Cannabinoid Medicine
An Overview

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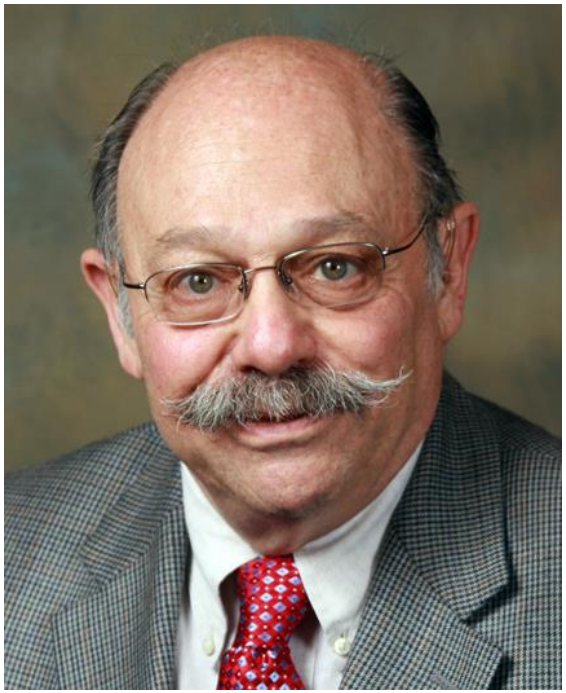


April 26, 2018
Orlando, Florida

American Academy of Cannabinoid Medicine

Presentation Overview

- INTRODUCTION
- HISTORY
- CLINICAL APPLICATIONS OF CANNABIS

Introduction

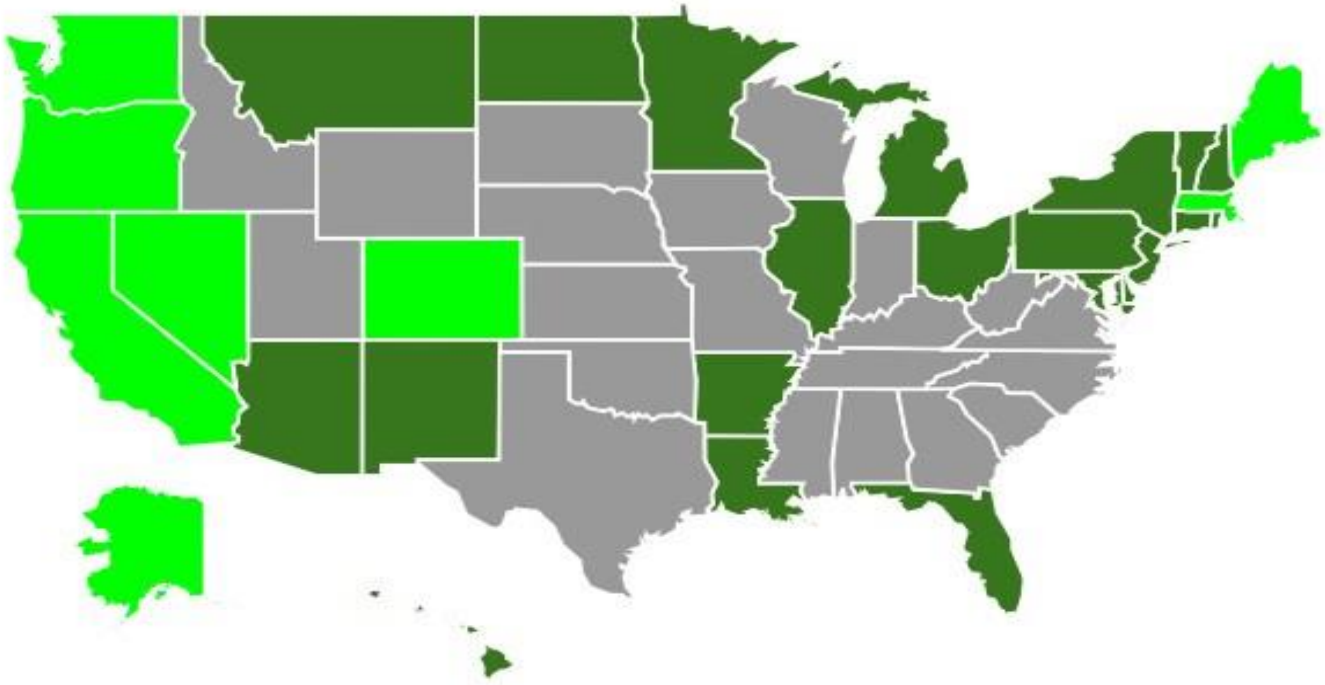
David Bearman, M.D.

- 15 years clinical cannabinoid medicine experience
- Former Medical Director SBRHA(now CenCal)
- Former Director/Health Officer Sutter County
- Vice President, American Academy of Cannabinoid Medicine
- Named Doctor of the Day by Wall Street Journal
- Author – *Drugs Are Not Tools of the Devil: How Greed and Discrimination Led to A Dysfunctional Drug Policy and How It Can Be Fixed*

This Lecture Will Address

- Brief History Of Medicinal Cannabis
- Endocannabinoid System
- Medical Utility of Cannabis and Cannabinoids
- Clinical Tips For Use of Medicinal Cannabis
- Case Studies
- Future Research

Medical Marijuana States



Brief History

Shen Nung
Ping Ts'oa Ching 2637 B.C.

Estimated date of the first known pharmacopia. Yes, it contained cannabis.

Cannabis medical attributes were well known in the ancient world. It was used as an analgesic, a childbirth anesthetic, for treating migraines, indigestion and insomnia.



Shen Nung

Sir William Osler
The Father of Modern Medicine

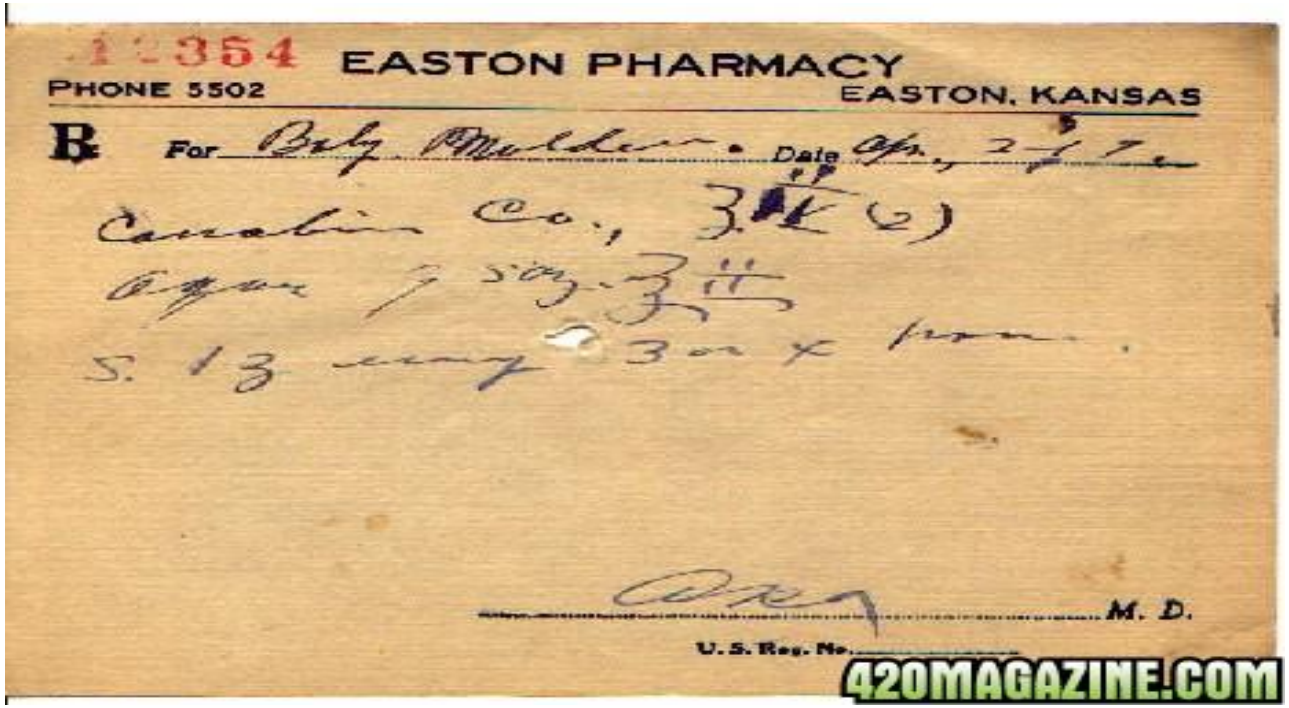
He wrote in the first textbook of Internal Medicine (1892) that stated:

Cannabis was the best migraine treatment.



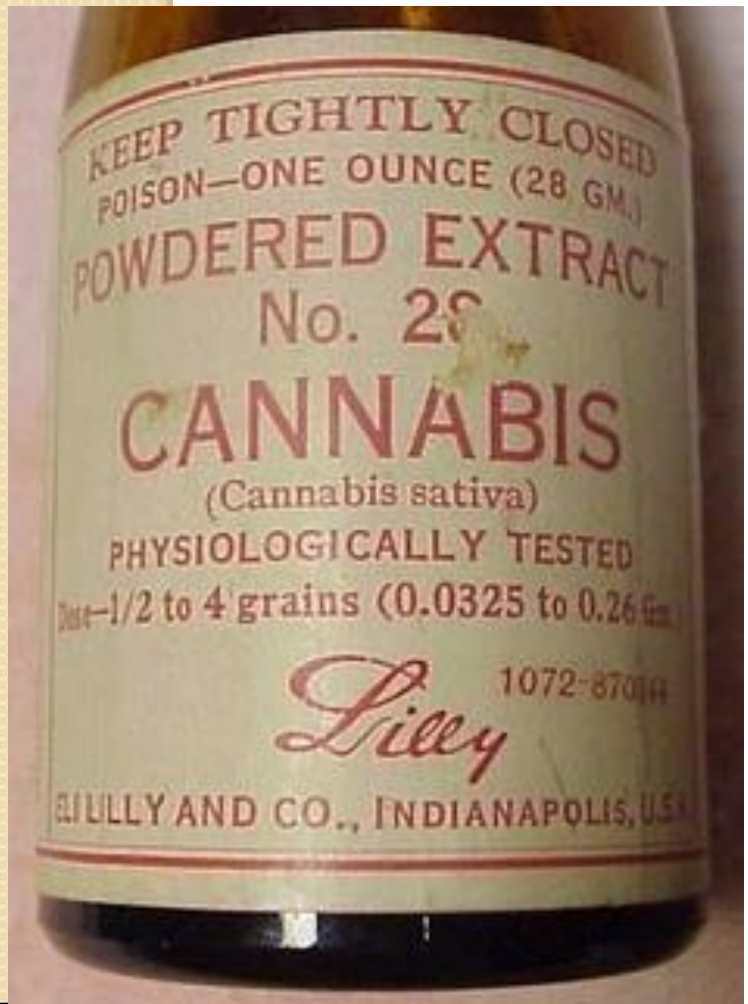
1920'S

In the 1920's, American doctors wrote millions of Rx per year that contained cannabis



L. Greensman, Marijuana Recommended Collide: The Blunt Trush – Joshua Blight and Mark Miller, Dec. 5, 2012

Major Pharmaceutical Companies Marketed Cannabis



Eli Lilly, Squibb, Merck, Sharp and Dohme, Smith Bros. all sold numerous forms of Cannabis in the late 19th and early 20th century

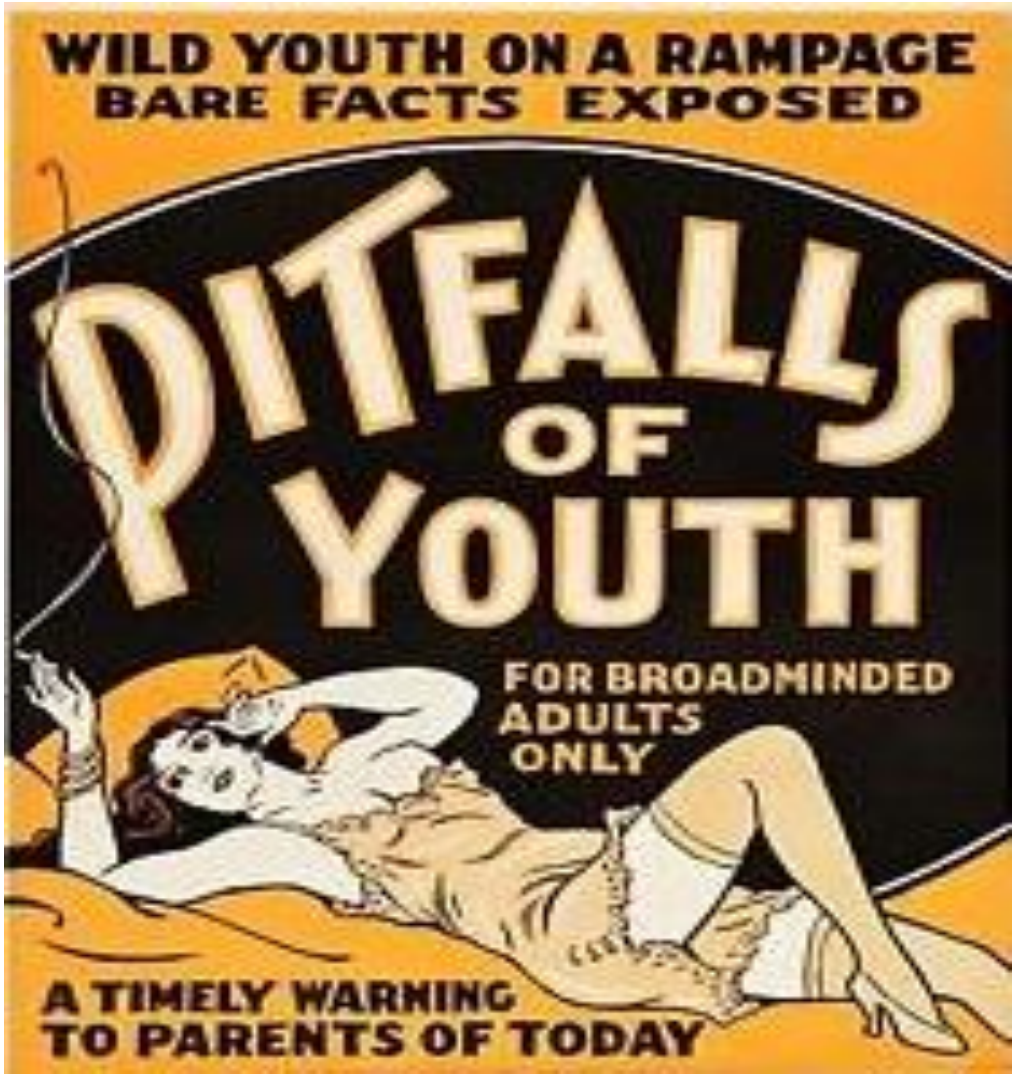
Phytochemicals Go Out of Style

- Millions of cannabis containing Rxs were written per year in 1920s and hundreds of thousands per year in the 1930s
- 28 OTCs containing cannabis available in 1937
- The use of herbal remedies(including cannabis) was eclipsed by the cult of modernism

- Manufactured pharmaceuticals seen as modern
- Cannabis was not standardized
- Herbal preparations more complex than single molecule manufactured pharmacueticals

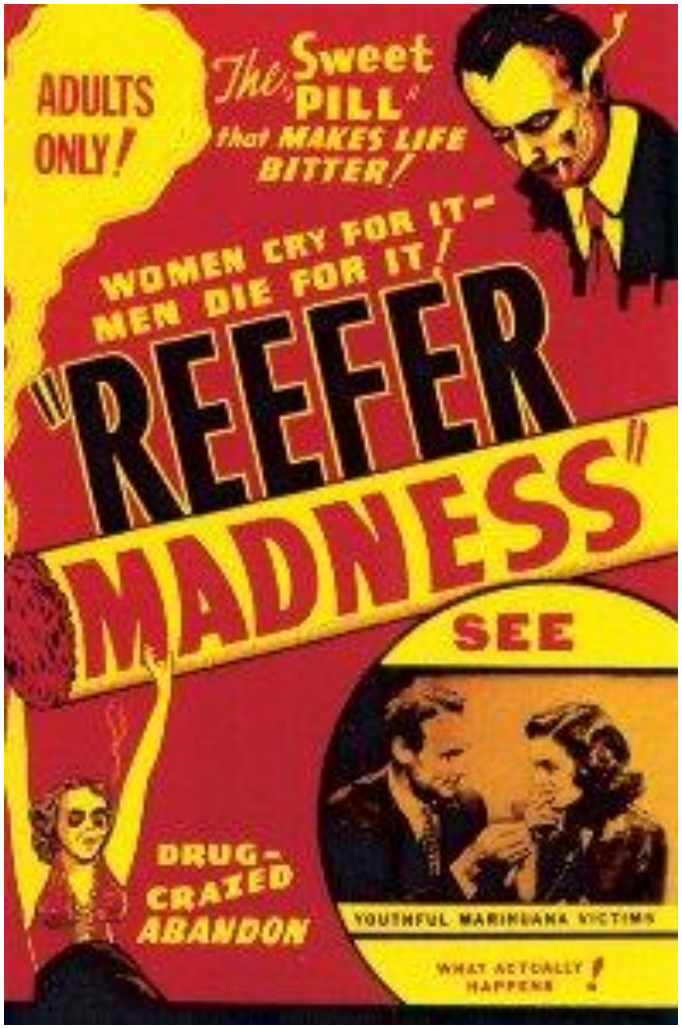
Prohibition Propaganda

Sex, Drugs and Jazz




ADULTS ONLY!
Exposed!
DIVULGING HERETOFORE UNHEARD OF
ORGIES OF YOUTH'S DISSIPATION
SENSATIONAL!
DARING!
BOLD!
MARIHUANA
SHATTERED HOPES!
TANGLED LIVES!

Who Can Forget Reefer Madness



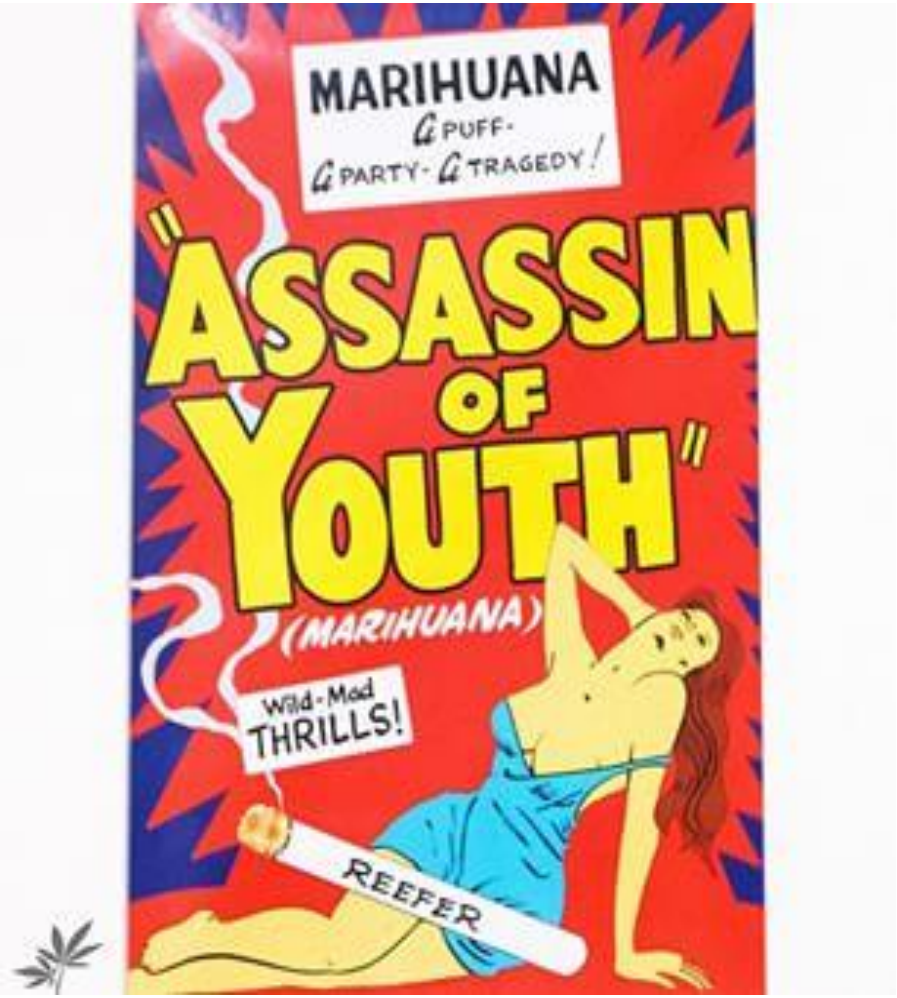
Cannabis Threatens The Establishment



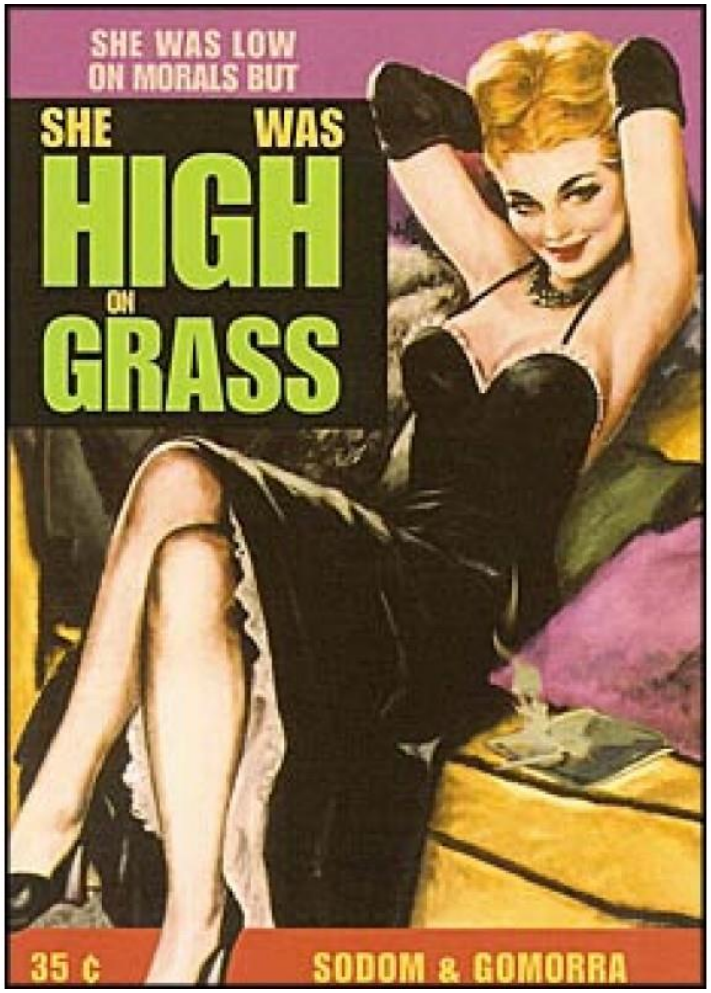
Sex, Drugs and Jazz



Beware? Really?



Pulp Fiction Demonizes Cannabis



Harry Anslinger's World



"There are 100,000 total marijuana smokers in the US, and most are Negroes, Hispanics, Filipinos and entertainers. Their Satanic music, jazz and swing, result from marijuana usage. This marijuana causes white women to seek sexual relations with Negroes, entertainers and any others."

- Harry J. Anslinger, "Testimony to US Congress supporting Marihuana Tax Act, 1937"

Marijuana Tax Act 1937 AMA Testimony

- The AMA opposed the Marijuana Tax Act(MTA)
- Dr. William Woodward, AMA Chief Legal Counsel, (*former Commissioner of Health of Wash.D,C and Boston, past president APHA*) gave Two hours of testimony against the MTA
- The AMA knew of no harm from the medicinal use of cannabis
- He pointed out that the federal government had no credible evidence .He had checked with several governmental entities including USPHS, Childrens Bureau, and Bureau of Prisons

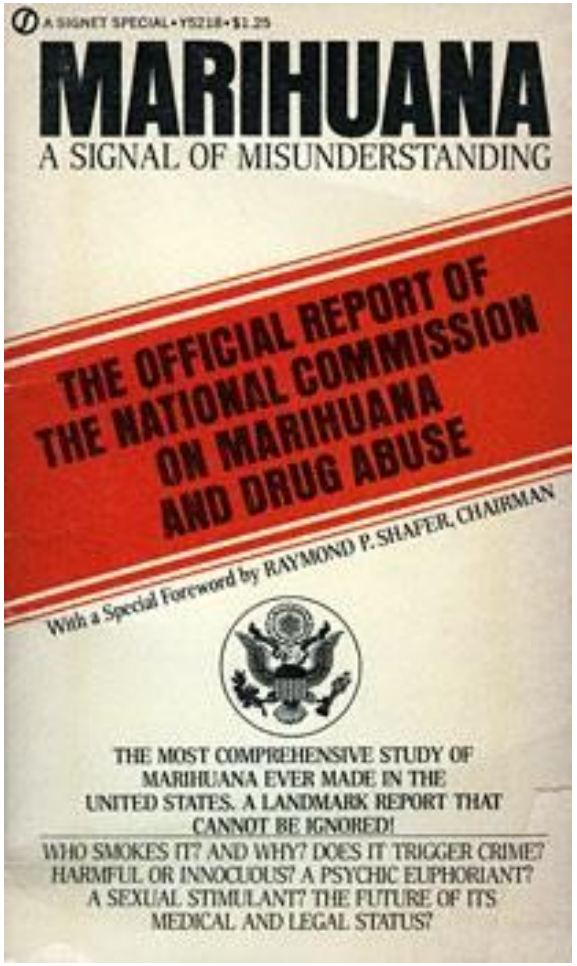
Dr. Woodward's Words

- "The AMA knows of no dangers from the medical use of cannabis"
- He checked with The Bureau of Prisons, Children's Bureau, Office of Education and divisions of mental health and pharmacy in the USPHS. None of them had one shred of evidence to support Mr. Anslinger's claims.
- He was critical of the use of the word marijuana because the American public was familiar with hemp and cannabis

1941 - Out of United States Pharmacopoeia



Nixon Marijuana Commission



Recommends legalizing recreational cannabis.
Nixon rejected it.

1978 - Federal Compassionate Access Investigational New Drug Program

The Compassionate Investigational New Drug program, or Compassionate IND, is a United States Federal Government-run Investigational New Drug program that allows a limited number of patients to use medical marijuana grown at the University of Mississippi.

It is administered by the National Institute on Drug Abuse. Closed to new entrants, there are four surviving patients who were grandfathered into the program.

Marinol – 1985

The AIDS Epidemic saw widespread use of cannabis by HIV/AIDS sufferers. Cannabis addressed appetite stimulation, relief of pain and depression.

The government's response was to encourage the development of synthetic THC. It was approved by the FDA in 1985. It is also approved for relief of nausea and cancer patients receiving radiation or chemo.

It's Trade name is Marinol, generic name is dranabinol.

Cannabinoid & Cannabis

- Marinol=1 cannabinoid
- Cannabis=80-100 cannabinoids



Introduction to Modern Medicinal Cannabis

1949 - H.H. Ramsey M.D. and Jean Davis M.D.

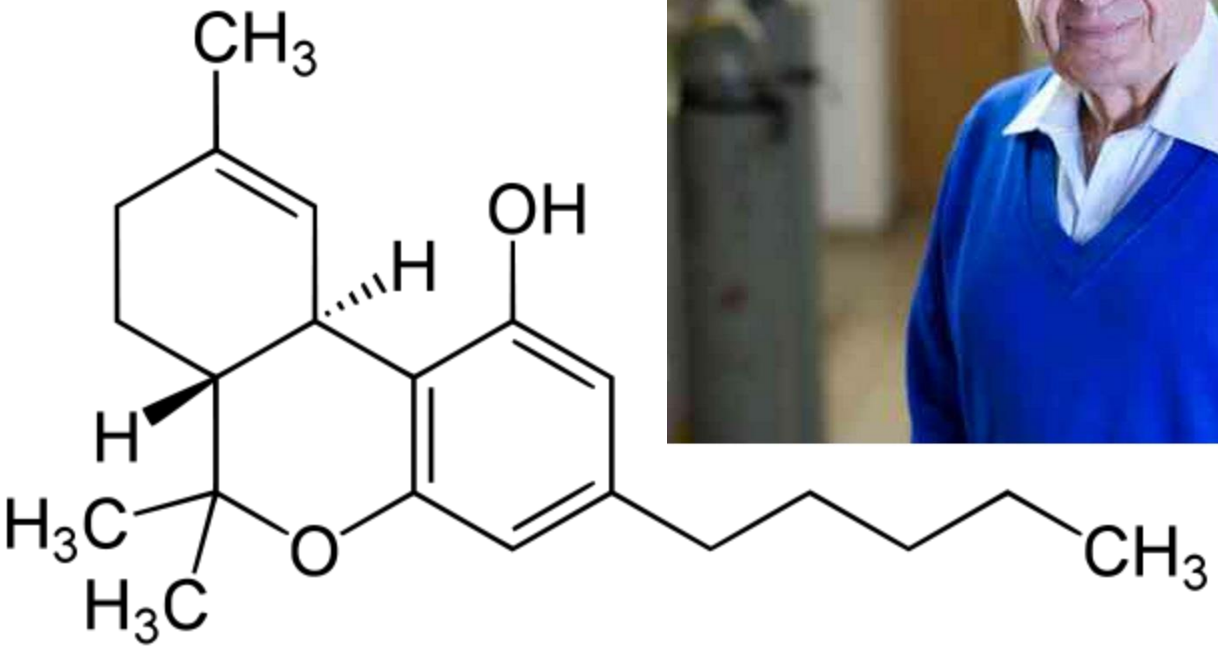
The first modern study on the medicinal value of cannabis. Seven subjects with intractable seizures. After treatment with cannabis 5 of the 7 subjects had no or extremely few seizures.

They concluded: ”The cannabinols herein reported deserve further trial in non-institutionalized epileptics.”

- *Federation Proceedings, Federation of American Society for Experimental Biology, vol. 8, lY49, p. 284.*

1964 – Dr. Raphael Mechoulam characterizes the structure of Delta 9 THC





Endocannabinoid Systen

- Modulation of Sensory input
- Dopamine
- Retrograde Inhibition
- CB1 & CB2 Receptors

The Endocannabinoid System

characterized circa 1992

The Endocannabinoid system is composed of:

RECEPTORS

- CB1 Receptors found largely in the brain
- CB2 Receptors found in the immune system and the periphery

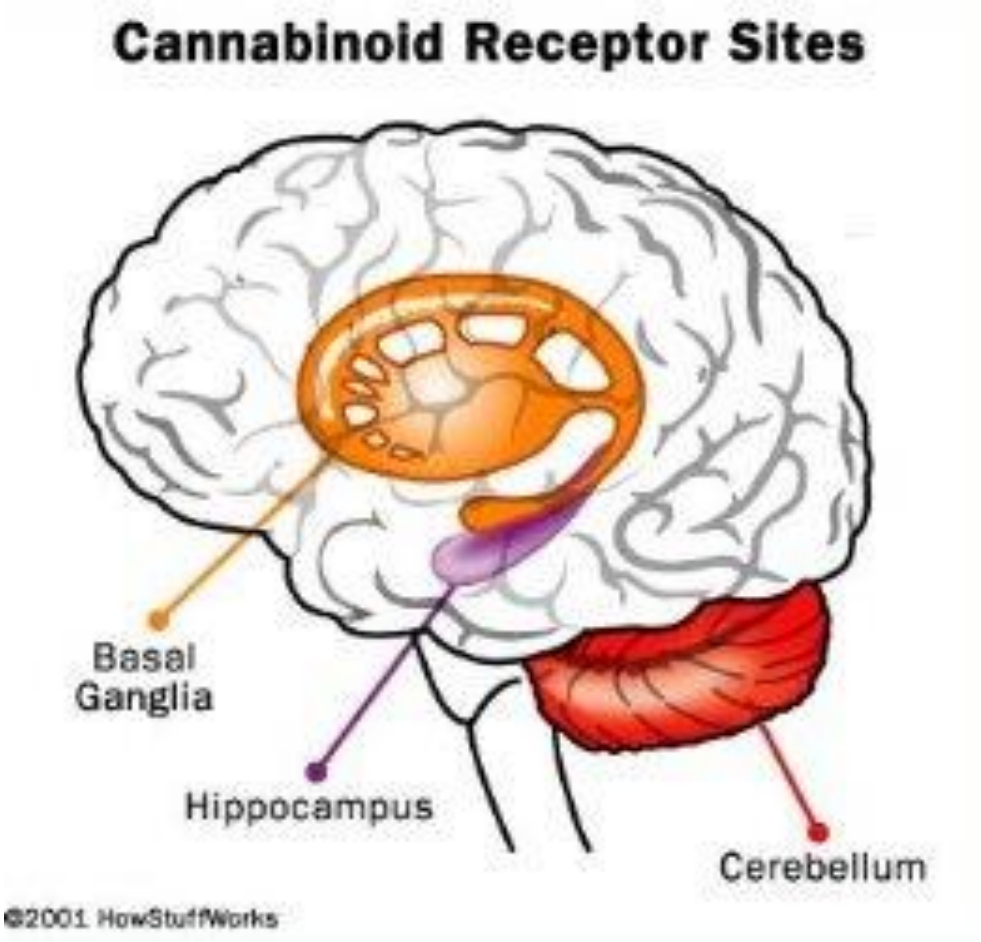
NUEROTRANSMITTORS

- Anandamide (AEA)
- 2-arachydonyl glycerol (2AG)

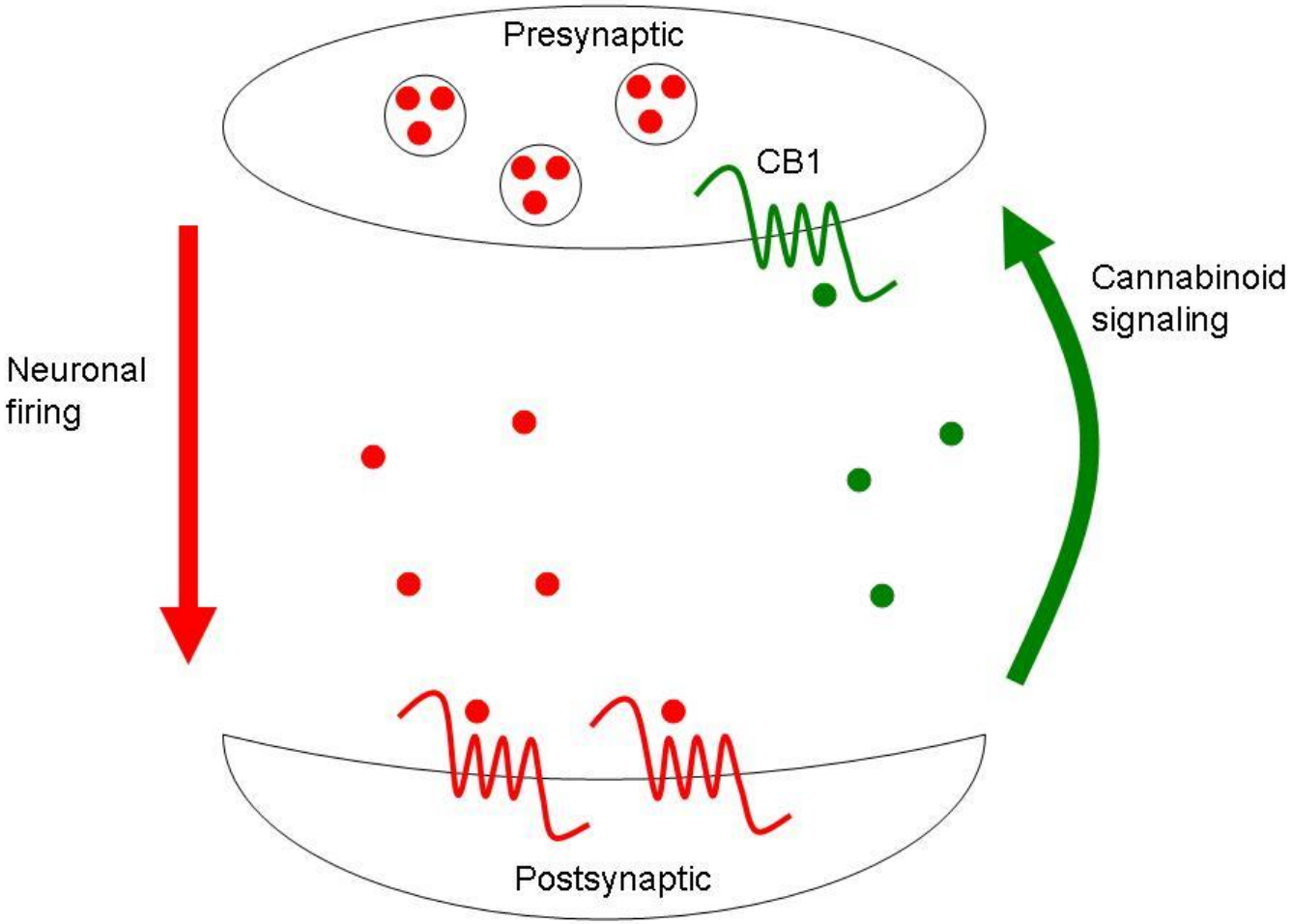
ENZYMES

- FAAH - enzyme that metabolizes anandamide
- MYGYL - enzyme metabolizes 2AG

Amygdala & Nucleus Accumbens Hippocampus -



Retrograde Inhibition

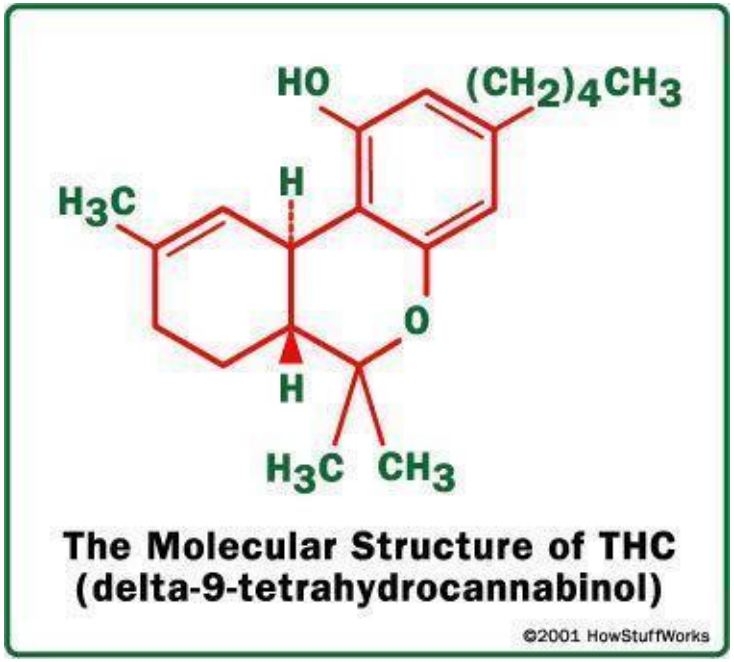


Cannabis: The Plant



Chemistry

- Cannabis 483 chemicals
- 80-100 cannabinoids(21 carbon molecule)
- Over 100 Terpenes
- Phenoids
- Flavinoids



Cannabinoids

21 carbon molecules that can block or stimulate CBI or CB2 receptors

Terpenes



Terpenes give cannabis its distinctive odor. There are over 100 terpenes in cannabis. They are found extensively in citrus fruit

Entourage Effect

Postulated by Mechoulam in 1999. It is the idea that the various constituents of the plant act in concert, that the effect of the whole is greater or more effective than the sum of its parts.

Many cannabinoids, terpenes and flavinoids acting together to cause a therapeutic benefit is the entourage effect

House of Lords, 1997

- The Science and Technology Committee of the House of Lords wrote a report on cannabis' potential medicinal benefit.

- The report is well done. It recognized the long medical history , anecdotal reports plus emerging research findings.

- This paved the way for research by GW Pharmaceuticals , manufacturers of Sativex.

- *Sativex(tincture of cannabis) is indicated for use in treating the symptoms of Multiple Sclerosis and neuropathic pain. It is governmentally approved in 20 countries*

GW Pharmaceuticals - 1999

In 1999 GW started doing research on tincture of cannabis(nabixamol) for relief of muscle spasms and neurological pain associated with Multiple Sclerosis.

(Reminder: disclosure-stockholder)

Sativex(nabixamol)

- A tincture of cannabis sublingual spray
- Available in Canada since 2005.



Clinical Standards

Be aware of your state's Ground Rules Set by Supreme Court and Medical Board

- California
- Mowrer decision (recommendation=prescription)
- Bearman v. LACSC-patient privacy
- Sparks v Kern County-Jay's cant practice medicine

Procedure for giving Approval/Recommendation

- Standards have been addressed by CMA, the Medical Board of California, and the American Academy of Cannabinoid Medicine and your State Board of Medicine

MBC Guidelines for Giving Approval/Recommendation

- Bonafide doctor-patient relationship
- Good faith H&P
- Review records
- Plan With Objectives
- A condition which will benefit from use of cannabis

My Criteria

- Screen on phone
  - Dx
  - What documentation do they have
  - Last time sought medical attention
  - How affects ADL
- Require old records
- Patient completes history form

My Criteria (cont.)

- 35 min.- 60 min. first appointment
  - Do H&P
  - Discuss State and Federal Law
  - Overview of science (ECS, GW, ETC)
- Keep good records
- Follow as medically appropriate
- Refer and/or treat as needed
- Document, Document, Document

Efficacy

- History
- Anecdotes
- State Studies in eight states
- GW Studies 1999 - present
- House of Lords Report
- IOM Report 1982 and 1999
- CMRC Studies 2000-2010
- 20,000 Research Studies

Safety

- Government reports from: India/Britain(1894), U.S. (1972), Britain (1968), Canada(1973), Australia, (1978) Panama Canal Zone(1916 & 1931)
- 1985 Delta 9 THC, FDA Approved
- 1986-1988 FDA Chief ALJ Young's Findings of Fact
- 2005 Tincture of Cannabis, Health Canada Approval
- 2006 FDA approves Phase III Sativex Clinical Trial
- 2010 EU approves Sativex

- *NOTE: Sativex is a whole plant alcohol extract from two strains of cannabis in a 1:1 ratio*

Routes of Administration

- **Respiratory**
- 1-smoking
- 2-Vaporizing
- **Sublingual**
- spray(Sativex/nabixamol)
- drops
- **Oral**
- tablets
- tincture
- other-tincture ,tea, in flavored drinks

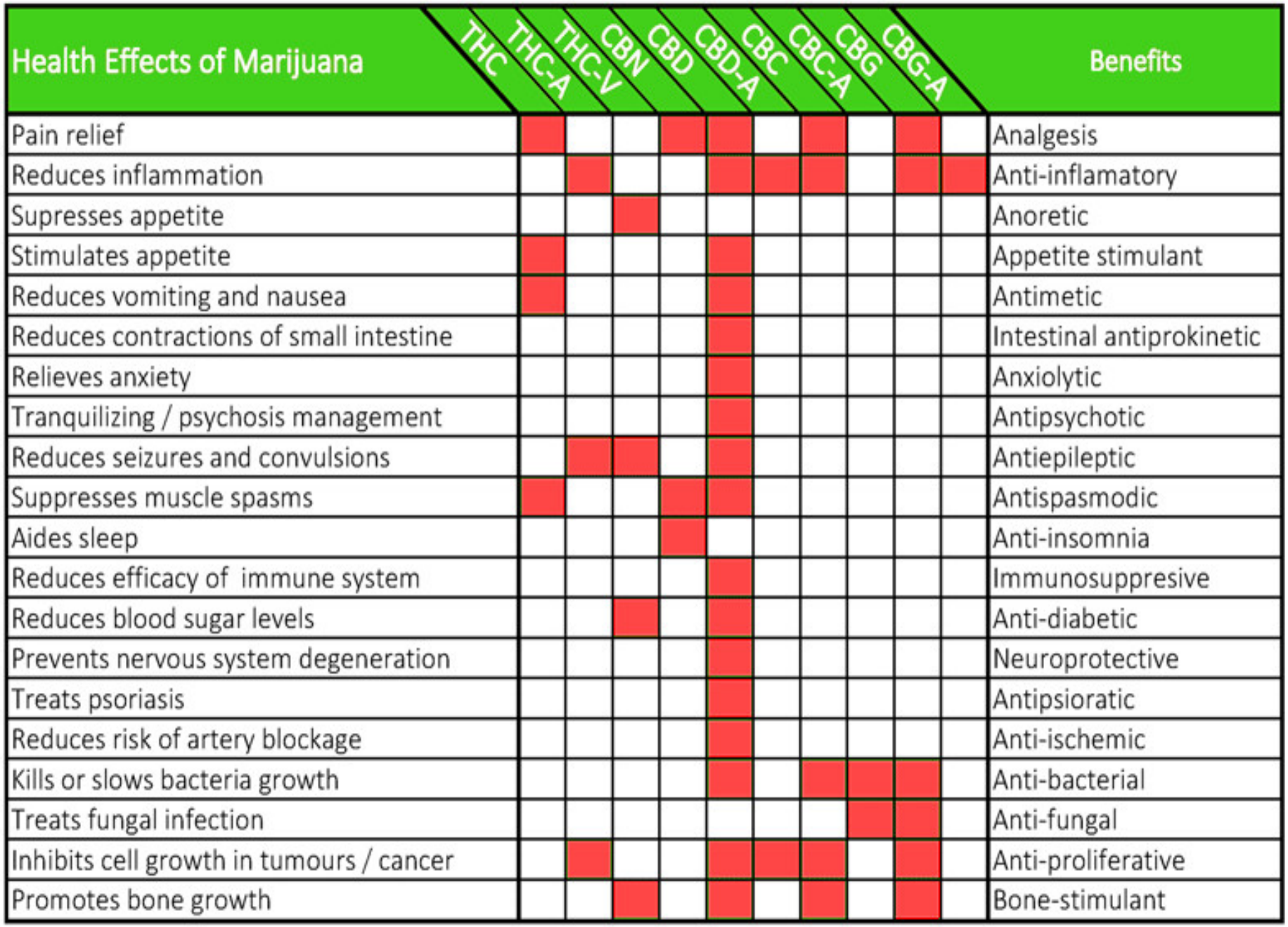
COMMON CANNABINOIDS

THC, THCA

CBD, CBDA

CBN, CBC

CBG, THCV


Health Effects of Marijuana
THC
THC-A
THC-V
CBN
CBD
CBD-A
CBC
CBC-A
CBG
CBG-A
Benefits
Pain relief
Analgesis
Reduces inflammation
Anti-inflamatory
Supresses appetite
Anoretic
Stimulates appetite
Appetite stimulant
Reduces vomiting and nausea
Antimetic
Reduces contractions of small intestine
Intestinal antiprokinetic
Relieves anxiety
Anxiolytic
Tranquilizing / psychosis management
Antipsychotic
Reduces seizures and convulsions
Antiepileptic
Suppresses muscle spasms
Antispasmodic
Aides sleep
Anti-insomnia
Reduces efficacy of immune system
Immunosuppresive
Reduces blood sugar levels
Anti-diabetic
Prevents nervous system degeneration
Neuroprotective
Treats psoriasis
Antipsioratic
Reduces risk of artery blockage
Anti-ischemic
Kills or slows bacteria growth
Anti-bacterial
Treats fungal infection
Anti-fungal
Inhibits cell growth in tumours / cancer
Anti-proliferative
Promotes bone growth
Bone-stimulant

COMMON TERPENES IN CANNABIS

Myrcene

Linalool

Limonene

Pinene

Beta Caryophyllene

Flumelene

Dose

- Many conditions(e.g. anxiety, ADD/ADHD, appetite stimulation, nausea) respond to as low as whole plant cannabis containing 2.5 mg of THC.
- You may also wish to add 2.5 CBD
- Sleep Aid- to go to sleep 5-10 mg; THC
- Analgesia 10-20mg of THC with equal or less CBD, generally 15mg THC, 15mg CBD

Isolates Vs Whole Plant

- *Cannabis is often more effective whole plants with*

  fewer side effects due to the entourage effect
- *THC alone may well be effective*
- *CBD alone can be effective*
- *Until Mechoulam rejects the* Entourage Effect you are better off with the whole plant

Therapeutic Applications Of Cannabis

- **Anti nauseant/Anti emetic**
- **Appetite stimulant**
- **Analgesic**
- **Anti epileptic**
- **Anti inflammatory**
- **Anxiolytic**
- **Anti spasmodic**
- **Anti depressant**
- **Sleep Aid**
- **PTSD treatment**
- **ADD/ADHD treatment**

Top 6 Conditions or Symptoms

- Pain
- Sleep Difficulties (Insomnia)
- Nausea
- Arthritis & Connective Tissue Disorders
- Migraine
- Anxiety

Other Commonly Treated Conditions

- ADD/ADHD
- Seizures
- Glaucoma
- Fibromyalgia, Restless Leg Syndrome, Reflex Sympathetic Dystrophy,CRPS
- Diabetic Peripheral Neuropathy
- Crohn’s Disease, IBS,Cyclical Vomiting Syndrome
- Depression
- PTSD

Seizure Case Example

- History of two intracranial bleeds
- Hemi paretic
- Intractable seizures
- With cannabis no seizures

Nuerodegenerative Diseases

- Multiple Sclerosis
- Parkinson's Disease
- Huntington's Disease
- Cerebellar Degeneration
- Alzheimer's Disease
- Amyelotrophic Lateral Scterosis

Parkinsons

- A painter has given me two lovely paintings because he is so grateful that cannabis has allowed him to continue painting

Mental Health

- Depression
- Anxiety/Panic Attacks
- Stress
- OCD
- Bipolar Disorder
- PTSD
- ADD/ADHD
- Autism/Asberger’s syndrome

Autism and Aspergers

- Recent case of 9 year old with autism who showed 30 % improvement(per special needs teacher and parents) in one week

Benefits to AIDS Patients

- Appetite stimulant
- Anti nauseant
- Anti depressant

Benefits to Cancer Patients

- Analgesic
- Anti Nauseant
- Appetite Stimulant
- Anti Depressant
- Anti proliferative (experimental & anecdotal)

Several Cancer Cases Cannabis Purported To Have Beneficial Effect

- 15 month old brain cancer
- SB doctor breast cancer
- Michelle Aldrich lung cancer
- Throat cancer metastatic to liver

ADD/ADHD

- Effective
- Retrograde Inhibition
- Fewer side effects than stimulants
- Can be used in conjunction with stimulants

Impact of Cannabis on ADD/ADHD

- Grades going from Ds and Fs to As & Bs
- Credited with graduating from Maritime Academy
- Credited with getting PhD
- Waitress Volunteering story of her son's improved focus concentration and grades

PTSD

- Treats and decreases anxiety
- Helps control anger
- Decreases nightmares
- Symptoms possibly related to increased dopamine transporter

Cannabis Use In Pregnancy

- Dr. Melanie Dreher, Dean of The School of Nursing at Rush Medical School, did her study in Jamaica in 1968.
- This study documented that children of women who smoked cannabis during pregnancy did better in school and reached their developmental landmarks sooner than children of women who did not smoke cannabis during pregnancy.

2005 Dr. Donald Tashkin Lung Cancer? NO!

He compared 1100 patients with respiratory wellness.

He determined cannabis does not cause lung cancer.

AMA November 2009

- Changes 2001 position that more research is needed to cannabis should be rescheduled so that more research can be done

- Joins over 100 health care organizations in support of medicinal cannabis. These include: American College of Physicians, American Nurse Association, American Public Health Association

The Law and Its Application

- THC (Marinol) is rescheduled to III (1999)
- Conant v. Walter (2000)
- Gonzalez v. Raich (2005)
- Tincture of cannabis (Sativex) meets FDA safety criteria (2005)
- Tincture of cannabis RX legal in 20+ countries (2010)
- Legal under state law in 23 states and the D.C.
- Rohrbachen Fam Amendment

Marijuana Research in the United States

California center For Medical Cannabis Research(CMCR)

- Founded 2000
- Funded by the State of California
- Located at UCSD School of Medicine
- 18 FDA approved smoked cannabis studies
- The center's report to the legislature came out in 2011

PTSD Study By Dr. Suzanne Sisley

- This is going on in Colorado
- She was a long time physician in the VA system in Arizona
- Her study was a rare study approved by the federal government but was blocked in Arizona by several state legislators
- Her research is privately supported inColorado

2015 Epidiolex

This is a high CBD whole plant alcohol extract tincture produced by GW Pharmacueticals. It is being tested as anti seizure medication at several states in the U.S.

A study this past spring reported a 50% drop in seizure frequency in the study population, children with intractable seizures

Sean McAllister,PhD.

- He is a researcher at California Pacific Medical Center Research Group
- He had done research on the treatment of mice with breast cancer with CBD.
- The study demonstrated that the CBD cured the mouse breast cancer
- Dr. McAllister is presently preparing to do a human breast cancer study with a cannabinoid or cannabinoids

Center for Medicinal Cannabis Research (CMCR)

- A summary of the Center's clinical trials, published in 2012 in the Open Neurology Journal, concluded: "Evidence is accumulating that cannabinoids may be useful medicine for certain indications."

Studies Available

- To date, there are over 20,000 published studies or reviews in the scientific literature referencing the cannabis plant and its cannabinoids, nearly half of which were published within the last five years.
- These numbers are according to a key word search on the search engine PubMed Central, the US government repository for peer-reviewed scientific research.

More for CMCR

- "The classification of marijuana as a Schedule I drug as well as the continuing controversy as to whether or not cannabis is of medical value are obstacles to medical progress in this area. Based on evidence currently available the Schedule I classification is not tenable; it is not accurate that cannabis has no medical value, or that information on safety is lacking."

Conclusion

- History
- Endocannabinoid System
- Legal
- Future

Where Are We and What's Next

Tincture of Cannabis : Epidiolex, Nabiximol

Delta 9 THC-Marinol Off Label Use

Strains ,Extracts, Synthetics

CBD, Phenoids, Terpenes, Other Constituents

Grinspoon: Pharmaceuticalization v Individualism

Plant v Synthetic

Top Needs

- Product Standardization
- Professionalism in growing, dispensing and prescribing
- Research on Cancer and PTSD
- Making Cannabis at least a Schedule II drug

Standards

- Label
  - All products
  - Dosage
  - Plant constituents
- M.D. Standards
  - Marginalize minimalists
  - SCC and AACM standards

Dispensaries

- Need to be professional
- Need to be regulated
- Should be like pharmacies
- Health spa model

Suggest Research Priorities

- Conditions
  - Cancer
  - PTSD
- Terpenes Role
- Minor Cannabinoid role
- Specific dosage

Areas to Focus On

- Standardization – plant, labeling, product
- Professionalism – M.D., dispensary
- Research
  - PTSD
  - Cancer
  - Epilepsy
- Education
  - Med School
  - CME
  - General Public

Advice To The Policy Makers

- Teach Med Students: The Endocannabinoid System
- Teach Pharmacists: To Make Tincture Of Cannabis
- Regulate Dispensaries Like Pharmacies
- Recognize Cannabis Medical Value & Safety
- Fund Cancer Research
- Treat PTSD with Cannabis

Thank you very much

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- Cannabinomics by *Christopher Fichtner, M.D.*
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- Cannabis and Cannabinoids by *Ethan Russo, M.D.* and *Franjo Grotenhermen, M.D*
- .
- Drugs are NOT Tools of the Devil: How Greed and Discrimination Led to Dysfunctional Drug Policy and How to Fix it, by *David Bearman, M.D.*
- Marijuana Medical Handbook; by Dale Gieringer, Ph.D., Ed Rosenthal, and Gregory T. Carter, M.D.

