury/intracranial haemorrhage associated disability, mortality, and other outcomes • Symptoms of anxiety in social anxiety disorders (CBD) • Symptoms of Tourette syndrome
Limited evidence of inefficacy	• Depressive symptoms in chronic pain or multiple sclerosis patients • Addiction abstinence • Symptoms of irritable bowel syndrome • Cancers, including glioma • Cancer-associated anorexia, cachexia syndrome and anorexia nervosa • Symptoms of amyotrophic lateral sclerosis • Chorea and some neuropsychiatric symptoms associated with Huntington disease • Dystonia
Insufficient evidence of efficacy or inefficacy	

▸ Practical considerations in medical cannabis administration and dosing. Caroline A. MacCallum, Ethan B. Russo

Adverse Effects

C.A. MacCallum, E.B. Russo

Table 4
Adverse events associated with cannabis-based medicines.

Side effect	Most common	Common	Rare
Drowsiness/fatigue	✓		
Dizziness	✓		
Dry mouth	✓		
Cough, phlegm, bronchitis (Smoking only)	✓		
Anxiety	✓		
Nausea	✓		
Cognitive effects	✓		
Euphoria		✓	
Blurred vision		✓	
Headache		✓	
Orthostatic hypotension			✓
Toxic psychosis/paranoia			✓
Depression			✓
Ataxia/dyscoordination			✓
Tachycardia (after titration)			✓
Cannabis hyperemesis			✓
Diarrhea			✓

▸ Practical considerations in medical cannabis administration and dosing. Caroline A. MacCallum, Ethan B. Russo

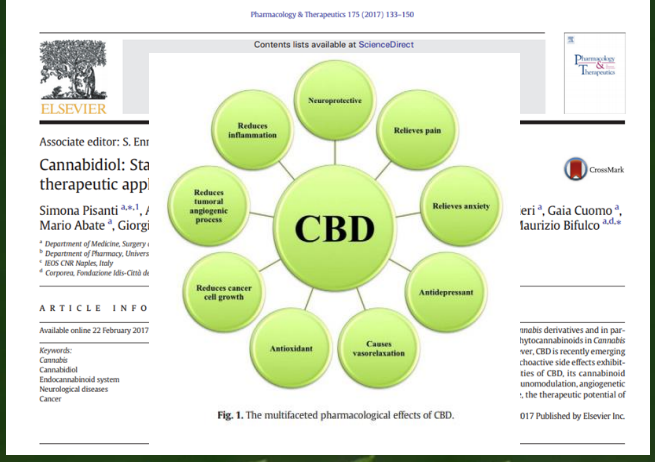


Fig. 1. The multifaceted pharmacological effects of CBD.

S. Pisanti et al. / Pharmacology & Therapeutics 175 (2017) 133–150

Table 2
Overview of CBD pharmacological effects

Disease	Effects
Alzheimer's disease	Antinflammatory, antioxidant, antiapoptotic in *in vitro* and *in vivo* models of Aβ-evoked neuroinflammatory and neurodegenerative responses.
Parkinson's disease	Attenuation of the dopaminergic impairment *in vivo*; neuroprotection; improvement of psychiatric rating and reduction of agitation, nightmare and aggressive behaviour in patients.
Multiple sclerosis	Improved signs of EAE in mice, antinflammatory and immunomodulatory properties.
Epilepsy	Anticonvulsant *in vitro* and *in vivo*; reduced seizures frequency in children and adults with treatment-resistant epilepsy.
Huntington's disease	Neuroprotective and antioxidant in mice transgenic models; no significant clinically important differences in patients.
Hypoxia-ischemia injury	Short term neuroprotective effects; inhibition of excitotoxicity, oxidative stress and inflammation *in vitro* and in rodent models.
Pain	Analgesic effect in patients with neuropathic pain resistant to other treatments.
Anxiety	Attenuation of the behavioural and glial changes in animal models of schizophrenia; anti-psychotic properties on ketamine-induced symptoms. Reduction of muscular tension, restlessness, fatigue, problems in concentration, improvement of social interactions in rodent models of anxiety and stress; reduced social anxiety in patients.
Depression	Anti-depressant effect in genetic rodent model of depression.
Cancer	Antiproliferative and anti-invasive actions in a large range of cancer types; induction of autophagy-mediated cancer cell death; chemopreventive effects.
Nausea	Suppression of nausea and conditioned gaping in rats
Inflammatory diseases	Antinflammatory properties in several in vitro and in vivo models; inhibition of inflammatory cytokines and pathways.
Rheumatoid arthritis	Inhibition of TNF-α in an animal model
Infection	Activity against methicillin-resistant *Staphylococcus aureus*
Inflammatory bowel and Chron's diseases	Inhibition of macrophage recruitment and TNF-α secretion *in vivo* and *ex vivo*; reduction in disease activity index in Chron's patients.
Cardiovascular diseases	Reduced infarct size through anti-oxidant and anti-inflammatory properties *in vitro* and *in vivo*.
Diabetic complications	Attenuation of fibrosis and myocardial dysfunction

S. Pisanti et al. / Pharmacology & Therapeutics 175 (2017) 133–150

Cannabis and Botanicals

- The Herb!!!
- (Herbal Medicine)

- All the rest of the herbs (botanical medicine)

Popularity of Cannabis and Botanical Medicine over the 25 years

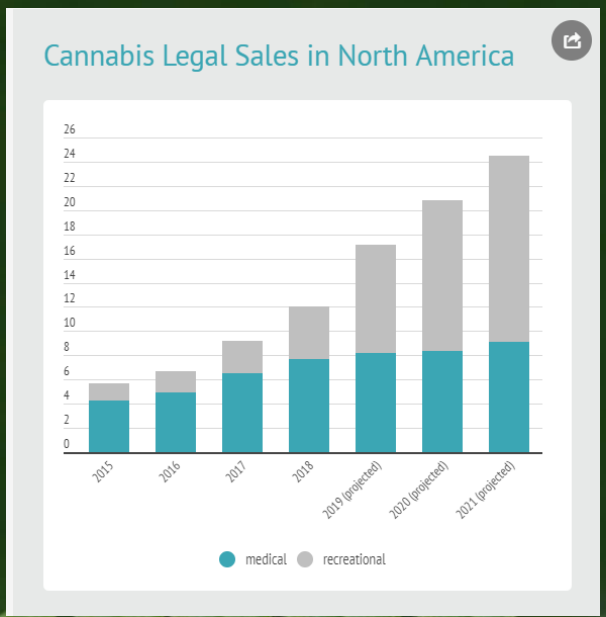
The use of Cannabis and Herbs Today

Cannabis
Legal Sales
9 Billion
2017#

Botanical medicine
Sales 8 billion 2017*

CNN wire, Jan 2017

* Herbal Gram issue 119, July 2018



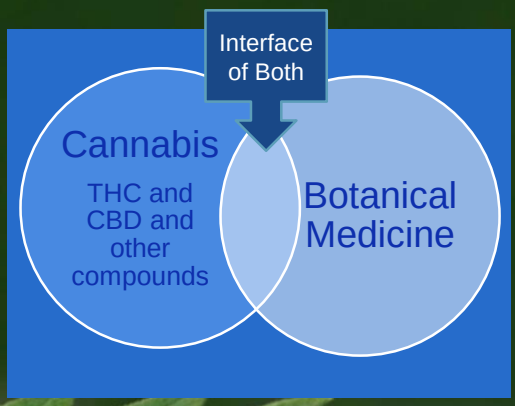
https://cannabusinessplans.com/cannabis-legal-market-size-projections

The Future of Cannabis and Botanicals

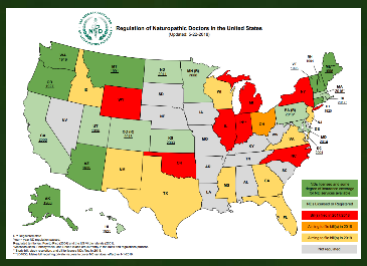
https://cannabusinessplans.com/cannabis-legal-market-size-projections/

The Future of Cannabis and Botanical Medicine

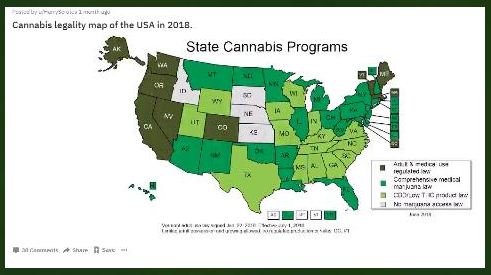
- Our patients will be using both at rapidly increasing rates
- What is the potential interactions?
- What is the potential synergy?
- What does the research say?



Naturopathic Regulation 2018



Cannabis Regulation 2018

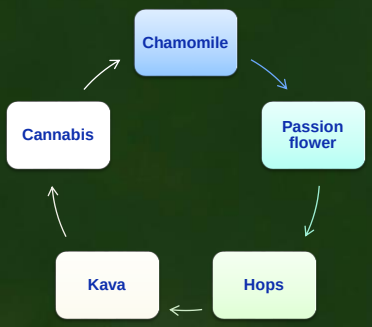


- 9 out of 10 LEGAL REC. STATES ARE LICENSED NATUROPATHIC MEDICINE STATES
- ALL STATES WITH NATUROPATHIC REGULATION HAVE LEGAL MEDICAL OR RECREATIONAL CANNABIS LAWS
- Our patients are using both Naturopathic medicine and Cannabis!
- Source: Natropathic.org

Naturopathic Therapeutic Order of Botanicals

Therapeutic Combinations /Use/ Synergy

Relaxation: Mild to Strong



Cannabis and Kava

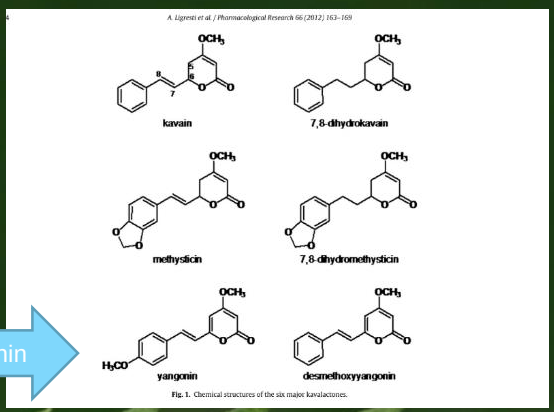
Similarities

Many cultivars
Anxiolytic (CBD)
Fast acting

- Actives in Kava
  - Kava lactones
  - 6 noble varieties
- Actives in Cannabis (545+)
  - Cannabinoids (60+)
  - Flavonoids
  - Steroids
  - Fatty acids
  - Terpenes

Kava Kava

Kava Lactones: 6 Noble Varieties



Yangonin

Pharmacological Research 66 (2012)163-169

Kavalactones and the endocannabinoid system: The plant-derived yangonin is a novel CB_1 receptor ligand

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Keywords:
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Natural products
Kava
Cannabinoid receptors
CB_1
CB_2
Endocannabinoid
FAAH
MAGL

ABSTRACT

...proteins of the endo-...folds for the design ...ones, a preliminary ...d nine kavalactone-...g their cannabinoid ...etabolic enzymes of ...cerol lipase (MAGL). ...binant CB_1 receptor ...mpounds exhibited ...f yangonin suggests that the endocannabinoid system might contribute to the complex human psychopharmacology of the traditional kava drink and the anxiolytic preparations obtained from the kava plant.

The CB1 receptor affinity of yangonin suggest that the endocannbinoid system might contribute to the complex human psychopharmacology of the traditional kava drink and the anxiolytic preparations obtained from the kava plant

Pharmacological Research 66 (2012)163-169

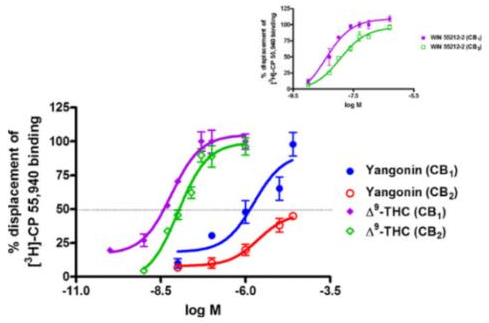

Fig. 3. Displacement curves of yangonin and the reference compound, THC. Also the displacement curves of WIN 55212-2, used for the determination of non-specific binding, are shown. Data are reported as mean ± SE of three experiments.

This study reports that yangonin, is a relatively good ligand of cannabinoid CB_1 receptors, although weaker than THC

Pharmacological Research 66 (2012)163-169

Cannabis and Echinacea

Similarities:

- Immune modulating
- Anxiolytic (CBD)
- Antiinflamatory
- Anti depression

- Actives in Echinacea
  - Alkamides
  - Polysaccarides
  - Cichoric acid
  - Caffeic acid
  - Glycoproteins

- Actives in Cannabis (545+)
  - Cannabinoids (60+)
  - Flavonoids
  - Steroids
  - Fatty acids
  - Terpenes

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Alkylamides from *Echinacea* Are a New Class of Cannabinomimetics

CANNABINOID TYPE 2 RECEPTOR-DEPENDENT AND -INDEPENDENT IMMUNOMODULATORY EFFECTS

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Alkylamides (alkamides) from *Echinacea* modulate tumor necrosis factor α mRNA expression in human monocytes/macrophages via the cannabinoid type 2 (CB_2) receptor (Gertsch, J., Schoop, R., Kuenzle, U., and Suter, A. (2004) *FEBS Lett.* 577, 563–569). Here we show that the alkylamides dodeca-2*E*,4*E*,8*Z*,10*Z*-tetraenoic acid isobutylamide (A1) and dodeca-2*E*,4*E*-dienoic acid isobutylamide (A2) bind to the CB_2 receptor more strongly than the endogenous cannabinoids. The K_i values of A1 and A2 (CB_2 ~60 nM; CB_1 >1500

the treatment of the common cold and upper respiratory infections are contradictory (4, 5). In contrast to the significant investments into the clinical assessment of the efficacy of *Echinacea* (6), the molecular mechanism of action of this medicinal plant has remained elusive, and comprehensive studies on the immunomodulatory actions of *Echinacea* constituents are scarce.

We have reported previously that unsaturated fatty acid *N*-alkylamides (alkylamides) from *Echinacea* preparations can modulate the

Echinacea and Cannabinomimetic

Our data demonstrate that alkylamides from *Echinacea* are a new class of CB_2-specific cannabinomimetics, which share the anti-inflammatory properties of anandamide and the cannabinoids from *Cannabis sativa* (19). With respect to the intracellular responses triggered via the CB_2 receptor, alkylamides from *Echinacea* resemble the endogenous cannabinoid 2-AG, which also stimulates Ca^{2+} transients in a CB_2 receptor-dependent manner (39, 46). The fact, however, that the anti-inflammatory effects exerted by cannabinomimetics are not strictly CB_2-dependent, as shown in this and previous studies (59, 60), raises the question about a possible common second target.

Echinacea preparations have been claimed to exert both stimulatory and inhibitory effects on immune cells (20–21). The evaluation of the immunomodulatory actions of alkylamides, which represent one of the most important constituent classes of *Echinacea*, thus constitutes an important step on the way to a better understanding of the molecular and pharmacological nature of these herbal remedies.

Cannabis and Ashwagandha

Similarities
- Immune modulating
- Anxiolytic (CBD)
- Neuroprotective

- Actives in Ashwagandha
  - Alkaloids
  - steroidal lactones withanolides (35) withaferins
  - Saponins

- Actives in Cannabis (545+)
  - Cannabinoids (60+)
  - Flavonoids
  - Steroids
  - Fatty acids
  - Terpenes

Ashwagandha Studies

ASHWAGANDHA FOR MEMORY AND COGNITION

Efficacy and Safety of Ashwagandha (Withania somnifera (L.) Dunal) Root Extract in Improving Memory and Cognitive Functions

Choudhary, D., Bhattacharyya, S., & Bose, S. (2017). Journal of Dietary Supplements, 1-14. Chicago

Conclusion: Ashwagandha may be effective in enhancing both immediate and general memory in people with MCI as well as improving executive function, attention, and information processing speed.

Cannabis and Holy Basil

Similarities
Immune modulating
Anti-oxidant
Anti-stress
Hypotensive
Anti-Cancer

- Actives in Holy Basil (7)
  - Terpenes
  - Flavonoids
  - Alkaloids
  - Phenols
  - Glycosides
  - Saponins
  - Tannins
- Actives in Cannabis (545+)
  - Cannabinoids (60+)
  - Flavonoids
  - Steroids
  - Fatty acids
  - Terpenes

PHYTOTHERAPY RESEARCH
Phytother. Res. **30**: 805–814 (2016)
Published online 22 February 2016 in Wiley Online Library
(wileyonlinelibrary.com) **DOI**: 10.1002/ptr.5584

Anti-stress Activity of *Ocimum sanctum*: Possible Effects on Hypothalamic–Pituitary–Adrenal Axis

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The present study investigated anti-stress potential of *Ocimum sanctum* in chronic variable stress (CVS) paradigm. Further, the possible mechanism of anti-stress was explored *in vitro* using cell and cell-free assays. Rats were administered *O. sanctum* followed by CVS regimen for a period of 16 days. On days 4, 8, 12, and 16, body weight and immobility time in forced swim test were measured. In addition, the possible inhibitory effect of *O. sanctum* and ursolic acid on cortisol release and CRHR1 receptor activity were studied in cell-based assays, while inhibitory effects on 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) and catechol-*O*-methyltransferase (COMT) were studied in cell-free assays. CVS group demonstrated less body weight gain and higher immobility time than *O. sanctum* administered groups, while oral administration of *O. sanctum* significantly increased body weight gain and decreased the immobility time. Further, *O. sanctum* and its constituents inhibited cortisol release and exhibited a significant CRHR1 receptor antagonist activity. Also, they had specific inhibitory activity towards 11β-HSD1 and COMT activity. Thus, *O. sanctum* was found to be effective in the management of stress effects, and anti-stress activity could be due to inhibition of cortisol release, blocking CRHR1 receptor, and inhibiting 11β-HSD1 and COMT activities. Copyright © 2016 John Wiley & Sons, Ltd.

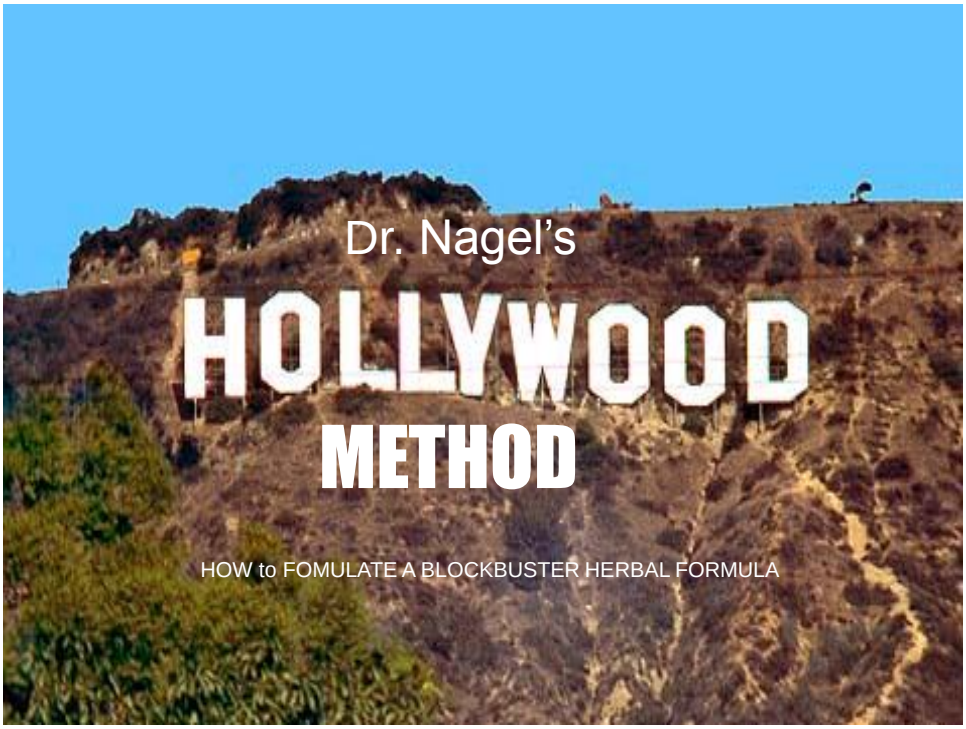
Keywords: anti-stress; catechol-*O*-methyltransferase; cortisol; corticotropin-releasing factor receptor 1; forced swim test; *Ocimum sanctum*.

Cannabis in formulation with botanicals

- Actions are widespread, cannabinoids are promiscuous!
- Inquiry: could concomitant use of botanical and cannabis make the results more predictable/reliable
- Synergy with other botanicals
- Use with other botanicals can support lower therapeutic doses
- Start low and go slow. Titrated dosing strategies.

- Dose alone as simple (low dosing, hormesis)
- Dose in combination with other herbs
  - Adaptogens
  - Tonics
  - Stimulates
  - Relaxants
  - Cooling and moistening

Dose as low dose herb



Herbal Formulations: Summary

- **Hollywood Film Players**
- Screen Writer
- Leading Actor or The Star
- Supporting Actors
- Behind-the-scenes cast
- Director
- Producer

- **Herbal Formula Players**
- **Overall Concept:**
- Star Acting Herb, Primary medicinal herb
- Supporting Herbs (2nd or co-primary herbs)
- Supporting background herb(s)
- Activator or Harmonizing herb
- Form of herbal product

The Activator, synergist

- *Cannabis AS AN ACTIVATOR!*
  - *THC*
  - *CBD*
  - *Terpenes*
- Similar to other so-called low-dose herbs
- Cayenne, Aconite

"Low Dose" or "Drop Dose" Botanicals

- Focus on the prescribing method
- Low or drop dosing
- Describes a group of plants that are not tonic herbs
- Everything low is now cool!

Commonly Used "Drop dose" Herbs

- *Aconitum*
- *Atropa belladonna*
- *Baptisia tinctoria*
- *Bryonia alba*
- *Cannabis spp.*
- *Capsicum annuum*
- *Convallaria*
- *Datura stramonium*
- *Digitalis purpurea*
- *Ephedra sinica*
- *Gelsemium*
- *Hyoscyamus*

- *Iris versicolor*
- *Leptandra*
- *Lithospermaum*
- *Lobelia inflata*
- *Lycopus viriginicus*
- *Pausinystalia yohimbe*
- *Phytolacca spp.*
- *Piscidia*
- *Podophyllum*
- *Rauwolfia*
- *Sanguinaria*
- *Tanacetum vulgare*
- *Veratrum alba*
- *Viscum album*

Commonly Used "Drop dose" Herbs

- *Ricinis (Castor bean)*
- *Sanguinaria*
- *Selenicereus (Cactus grandiflorus)*
- *Tanacetum vulgare*
- *Veratrum alba, viride*
- *Viscum album, flavescens*

Potency of Low-Dose Tinctures

- Highest quality is important, many are imported from Europe.
- Choose suppliers carefully, many don't carry them now because of liability issues.
- Ask for assayed levels of potent components if possible. For example, *Rauwolfia*
- Assayed is not the same as a standardized drug.
- Consider interactions with compounding.
- Do not make these yourself!

Eclectic Physician System of Dosing

- Used uniformly made specific medicines. (Lloyd Brothers Pharmacy)
- Prescribed for specific symptoms.
- Commonly prescribed 5 to 10 drops of specific medicine to 4 ounces of water. Patients took 1 teaspoon 3 times a day.
- Used herbs in homeopathic doses. (1x)

Lloyd on Dose from Materia Medica 1922

"As a rule, doses usually administered are far in excess of necessity and it its better to err on the side of insufficient dosage and trust to nature, than to overdose to the present or future harm or danger to the patient."

"With potent drugs especially should the greatest care be had to give the smallest possible quantities that will achieve results, and never to give them without a well defined indication."

Dr. Harvey Felter from The Eclectic Materia Medica, Pharmacology and Therapeutics. 1922 pg 38 .

Low Dose Dosing by Felter

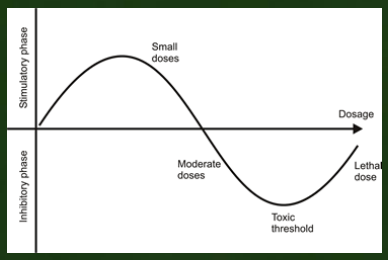
"It remains a clinical fact that many drugs of supposedly non potent character, when given in minute doses, best influence conditions of disease, even though no explanation of the action can be given.

"The fractional dose of *Matricaria* or of *Pulsatilla* effects a positive control over nervous phenomena that cannot be duplicated by the more powerful agents or doses."

Dr. Harvey Felter from *The Eclectic Materia Medica, Pharmacology and Therapeutics*. 1922, p. 38.

Hormesis / Ultra low dose

- Hórmēsis (Greek): to set in motion, excite
- Biphasic dose responses
- U or J-shaped stimulation
- Low doses can stimulate physiology and support homeostatic mechanisms
- Higher doses can inhibit physiology and suppress homeostatic mechanisms



Hormesis and Pharmacology by Edward Calabrese, 2009

THE SIX TISSUE STATES

Heat / Excitement

Tension/ Wind

Dry/ Atrophy

- Damp/ Stagnation

Relaxation/ Damp

Cold / Depression

Source: Earthwise Herbal, by Matt Wood, North Atlantic Press, 2009

6 Tissue States by Matt Wood

Tissue State	Treatment	Taste	Pharmacology
Heat/Excitation	Cooling	Sour	Flavonoids, cyanogens
Cold/Depression	Warming	Pungent	Aromatics, volatile oils
Dry/Atrophy	Moistening	Salty	Mucilages, emollients
	Nourishing	Sweet	Carbohydrates
Damp/Stagnation	Purifying	Bitter	Bitters
Wind/Tension	Relaxing	Acrid	Acrid bitters
Damp/Relaxation	Tightening	Astringent	Tannins

Source: Earthwise Herbal, by Matt Wood, North Atlantic Press, 2009

Cannabis and 6 Tissue States

Formulation Basics

What are your Cannabis types

- Whole flower with all parts (Entourage Effect)
- High THC, low THC
- Balanced (1:1)
- Raw or decarb flower
- Tinctures, oils
- Isolated extracts
  - THC high
  - CBD High

CANNABIS

- The great trickster
- The great relaxer
- The great stimulator
- The great synergist
- Bring people and plants together
- The Great Everything herb!
- Attitude of Gratitude

Make your own tincture

INGREDIENTS:

- 1 pint (8 oz) of hard liquor such as brandy, vodka or Everclear (use the highest proof available).
- 2 ounces of Cannabis (Use 1:1 or 2:1 strain)
- Blender, strainer, cheesecloth, paper bag, coffee filter
- 1-pint glass mason jar with lid
- Small brown or blue glass bottles with droppers
- Funnel to fit into the small dropper bottles

ACTIVATING THE CANNABINOIDS: DECARBOXYLATION

- The most potent medical benefits of cannabis are achieved by activating the cannabis with heat. Is known as decarboxylation.
- Grind the cannabis in a blender, coffee grinder, or food processor into small particles, but not powder.
- Preheat oven to 325°F. Many consumer ovens' thermostats are inaccurate, so please verify the temperature with an oven thermometer.
- Spread the ground cannabis evenly on a baking sheet.
- Bake at 325°F for five minutes or until the first signs of smoke or vapor can be seen.
- Alternative: 240°F for 45-60 minutes. While this takes longer, it may do a better job of preserving essential oils and other therapeutic substances in cannabis
- Source: Healer.com

Maceration of Cannabis

- **Method 1: COLD EXTRACTION**
  - Place ground and activated cannabis in the 1-pint mason jar.
  - Fill the jar with high-proof alcohol, leaving a half inch at the top. Apply lid.
  - Place the lidded mason jar with the alcohol and cannabis in it in a paper bag and place the paper bag in the freezer. Shake the jar once a day for three to four days.
- **METHOD 2: DARK PLACE EXTRACTION**
  - Place ground and activated cannabis in the 1-pint mason jar.
  - Fill the jar with high-proof alcohol, leaving a half inch at the top. Apply lid.
  - Place the jar in a brown paper bag in a cool, dark place. Shake for a few minutes every day for three to four weeks. (Some experts recommend up to six months for a stronger preparation.)
- Strain with cheese cloth and coffee filters, store in amber dropper jars
- Dose depends on strain, consider that you can extract 80% of EC
- Source: healer.com

Resources

- Research: Dr Ethan Russo
  https://www.researchgate.net/profile/Ethan_Russo
- Leafy.com : Industry website
- www.drcarolinemaccallum.com/cannabis-resources/
- A woman's guide to Cannabis, by Nikki Furrur
- Dr Sulak: https://healer.com/category/cannabis-and-opioids/

Thank you !

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