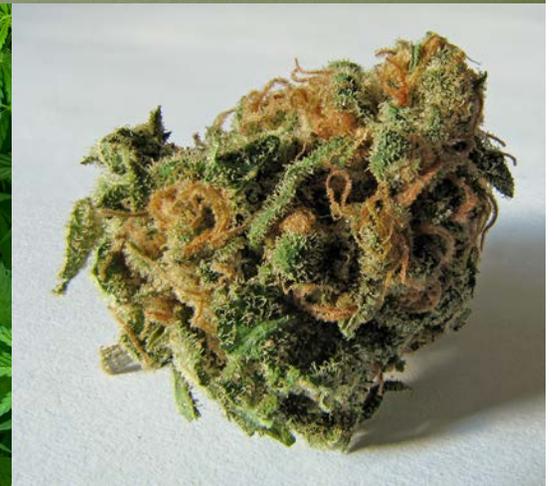
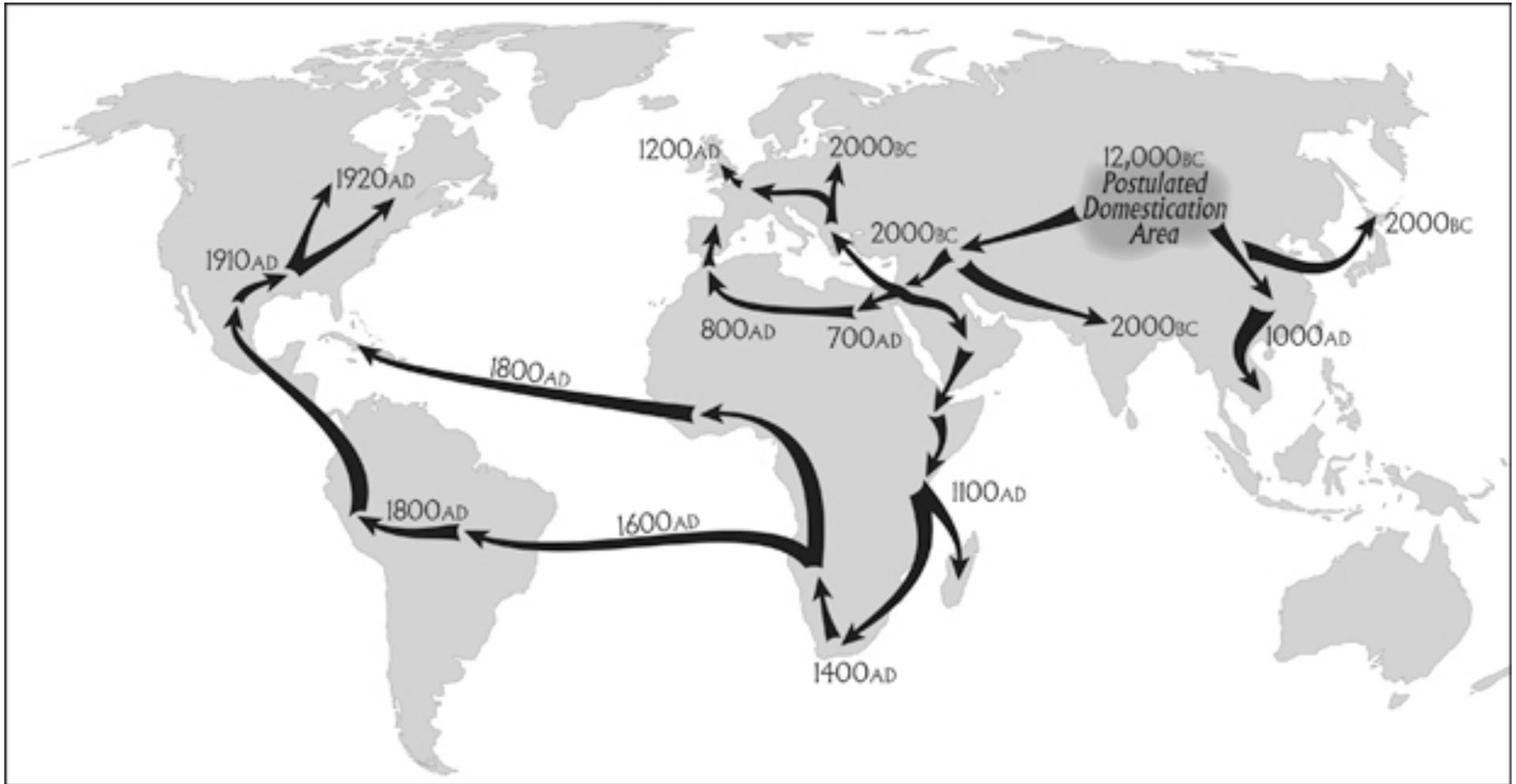


Demystifying Cannabis

Traditional Roots Conference
May 15 2015





Cannabis History

- ❖ Central Asia origins
 - ❖ Expansion of “landraces” to new climates, forming new varieties
- ❖ Oldest recorded use: 2700BCE in Northern China
 - ❖ Hemp seeds (Ma Ren) – TCM moistening/laxative digestive remedy
 - ❖ Flowers (Ma Fen) – used in Han Dynasty texts for certain types of pain
- ❖ Ayurvedic use
 - ❖ Bhang
 - ❖ Ganga
 - ❖ Hashish
 - ❖ Most preparations involve boiling in milk
 - ❖ Qualities: hot, sharp, penetrating in energy
 - ❖ Increases pitta, reduces kapha; relieves pain, promotes sleep

Entering Western Medicine



- ❖ William O'Shaughnessey
- ❖ 1850: Cannabis in USP
 - ❖ Tincture, fluid extract
- ❖ Eclectic use: King's American Dispensatory
- ❖ 1910-1920: recreational use by border town migrants, jazz musicians
- ❖ Maligned with 'social ills and deviance'

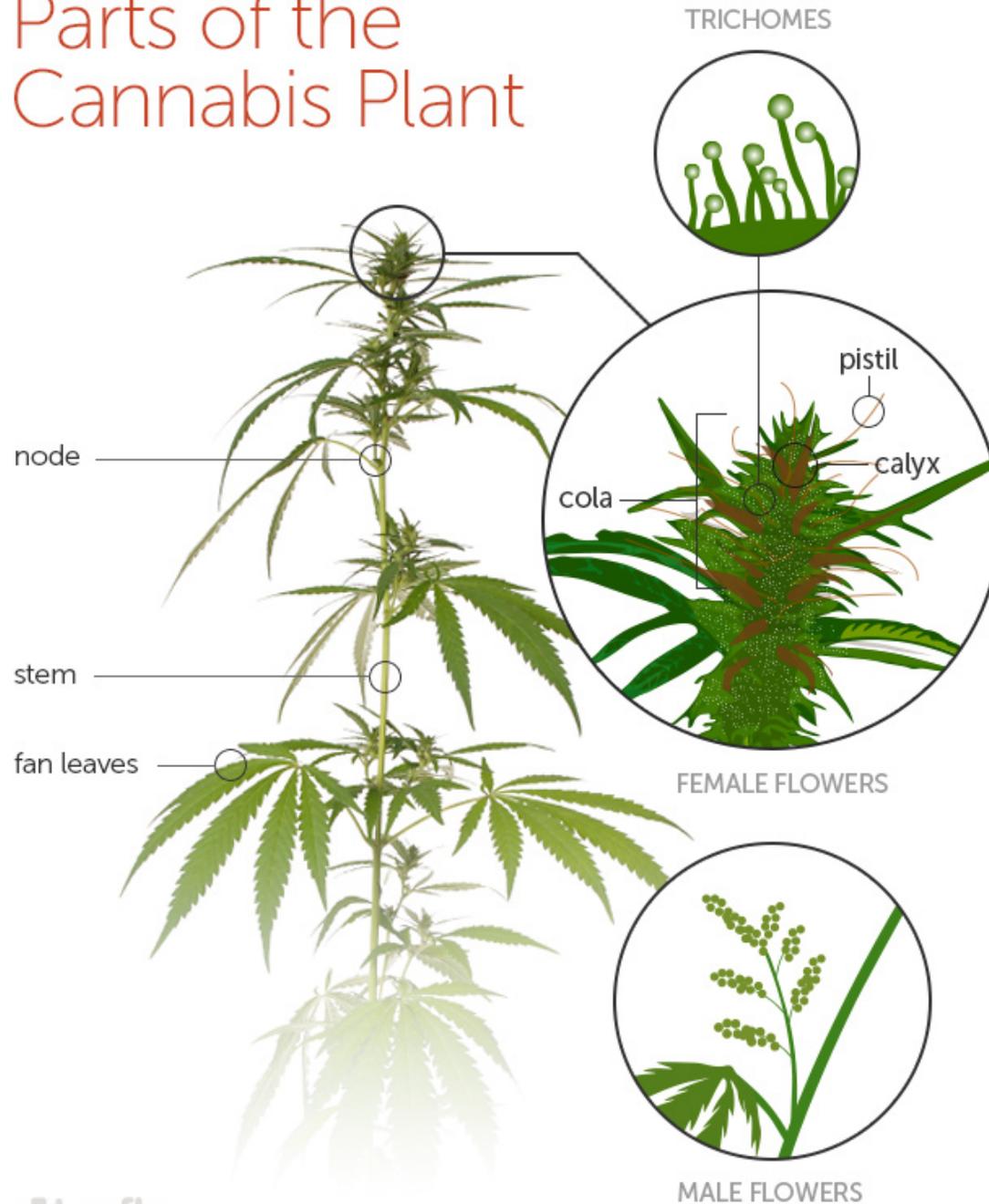
Prohibition

- ❖ 1937 Marihuana Tax Act
 - ❖ Opposed by AMA
- ❖ THC discovered in 1960's
- ❖ Schedule 1 designation in 1970
- ❖ NIDA mandate in effect for cannabis research
 - ❖ Negative effects research – dependence, driving, withdrawal
- ❖ Indoor growing methods

State of the Science

- ❖ NIDA mandate
 - ❖ National Institute for Drug Abuse
 - ❖ Negative effects, not therapeutics
 - ❖ Non-representative cannabis (2-4% THC)
- ❖ Highly biased literature from US studies
- ❖ Most research from Israel, Western Europe
- ❖ Data is preclinical and anecdotal (internet)
- ❖ Hyperbole, excitement, little data

Parts of the Cannabis Plant





Glandular Trichome

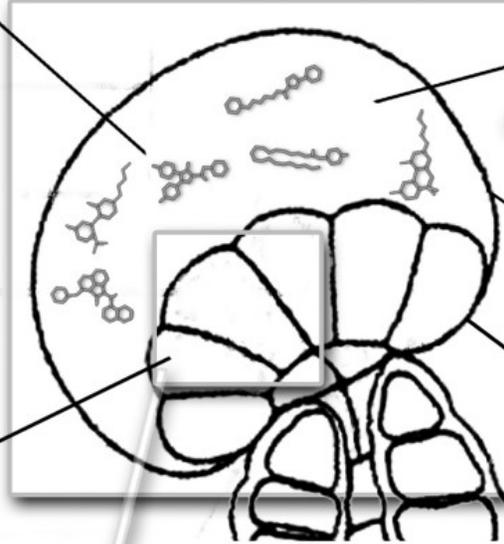
manufacturing and storing phytocannabinoids

Trichome Head

Cannabinoids

Secretory Reservoir

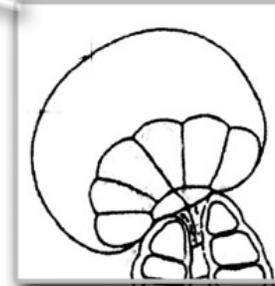
Terpenes



Trichome cross section

Waxy surface Layer

Rosette of Gland Cells



Resin Gland Disk Cell

Cannabinoids

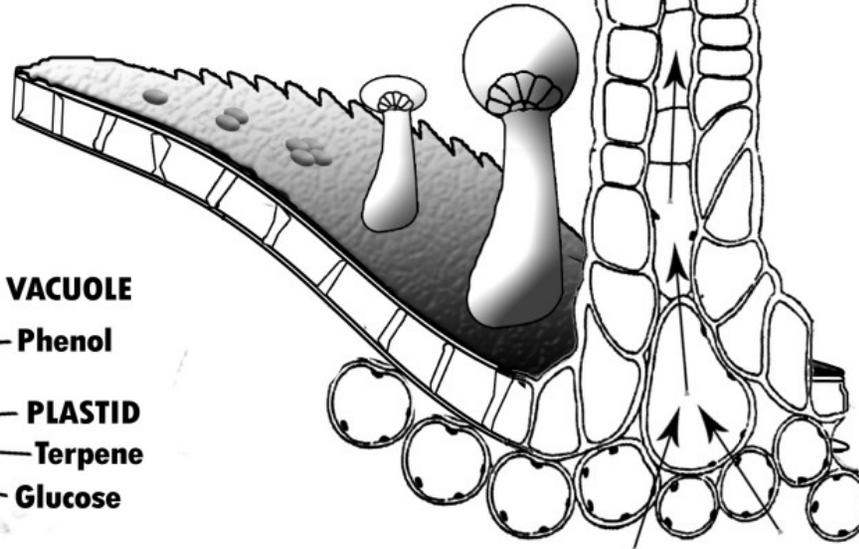
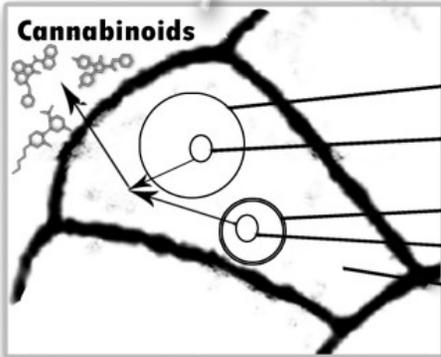
VACUOLE

Phenol

PLASTID

Terpene

Glucose





Sativa vs Indica

energy
stimulating
head high
cerebral
uplifting
creativity
focus
fights depression

couch-lock
chilling
appetite
body high
deep relaxation
sleep aid
pain + nausea relief
stress + anxiety relief

Endocannabinoid System (ECS)

- ❖ Pain response, hunger, stress response, cell development and cancer
 - ❖ “Eat, Sleep, Relax, Protect” – Di Marzo
- ❖ Discovered in early 1990’s
- ❖ Focus of biomedical research due to role in homeostasis
- ❖ Composed of cannabinoid receptors (CBRs) and endocannabinoids
- ❖ Modulates Cannabis therapeutics and psychoactivity

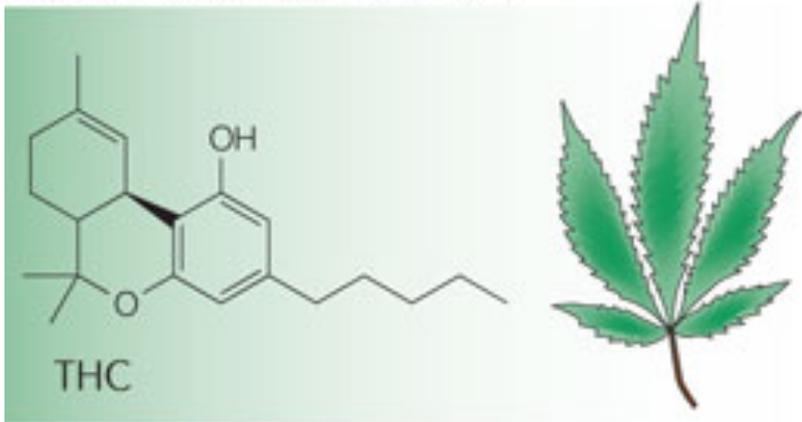
Cannabinoid receptors (CBRs)

- ❖ CB1 – CNS distribution
 - ❖ Medulla, hypothalamus, hippocampus, cerebral cortex, basal ganglia, spinal cord
 - ❖ THC is CB1 agonist
 - ❖ Reduces refractory period between synapses
- ❖ CB2 – Immune cells and tissues
 - ❖ Immune function and inflammation
 - ❖ Lymphoid/immune tissues
 - ❖ Tonsils, spleen
 - ❖ Immune cells
 - ❖ B cells
 - ❖ T cells
 - ❖ NK cells

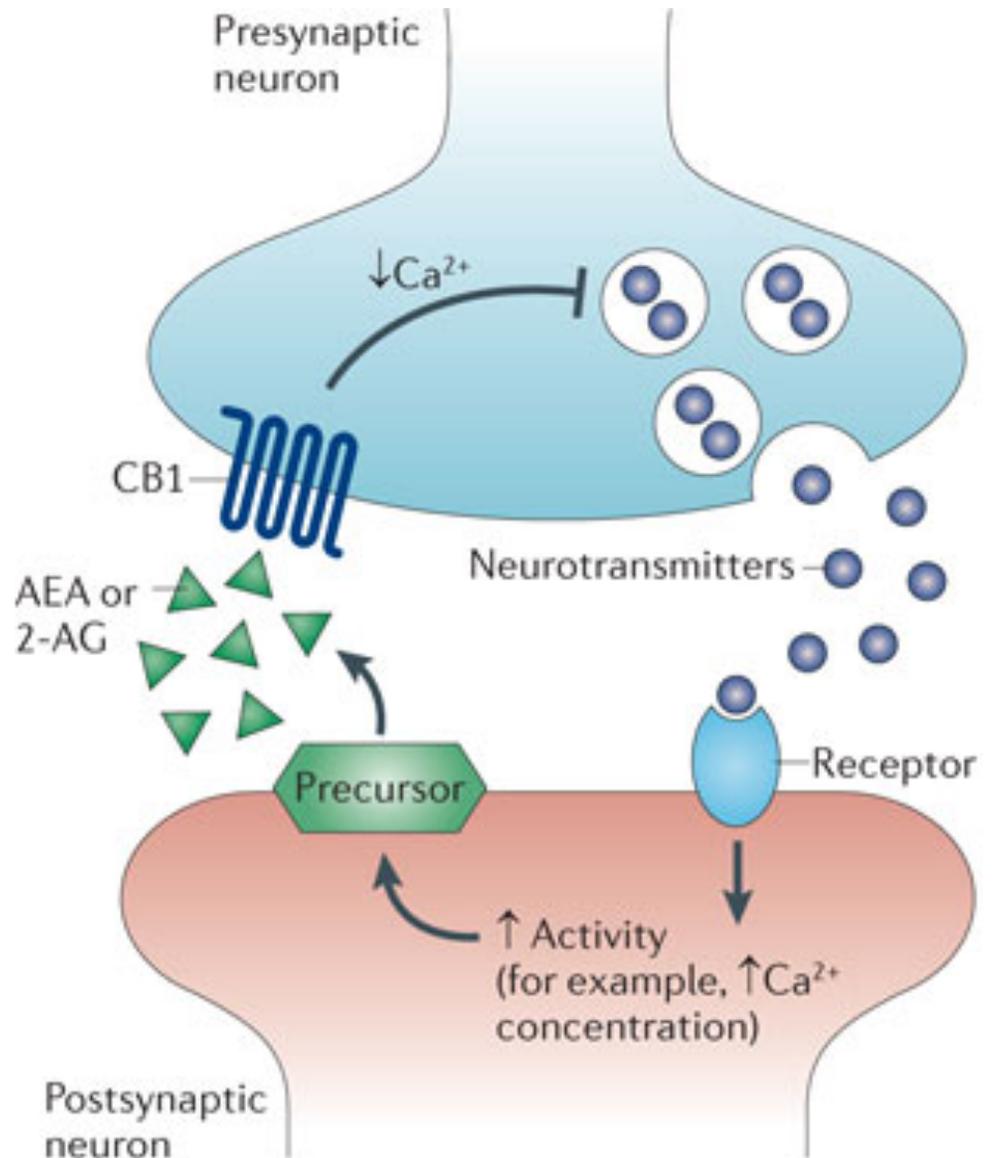
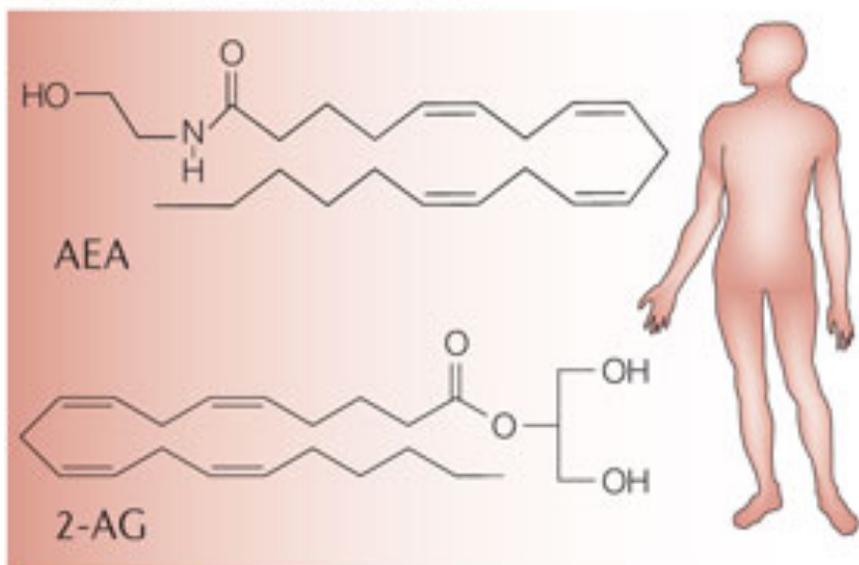
Endocannabinoids

- ❖ Lipid signaling molecules
- ❖ 2-AG
 - ❖ Neural inflammatory responses
- ❖ Anandamide
 - ❖ Ananda=bliss
 - ❖ Memory (ability to forget), eating behavior, pleasure

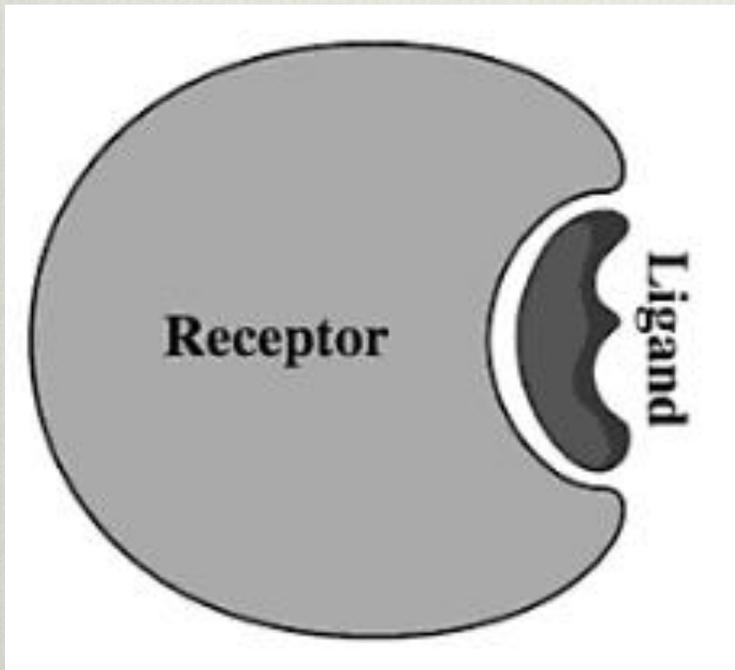
Plant-derived cannabinoid



Endogenous cannabinoids



Human and cannabis *coevolution?*



- ❖ ECS - 600,000,000 years ago
- ❖ Cannabis - 34,000,000 years ago
- ❖ ECS present in all mammals, vertebrates, and Hydra genus
- ❖ Vestigial receptor hypothesis

ECS Cont'd

- ❖ Major role in homeostasis
 - ❖ Neuroendocrine function
 - ❖ Lipid metabolism
 - ❖ Cardiovascular disease
 - ❖ Musculoskeletal health
- ❖ Alterations reported in nearly all human disease
- ❖ Can be stimulated or suppressed
 - ❖ *Endocannabinoid Deficiency Syndrome* – Ethan Russo

ECS: key to Cannabis therapeutics

- ❖ Cannabinoids supplement and stimulate the ECS
- ❖ Effects on person depend on ECS “tone” and background activity
 - ❖ Chronic smokers and recreational users vs. abstainers
- ❖ **Cannabis can have varying effects on people depending on their ECS tone and activity**

Cannabinoids

- ❖ Endocannabinoids
- ❖ Synthetic cannabinoids
 - ❖ Marinol, Cesamet, research materials
- ❖ **Phytocannabinoids**
 - ❖ 100+ in Cannabis

THC

- ❖ CB1 – CNS activity
- ❖ psychoactive
- ❖ Affects dopamine, serotonin, norepinephrine
 - ❖ Pain
 - ❖ Appetite
 - ❖ Nausea and vomiting
 - ❖ neuroprotective
- ❖ Strains can contain up to 30%
- ❖ Concentrates up to 95%

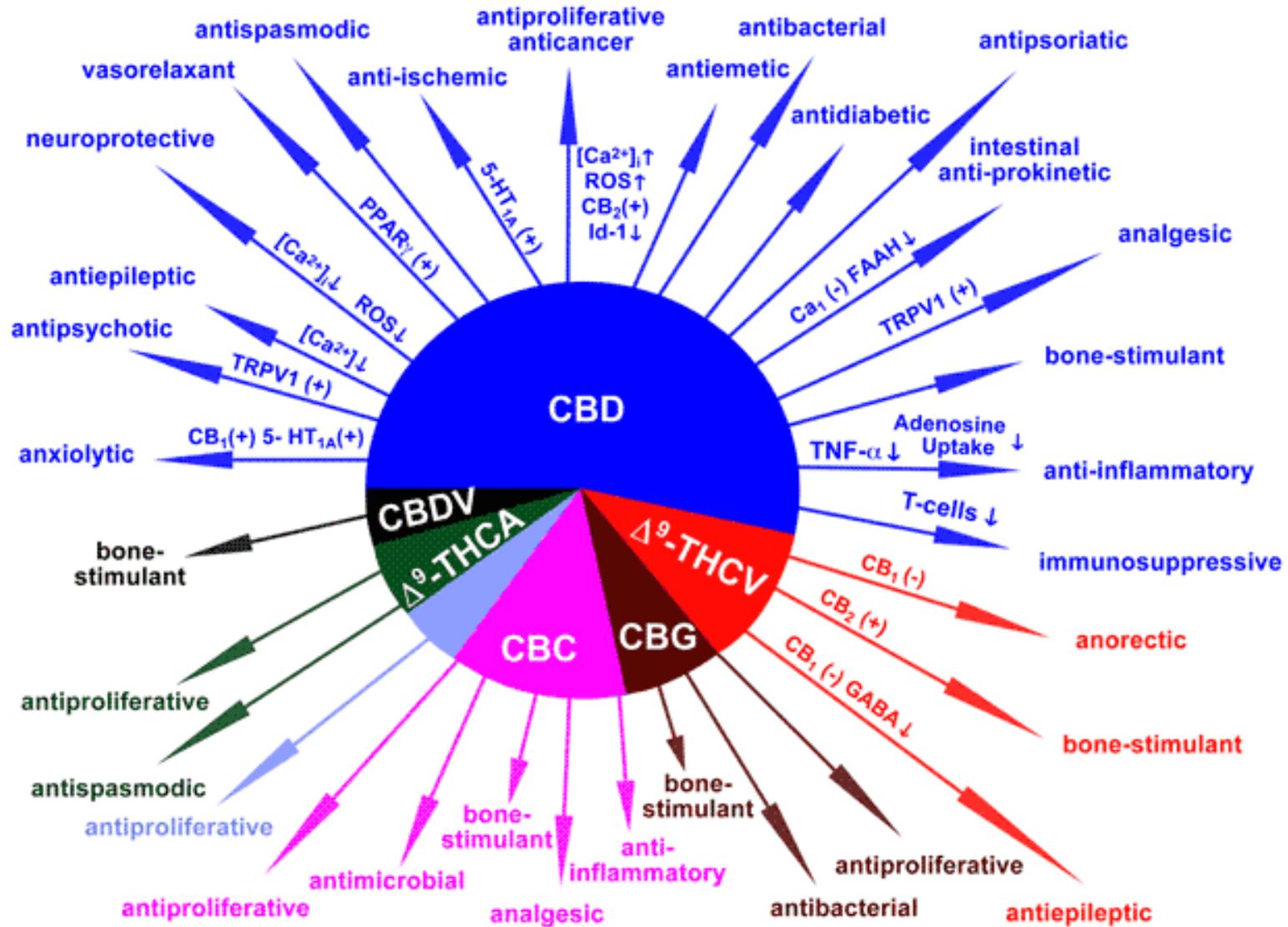
CBD

- ❖ Nonpsychoactive
- ❖ CB2 – Immune function and inflammation
- ❖ Antipsychotic
- ❖ Pediatric seizure disorders
- ❖ Modulates psychoactivity of THC
- ❖ low-THC/high CBD strains
 - ❖ Harlequin
 - ❖ AC/DC
- ❖ CBD-only products, CBD-specific laws

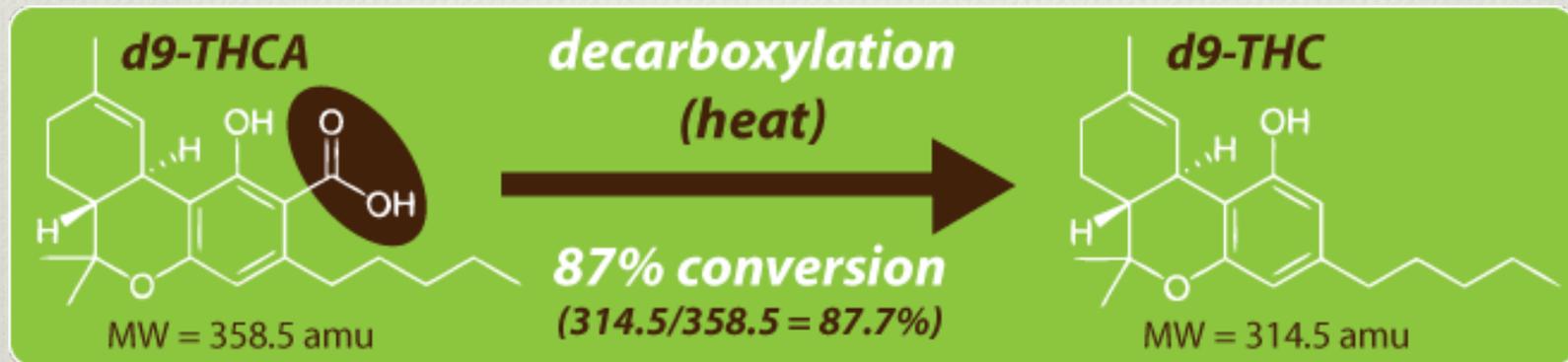
- ❖ CBG - cannabigerol
 - ❖ Precursor molecule, antiinflammatory, analgesic
- ❖ THCV - tetrahydrocannabivarin
 - ❖ Antispasmodic, analgesic, antiinflammatory
- ❖ CBC - cannabichromene
- ❖ CBN – cannabinol
- ❖ Minor cannabinoids
 - ❖ D-8-THC
 - ❖ CBE
 - ❖ CBT
 - ❖ CBL
 - ❖ CBND
 - ❖ Neuroprotection, analgesia, antispasmodic, antiinflammatory

Pharmacological actions of non-psychotropic cannabinoids

(with the indication of the proposed mechanisms of action).

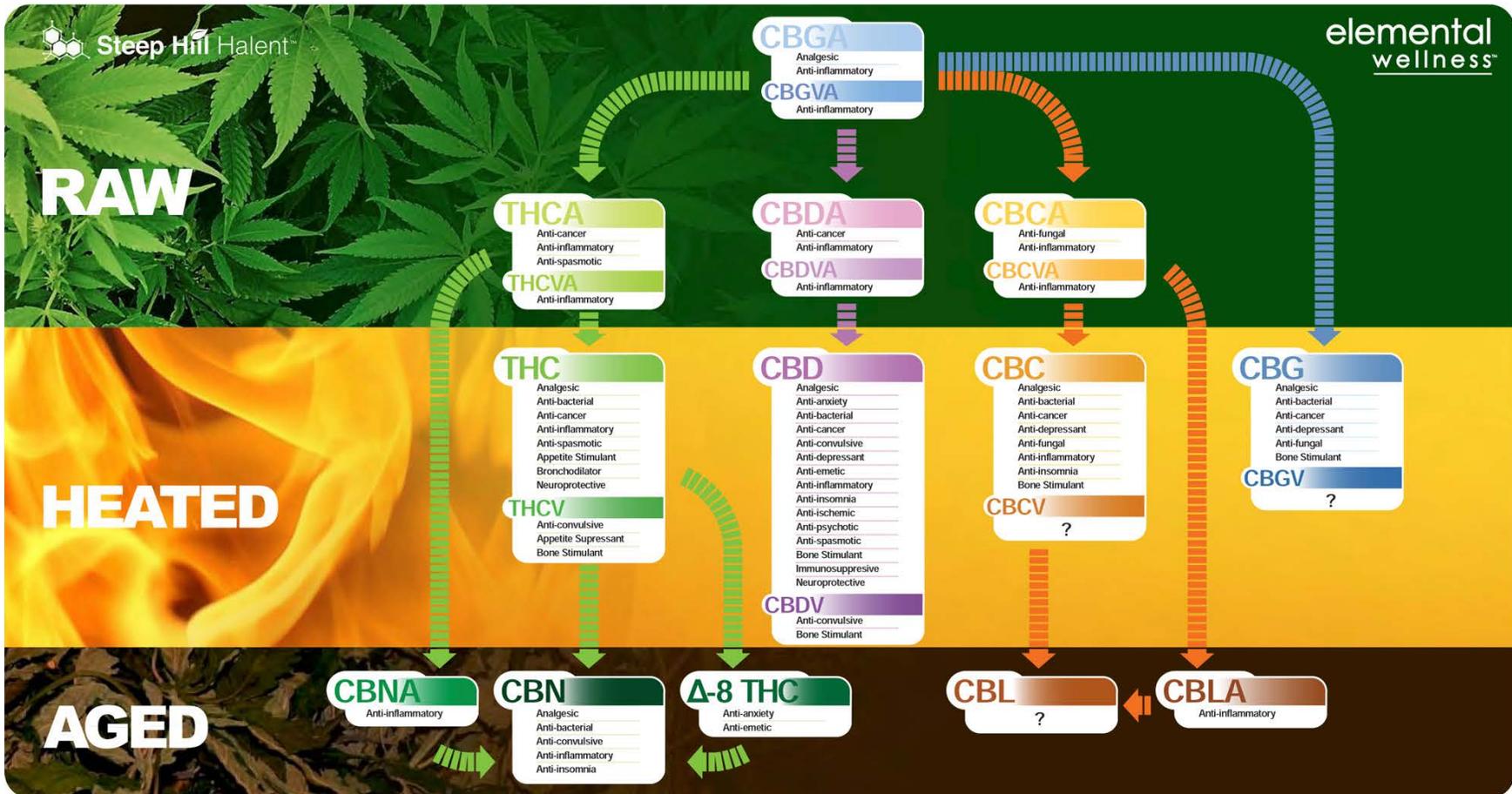


Decarboxylation



UNDERSTANDING MEDICAL CANNABIS

Cannabinoids and Their Therapeutic Effects



Terpenes

- ❖ Limonene (citrus)
 - ❖ Antidepressant, anxiolytic, antioxidant
- ❖ Pinene (conifers)
 - ❖ Antiinflammatory, neuroprotective, bronchodilator
- ❖ Myrcene (hops, lemongrass)
 - ❖ Antiinflammatory, analgesic, sedatives
- ❖ Linalool (lavender, tulsi)
 - ❖ Antidepressant, analgesic, anxiolytic, anticonvulsant
- ❖ B-caryophyllene (black pepper, cardamom, oregano)
 - ❖ Antiinflammatory, CB2

Whole Plant Synergy

- ❖ THC: CBD ratio
 - ❖ Alleviation of side effects, enhancement of medicinal activity

- ❖ Entourage effect: terpenes and cannabis therapeutics
 1. Multi-target effects
 2. Pharmacokinetic effects (improved solubility or bioavailability)
 3. Interactions affecting bacterial resistance
 4. Modulation of adverse events

Themed Issue: Cannabinoids in Biology and Medicine, Part I

REVIEW

Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects

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Keywords

cannabinoids; terpenoids;
essential oils; THC; CBD;
limonene; pinene; linalool;
caryophyllene; phytotherapy

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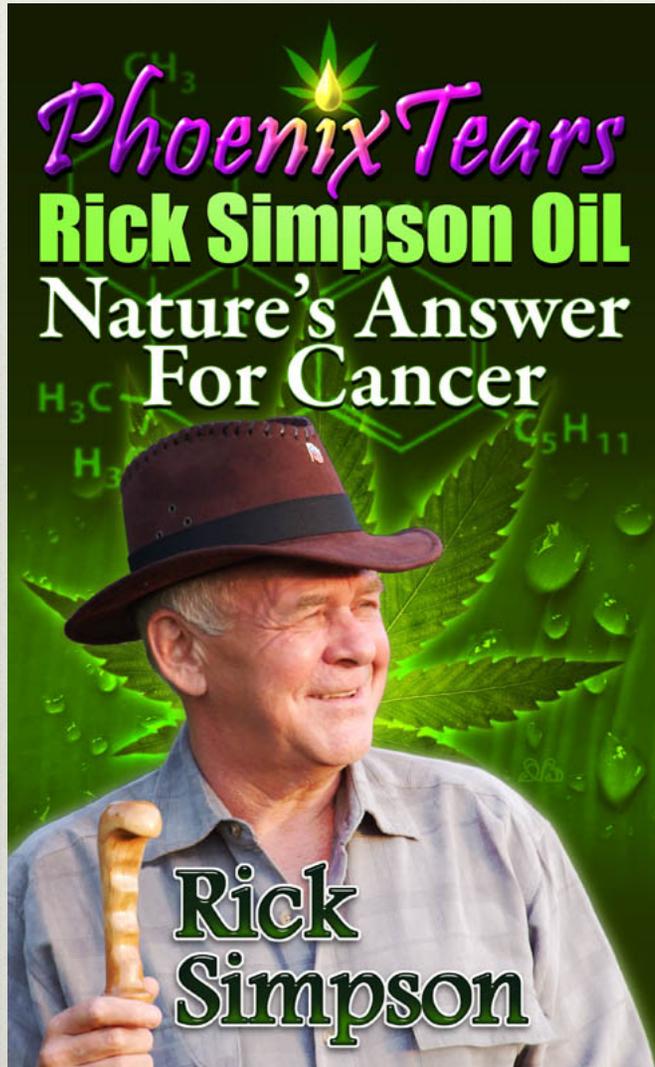
12 January 2011

Tetrahydrocannabinol (THC) has been the primary focus of cannabis research since 1964, when Raphael Mechoulam isolated and synthesized it. More recently, the synergistic contributions of cannabidiol to cannabis pharmacology and analgesia have been scientifically demonstrated. Other phytocannabinoids, including tetrahydrocannabivarin, cannabigerol and cannabichromene, exert additional effects of therapeutic interest. Innovative conventional plant breeding has yielded cannabis chemotypes expressing high titres of each component for future study. This review will explore another echelon of phytotherapeutic agents, the cannabis terpenoids: limonene, myrcene, α -pinene, linalool, β -caryophyllene, caryophyllene oxide, nerolidol and phytol. Terpenoids share a precursor with phytocannabinoids, and are all flavour and fragrance components common to human diets that have been designated Generally Recognized as Safe by the US Food and Drug Administration and other regulatory agencies. Terpenoids are quite potent, and affect animal and even human behaviour

Clinical Applications

- ❖ Cancer
 - ❖ Hyperbole, preclinical evidence
 - ❖ Palliative effects, antineoplastic effects at higher doses
 - ❖ Side effects alleviated by CBD, terpene-rich botanicals
- ❖ Pediatric seizure disorders
 - ❖ CBD
- ❖ Pain
 - ❖ Muscle spasticity
 - ❖ Gynecological pain
 - ❖ Opiate adjunct (dose reduction)
 - ❖ Opioid system: sister system
- ❖ IBD – Crohn's (CBD-rich oil)

Rick Simpson



- ❖ *“High grade hemp oil when made and used according to my instructions seems to work on all types of cancer and I am not aware of any type of cancer that it would not be effective to treat.”*
- ❖ *“After years of experience in dealing with patients who suffered from all types of medical problems I can honestly say I do not know of any condign for which the oil is not an effective treatment.”*

Qualifying Conditions: OR

- ❖ Cancer
- ❖ Glaucoma
- ❖ Alzheimer's
- ❖ HIV/AIDS
- ❖ Cachexia (wasting syndrome)
- ❖ Severe pain
- ❖ Severe nausea
- ❖ Seizures
- ❖ Persistent muscle spasms
- ❖ Multiple sclerosis

Qualifying Conditions: WA

- ❖ Cancer
- ❖ HIV/AIDS
- ❖ Multiple sclerosis
- ❖ Epilepsy or other seizure disorder
- ❖ Spasticity disorders
- ❖ Intractable pain
- ❖ Glaucoma
- ❖ Crohn's disease
- ❖ Hepatitis C
- ❖ Diseases not listed that include symptoms of nausea, vomiting, wasting, appetite loss, cramping, seizures, muscle spasms, or spasticity

Qualifying Conditions: CA

- ❖ Cancer
- ❖ Glaucoma
- ❖ HIV/AIDS
- ❖ Parkinson's disease
- ❖ Multiple sclerosis
- ❖ Damage to the nervous tissue of the spinal cord with objective neurological
- ❖ indication of intractable spasticity
- ❖ Epilepsy
- ❖ Cachexia/Wasting syndrome
- ❖ Crohn's disease
- ❖ Post-traumatic stress disorder (PTSD)

- ❖ Counseling clients on self-medication
- ❖ Incorporating smoking into protocols
- ❖ Tincture use
 - ❖ Rare, as inhalation is often better route
 - ❖ Pain - with California poppy, Piscidia
 - ❖ Appetite stimulation – with Ginger, Angelica
- ❖ Botanicals for chronic smokers
 - ❖ Lung support herbs: mullein, plantain, marshmallow, Reishi mushroom
 - ❖ Memory support herbs: Calamus, Gotu kola
 - ❖ Cravings and withdrawal: Magnolia bark

Dried herb



- ❖ *Cannabis inflorescence*
- ❖ Dried female flowers
- ❖ Inhalation
- ❖ Starting base for other preparations
- ❖ Test for microbes, pesticide residues
- ❖ Dispensary lab reports

Cannabis oil



- ❖ RSO, hemp oil, Constance oil
- ❖ Evaporated tincture
- ❖ Vaporizer, ingested in capsules
- ❖ Solvent residues
- ❖ Recreational: BHO, wax, shatter

Medibles



ROA

Inhalation

- ❖ 10-30% bioavailability
- ❖ Onset in seconds
- ❖ Vaporizing: cleaner alternative
- ❖ Dried herb, oil concentrate
- ❖ Pain, nausea, appetite
- ❖ Ease of dose titration

Ingestion

- ❖ 6-10% bioavailability
- ❖ Delayed onset
- ❖ 11-OH-THC
- ❖ Unpredictable effects
- ❖ Good for high dose treatment

ROA

Mucosal application

- ❖ Buccal, rectal
- ❖ 34-46% bioavailability
- ❖ 10 minute absorption
- ❖ Oil concentrates
- ❖ Used in cancer support settings

Topical

- ❖ Infused oils, salves, liniments
- ❖ Local inflammation, pain, dermatitis, psoriasis

Dosing

- ❖ Low vs. high dose treatment
 - ❖ Low: 2.5-5mg – self titrate for symptom management
- ❖ High dose antineoplastic treatment
 - ❖ Up to 1g/day
 - ❖ Build up incrementally over 4 weeks
 - ❖ Side effects and withdrawal

Determining THC content

- ❖ Know THC% in herb
- ❖ Calculate total THCMg in 1g herb
 - ❖ 15% THC, 150mg THC in 1g sample
 - ❖ Estimate 25% bioavailability
 - ❖ 37.5mg absorbed
 - ❖ Targeted dose was 3.75mg, .1g needed

Toxicity

- ❖ No one has ever died from a cannabis overdose
- ❖ LD50 of THC: 1,270 mg/kg
- ❖ 1500lbs smoked in 15 minutes

Debunked Safety Concerns

- ❖ Increase in lung cancer risk
 - ❖ Bronchial and pulmonary inflammation/irritation
- ❖ Observable cognitive deficits

Adolescents

- ❖ ECS engaged during adolescent development
- ❖ Adolescent brains vs. adult brains
- ❖ More sensitivity to negative side effects of cannabis
 - ❖ Memory impairment
 - ❖ Cognitive functioning
 - ❖ Psychosis
- ❖ Do not use (exception: pediatric seizure disorders)

Psychiatric Disorders

- ❖ Correlations between cannabis and psychiatric disorders
- ❖ Genetic predispositions
 - ❖ COMT polymorphisms
 - ❖ Akt1 gene variants
- ❖ Close clinical monitoring
- ❖ THC concentrates
- ❖ CBD – implicated for management as antipsychotic

Pregnancy

- ❖ Use in morning sickness
- ❖ Mixed research on influence of cannabinoids on fetal brain development
- ❖ Cannabinoids found in nursing mother's milk
- ❖ Short term use likely OK, discourage for long term

Dependence and Withdrawal

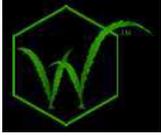
- ❖ Dependencies possible, likely psychological as opposed to physiological
- ❖ Withdrawal symptoms from treatment may include-
 - ❖ loss of appetite
 - ❖ irritability and aggression
 - ❖ anxiety and restlessness
 - ❖ ECS reset
 - ❖ Treat with CBD, Magnolia bark

Drug Interactions

- ❖ Opioids – beneficial interactions
- ❖ NSAIDs inhibit effects of THC
- ❖ Antidepressants – may decrease effects in SSRIs
- ❖ CYP3A4 – in vitro effects
 - ❖ Clinical relevance unknown

QA/QC

- ❖ Microbial contaminants
 - ❖ Dried herb, not likely a concern with extracts
- ❖ Solvent residues
 - ❖ Oil concentrates
- ❖ Pesticide residues
- ❖ Heightened concerns in immune compromised patients



CERTIFIED CANNABACEUTICALS™ CERTIFICATE OF ANALYSIS

The Werc Shop

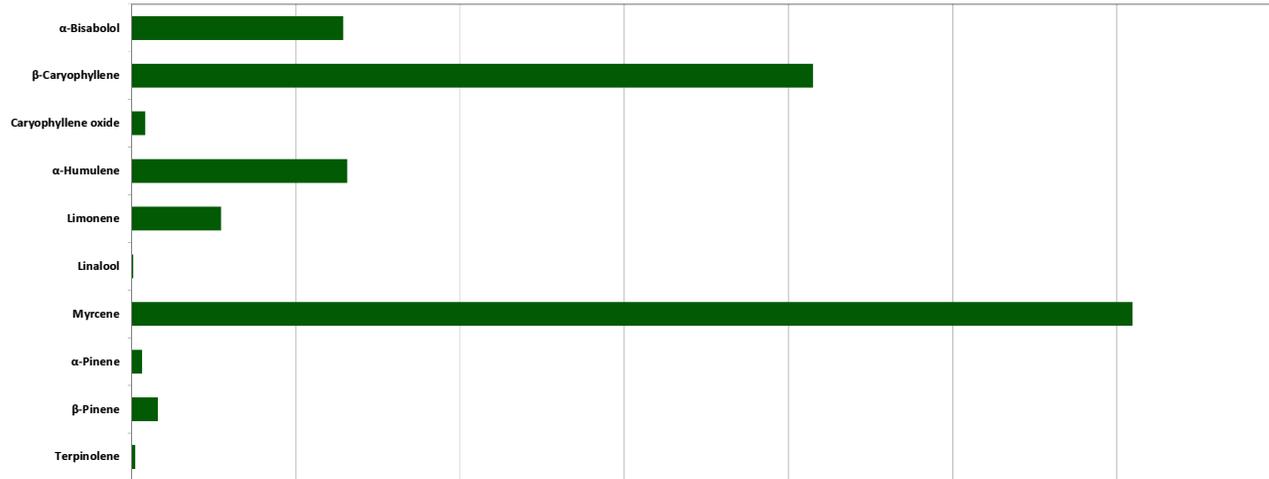
Providing Knowledge Through Information™



Contact Us: 855.734.6640
erby-WA@thewercshop.com
www.thewercshop.com

Analysis Performed For: WERC			CANNABINOIDS (weight %)											MICROBIOLOGICAL (CFU)					MOISTURE	VISUAL			
Sample Name/ID	Manifest Lot/Batch ID	Tested On Date	MAXIMUM AVAILABLE			I-502 REQUIRED			ADDITIONAL CANNABINOIDS					< 100,000	< 10,000	< 1,000	< 1,000	Absent		% Loss on Drying	% Stems	% Other	
			Δ ⁹ -THC Max.	CBD	Max.	Δ ⁹ -THC	Δ ⁹ -THCA	CBD	Δ ⁹ -THC + Δ ⁹ -THCA + CBD	CBDA	CBGA	CBG	CBC	CBN	Total Aerobic Count	Total Yeast & Mold	Total Coliforms	Bile-Tolerant Gram Negative	E. coli				Salmonella
BBB-Super-Lemon-Haze	xxxx-xxxx-xxxx-xxxx	4/20/2014	19.96	0.23		1.69	20.82	0.21	22.72	0.02	0.18	0.58	0.05	ND	Pass	Pass	Pass	Pass	Pass	Pass	9.42%	1	0

Terpenes	mg/g
α-Bisabolol	2.56
Caryophyllene	8.25
Caryophyllene Oxide	0.16
α-Humulene	2.61
Limonene	1.08
Linalool	0.01
Myrcene	12.12
α-Pinene	0.12
β-Pinene	0.31
Terpinolene	0.04
Sum of Terpenes	27.27



*Cannabis samples can show considerable intra- and inter-plant variability. The test results presented above are accurate only for the sample analyzed. Depending on sampling protocols followed by the sample creator/collector these results may not be representative of the entire product lot/batch.

The Werc Shop uses high performance liquid chromatography (HPLC) for determining cannabinoid content. Cannabaceuticals™, Providing Knowledge Through Information™, Werc™, the W Logo, Erby™ and the "CC" are trademarks of The Werc Shop, Inc.

Maximum CBD Wt% is calculated assuming all CBDA is completely converted upon heating.
 Maximum THC Wt% is calculated assuming all THCA is completely converted upon heating.

**Standards for CFU levels established in compliance with WA I-502 for each product class

The Werc Shop™

An Independent Laboratory

Providing Safety Through Information™

Look for this logo to know your medicine has been independently tested by well trained scientists with a passion for cannabis!

Cannabaceutical™:
New medical classification created by The Werc Shop to clearly describe Medical Cannabis containing products.

%= The Wt. % (weight percent) of the chemical that is present.
If you have 1000 mg of concentrate (or 1g) you have 169.9 mg of THC available via inhalation.

Cannabaceutical™ Facts

Tested On: **April 20, 2012**

True OG

Hybrid
Indoor

Strain Name

Strain Type
Grow Envir.

Δ⁹-THC Max:	16.99 %	Sum of Top Terpenes	27.6 mg/g
Δ ⁹ -THCA	18.99 %	Limonene	9.5 mg/g
Δ ⁸ -THC	0.33 %	Myrcene	5.5 mg/g
CBD Max:	0.28 %	β-Caryophyllene	5.0 mg/g
CBDA	0.08 %	Germacrene B	2.3 mg/g
CBD	0.21 %	Valencene	1.9 mg/g
CBG Max	0.65 %	β-Pinene	1.8 mg/g
Δ ⁹ -THCVA	0.10 %	Linalool	1.6 mg/g
CBN	ND %		
Pesticides Screen PASS		Microbial Screen GOLD	

Terpenes:
Responsible for the smell and taste attributes. Terpenes are known to modify the effects of THC and impact the overall medicinal effect of the strain. Also useful information for breeding.

CBG is a degradation product of THC. Not found in fresh flowers, can be in edibles.

CBG is a non-psychoactive anti-inflammatory cannabinoid.

Safety Screens:
Screening for 100's of molds and bacteria and over 30 different pesticides.

CBDA is a very potent anti-inflammatory agent. This is only available when consumed orally and the plant has not been heated before consumption.

THCA is an excellent anti-inflammatory agent. This is only available when consumed orally and the plant has not been heated before consumption.

CBD helps with pain & inflammation, is an anti-convulsant, anti-arthritis and neuroprotective agent that does not induce psychoactivity. CBD modulates the effects of THC to provide a non-psychoactive treatment alternative.

Myrcene: Effects intake of THC by brain cells to increase the overall effects of THC when ingested together.

Linalool: Floral smelling, is believed to provide some anti-cancer effects and is known to cause severe sedation.

Limonene: Has a citrus scent and may possess anti-cancer, anti-bacterial, anti-fungal and anti-depression abilities.

Pinenes: Pine odor, bronchodilator that opens the lungs to more THC absorption. It also increases focus, self-satisfaction, and energy.

Caryophyllene: Sweet, woody, clove taste responsible for anti-inflammatory and neuroprotective effects through CB₂ receptor activation.

THC offers relief for neuropathic pain, stimulates appetite and reduces vomiting associated with chemotherapy. THC can be useful to reduce inflammation and also offers neuroprotective effects. Patients should note THC can induce psychoactive, or cerebral, effects as well. Too much THC can cause unease, anxiety and overall discomfort.

TheWercShop.com

310-703-9567

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the Science of Dank
www.tgagenetics.com

\$12	\$20	\$40	\$80	\$130	\$260
\$10	\$17	\$35	\$70	\$120	\$240
\$8	\$15	\$30	\$60	\$110	\$200

