CANNABIS Madness or Medicine

Uma Dhanabalan, MD MPH FAAFP MRO

Global Health & Hygiene Solutions, LLC
TotalHealthCareTHC.com

Family Medicine, Occupational & Environmental Medicine, Cannabis Medicine

Objectives

- The History of Marijuana
- The Endocannabinoid System (ECS)
- Cannabinoids
- Delivery Systems

The Origin



Cannabis

- Family: Cannabaceae
- **Genus**: Cannabis Sativa
- Species: Cannabis Sativa, Cannabis Indica, Cannabis Ruderalis
- **Etymology**: "Canna" meaning stalk/cane, "Bis" meaning 2 sexes (Babylonia)
- AKA: Marijuana, Marihuana, Pot, Weed, Grass, Mary Jane, Bud, Ganja, Reefer, Hash
- > 480+ Chemicals, > 80+ Cannabinoids

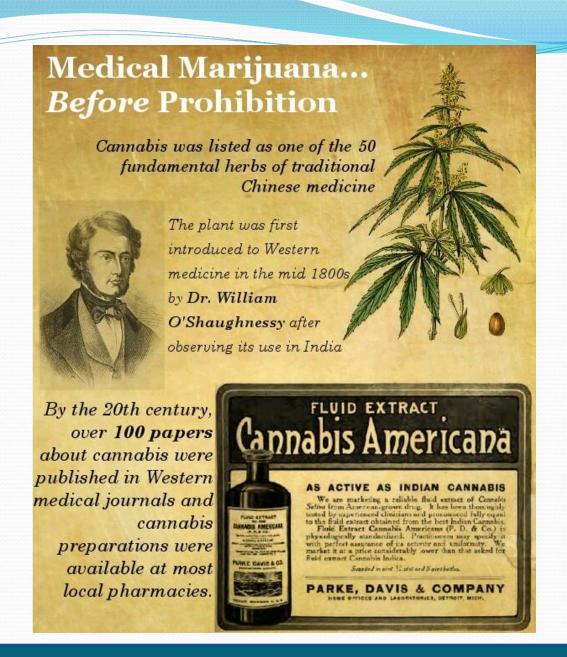
History - Medicine

- 1500 BC Chinese Pharmacopeia, the Rh-Y National Institute on Drug Abuse (NIDA)
- 1450 BC Holy anointing oil, Hebrew version Exodus (30:22-23), *kaneh-bosem*, extracted into olive oil, along with a variety of other fragrant herbs Book of Exodus
- 1213 BC Egyptians use for Glaucoma, Inflammation, and Enemas Lise Manniche, PhD An Ancient Egyptian Herbal, 1989
- 1000 BC India to treat a wide variety of ailments US National Commission on Marihuana and Drug Abuse

History - Medicine

- 600 BC It could quicken the mind, prolong life, improve judgment, lower fevers, induce sleep and cure for dysentery. **Ayurveda** The Sushruta Samhita, written in Sanskrit, text of medicine, anti-phlegmatic and a cure for leprosy. Jonathon Green, Cannabis, 2002
- 70 AD Pedanius Dioscorides, Greek physician studied many plants, *De Materia Medica* (*On Medical Matters*) Martin Booth, Cannabis: A History, 2005





PHARMACOPŒIA

OF THE

UNITED STATES OF AMERICA.

BY AUTHORITY OF THE

NATIONAL MEDICAL CONVENTION,

HELD AT

WASHINGTON,

A. D. 1850.



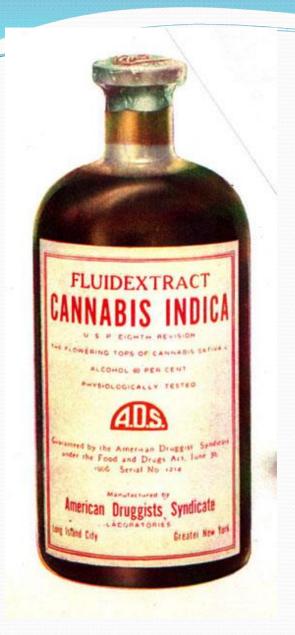
PHILADELPHIA:
LIPPINCOTT, GRAMBO, & CO.
successors to gridg, Elliot, & co.
1851.

W

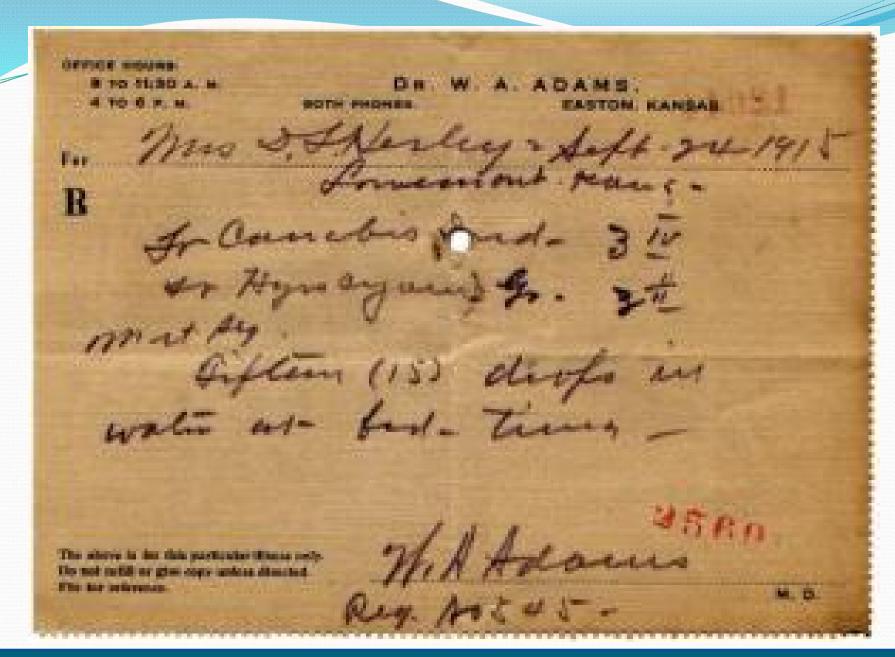
1850

- Marijuana: to the USA
- Marijuana as treatment for: neuralgia, tetanus, typhus, cholera, rabies, dysentery, alcoholism, opiate addiction, anthrax, leprosy, incontinence, gout, convulsive disorders, tonsillitis, insanity, excessive menstrual bleeding, uterine bleeding, and others.
- Patented marijuana tinctures were sold.

Medical Marijuana Law, 2007







- 1890 Queen Victoria's personal physician, prescribes cannabis for menstrual cramps.
- Sir Reynolds writes in the first issue of The Lancet, "When pure and administered carefully, [cannabis] one of the of the most valuable medicines we posses."
- 1898 The Spanish American War erupts, Panco Villa seizes 800,000 acres of timberland belonging to William Randolph Hearst.
- Hearst begins a 30-year propaganda campaign denouncing Spaniards, Mexicans, Blacks, and Latinos, portraying Mexicans as lazy pot-smoking layabouts.
- 1906 US Congress passes Pure Food and Drug Act, requires labeling of cannabis in over the counter remedies and food

- 1893-1894 Indian Hemp Commission
 - Analgesic, restores energy, induce contractions, antidiuretic, hay fever, cholera, dysentery, gonorrhea, diabetes, impotence, urinary incontinence, swelling of the testicles, granulation of open sores, chronic ulcers, insomnia, relief of anxiety, protection against cholera, stimulate appetite, aid to concentration of attention.
 - Cannabis has no addictive properties, and a number of positive emotional and social benefits.

- December 17, 1914. The Harrison Narcotics Tax Act of 1914 was approved, "a special tax on all persons who produce, import, manufacture, compound, deal in, dispense, sell, distribute, or give away opium or coca leaves, their salts, derivatives, or preparations, and for other purposes."
- 1914 1918 World War I
- 1920 1933 Prohibition of Alcohol
- 1929 1941 The Great Depression

- US Department of Treasury creates Federal Bureau of Narcotics
- Harry Jacob Anslinger Commissioner of the Federal Bureau of Narcotics
- Architect of national prohibition. His case rested on two fantastical assertions: that the drug caused insanity; that it pushed people toward horrendous acts of criminality."
 "The Federal Marijuana Ban Is Rooted in Myth and Xenophobia," New York Times, July 29, 2014
- Campaign by the U.S. Federal Bureau of Narcotics and Dangerous Drugs sought to portray marijuana as a powerful, addicting substance that would lead users into narcotics addiction. "Gateway Drug"

Beware! Young and Old-People in

Marthura Covers

This



may be handed you

by the friendly stranger. It contains the Killer Drug "Marihuana"—a powerful narcotic in which lurks

Murder! Insanity! Death!

WARNING!

Dope peddlers are shrewd! They may put some of this drug in the or in the tobacco cigarette.

WRITE FOR DETAILED INFORMATION, ENCLOSING 12 CENTS IN POSTAGE — MAILING COST

Address: THE INTER-STATE WARCOTIC ASSOCIATION

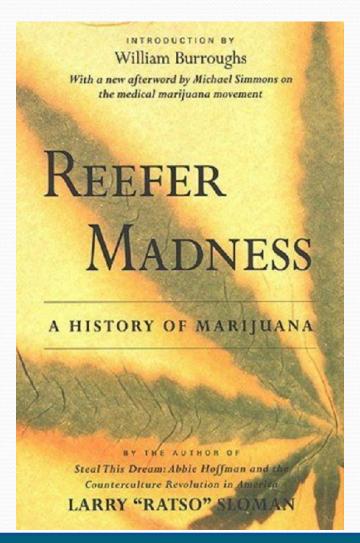
(Incorporated not for profit)

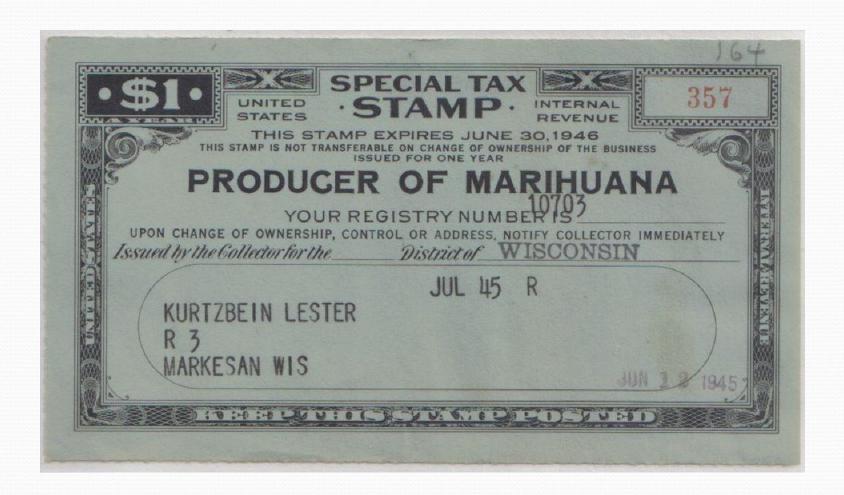
53 W. Jackson Blvd.

Chicago, Illinois, U. S. A.

ANTERIOR STANDAR PORTER in part of the indicational company described the day, the deviation on the district image of the control of the cont







A Brief History of...

Marijuana Law



1619



1st N. American marijuana law forces farmers to grow hemp

Jamestown Colony, Virginia

1850

Cannabis extract widely recommended & sold overthe-counter in Western pharmacies



1915-1927



Influx of Mexican immigrants into the US ..

9 states pass laws outlawing the 'marihuana' they smoked

"All Mexicans are crazy and this stuff [marihuana] is what makes them crazy"

-Texas senator on the floor of the Senate

1929-1936

Recreational marijuana use spreads among minorities...

"Reefer makes Darkies think they're as good as white men"



"I wish I could show you what a small marihuana cigarette can do to one of our degenerate Spanishspeaking residents. That's why our problem is so great"

Harry J. Anslinger is appointed as head of the Federal Bureau of Narcotics

1937

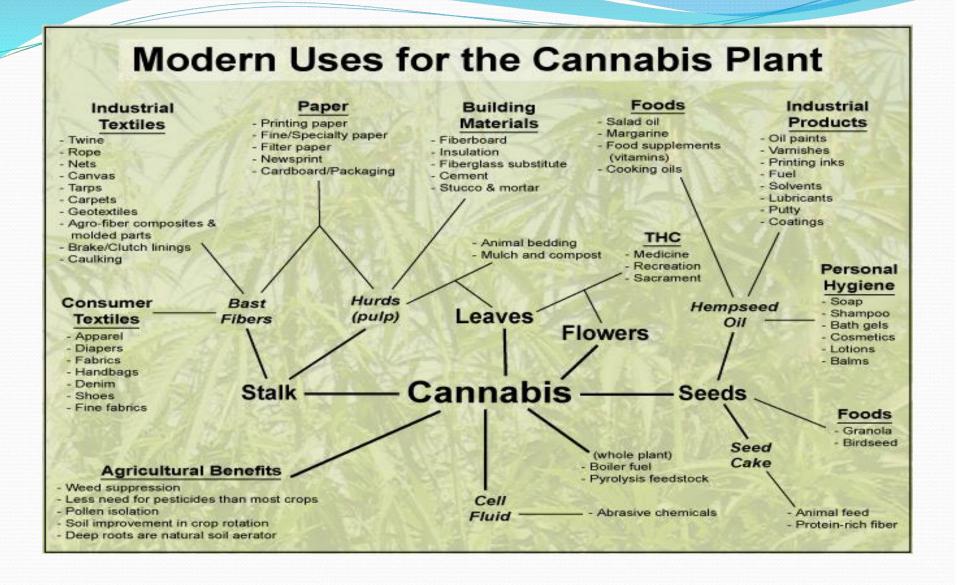
Anslinger proposes Marihuana Tax Act to Congress and testifies:

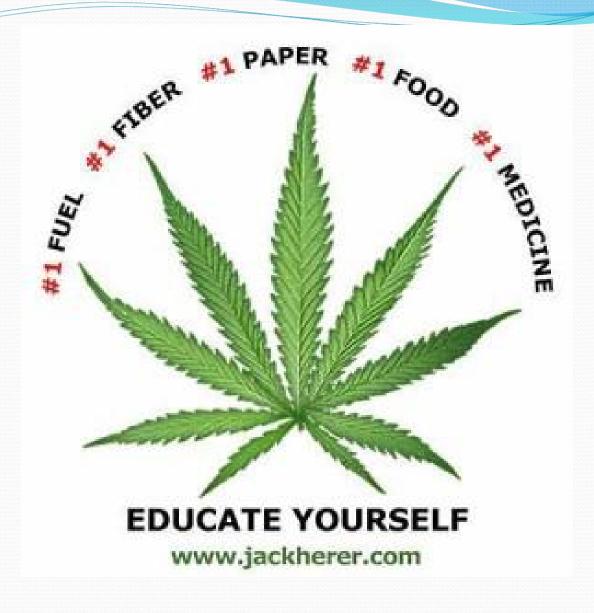
"Marijuana is the most violent drug in the history of mankind"

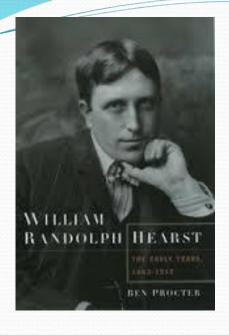
Act passes...

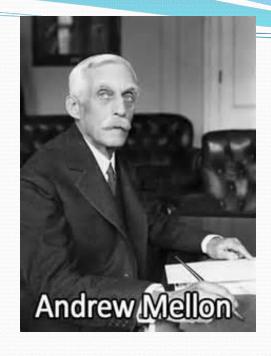
Marijuana is **Prohibited**



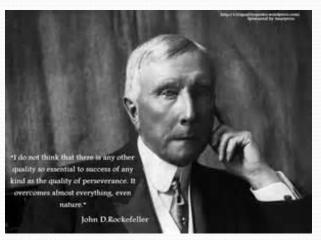




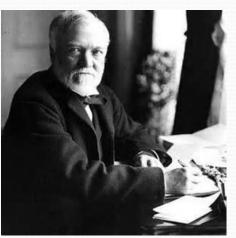








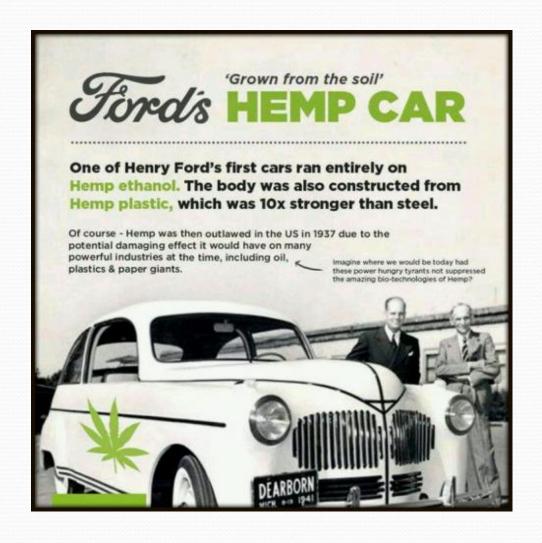




1938 - Popular Mechanics

- " It tells about the new machine for harvesting hemp which "solves a problem more than 6,000 years old."
- Increased hemp production "will displace imports of raw material and manufactured products" and calls hemp the "standard fiber of the world."
- Hemp can "produce more than 25,000 products, ranging from dynamite to Cellophane."
- The 1st time in U.S. history the term 'billion-dollar' is applied to the potential for an agricultural harvest.





- U.S. government overrides its own ban on hemp and distributes 400,000 pounds of hemp seed to U.S farmers who produce 42,000 tons of hemp fiber annually to support the war effort until 1946.
- U.S. farmers, including youthful 4-H Club members, are inundated by "Uncle Sam" with incentives to grow hemp.
- The U.S.D.A. makes it mandatory for farmers to attend showings of the "Hemp For Victory" film. Farmers and their sons who agree to grow hemp are exempt from military service, even though America is at war.

The US Pharmacopoeia admitted marijuana as a recognized medicine in 1850 under the name Extractum Cannabis or Extract of Hemp, and listed it until 1942. Fluid extracts were marketed by The Smith Brothers, Parke Davis, Squibb, Lilly, Burroughs Wellcome, and other leading drug manufacturers

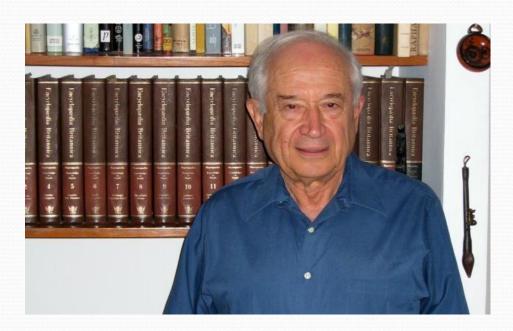
Cannabis Extractum Recognized 1850

• American Medical Association (AMA) "Report 10 of the Council on Scientific Affairs," 1997

- 1938 Mayor Fiorello LaGuardia requests that the New York Academy of Medicine conduct an investigation of marijuana.

 Cannabis Dependence: Its Nature, Consequences, and Treatment, 2006
- 1944 The practice of smoking marihuana does not lead to addiction of morphine or heroin or cocaine and no effort is made to create a market for these narcotics by stimulating the practice of marihuana smoking. Marihuana is not the determining factor in the commission of major crimes. The publicity concerning the catastrophic effects of marihuana smoking in New York City is unfounded. LaGuardia Committee Report on Marihuana
- 1950-60s An accessory of the beat generation, used by college students and "hippies" and became a symbol of rebellion against authority.
- 1970 The Controlled Substances Act of 1970 classified marijuana along with heroin and LSD as a Schedule I drug, having the relatively highest abuse potential and no accepted medical use.

Dr. Raphael Mechoulam



- "Grandfather of Cannabis"
- 1964, discovered THC as the psychoactive component of the cannabis plant
- 1992, discovered the 1st Endocannabinoid-"Anandamide"
- Sanskrit: Eternal bliss and supreme joy

1975 - 1999

- 1975 Robert Randall, suffered from glaucoma, arrested for cultivating marijuana
- 1978 Investigational New Drug (IND)
- 1992 Flood from AIDS patients, Bush closed the program for new applicants.
- December 1, 1999 U.S. Department of Health and Human Services updated its medical marijuana policy, restating that the IND program would not be reopened.

2002 - Marijuana Policy Project

- The United States
 Government as
 represented by the
 Department of Health
 and Human Services was
 granted a U.S. Patent
 (#6630507)
- On any and all uses and applications of: Cannabinoids as antioxidants and neuroprotectants.



(12) United States Patent Hampson et al.

(10) Patent No.: US 6,630,507 B1 (45) Date of Patent: Oct. 7, 2003

(54) CANNABINOIDS AS ANTIOXIDANTS AND NEUROPROTECTANTS

- (75) Inventors: Aidan J. Hampson, Irvine, CA (US); Julius Axelrod, Rockville, MD (US); Maurizio Grimaldi, Bethesda, MD (US)
- (73) Assignce: The United States of America as represented by the Department of Health and Human Services, Washington, DC (US)
- (*) Notice: Subject to any disclaimer, the term of this

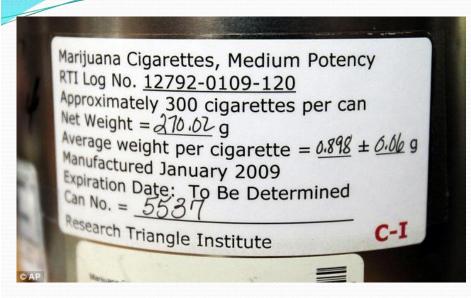
OTHER PUBLICATIONS

Windholz et al., The Merck Index, Tenth Edition (1983) p. 241, abstract No. 1723.*

Mechoulam et al., "A Total Synthesis of d1–∆¹-Tetrahydrocannabinol, the Active Constituent of Hashish¹," Journal of the American Chemical Society, 87:14:3273–3275 (1965).

Mechoulam et al., "Chemical Basis of Hashish Activity," Science, 18:611–612 (1970).

Ottersen et al., "The Crystal and Molecular Structure of Cannabidiol," *Acta Chem. Scand. B* 31, 9:807–812 (1977). Cunha et al., "Chronic Administration of Cannabidiol to Healthy Volunteers and Epileptic Patients¹," *Pharmacology*, 21:175, 195 (1980).



Elvy Musikka, who suffers from glaucoma, smokes marijuana she regularly receives from the U.S. Government.



- Voters passed the Massachusetts Medical Marijuana Initiative on November, 6.
- Ballot Question 3, "An Initiative Petition for a Law for Humanitarian Medical Use of Marijuana" passed with a 63.3% vote and with a majority in 349 of 351 communities
- Massachusetts was the 18th state to legalize the medical use of marijuana.

GHHS. LLC 2015

Study: State Medical Marijuana Laws Associated With Lower Induced Opiate-induced Fatalities

- University of Pennsylvania, the Albert Einstein College of Medicine in New York City, and the Johns Hopkins Bloomberg School of Public Health in Baltimore conducted a time-series analysis of medical cannabis laws and state-level death certificate data in the United States from 1999 to 2010 a period during which 13 states instituted laws allowing for cannabis therapy.
- "States with medical cannabis laws had a 24.8 percent lower mean annual opioid overdose mortality rate compared with states without medical cannabis laws."
- Specifically, overdose deaths from opioids decreased by an average of 20 percent one year after the law's implementation, 25 percent by two years, and up to 33 percent by years five and six. *JAMA Intern Med.* 2014;174(10):1668-1673

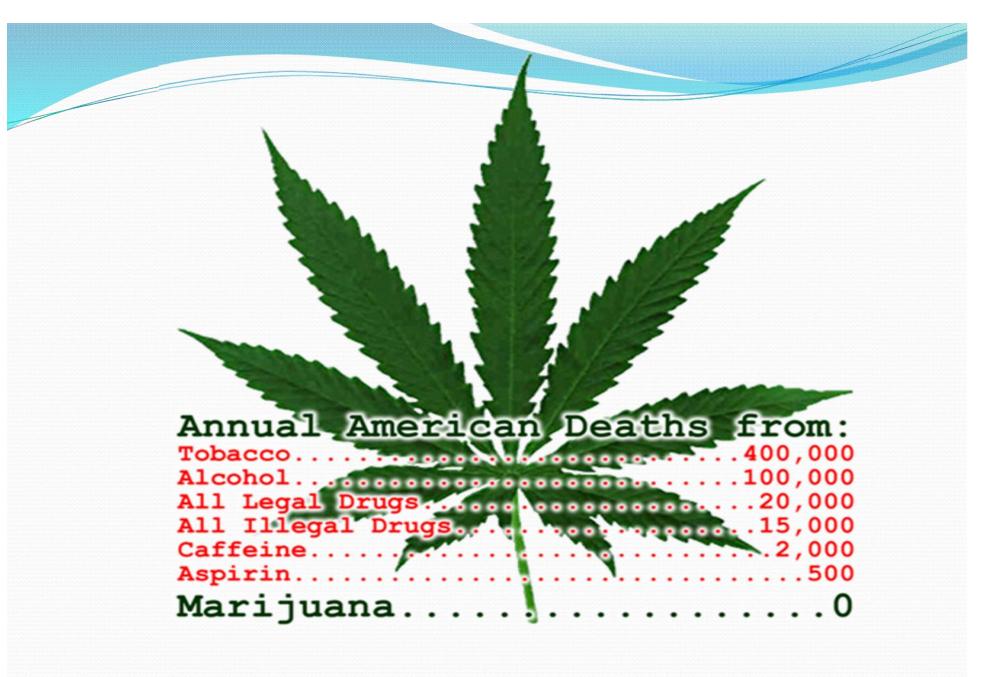
Causes of Death 2013

A 11	
AII	Causes
1 111	Causes

- Major Heart Disease
- Malignant Neoplasm
- Respiratory Diseases
- Accidents
- MVA
- Alzheimer's Disease

2,596,993 • Diabetes M	lellitus 75,578	3
796,494 • Drug-Indu	ced Death 46,471	L
584,881 • Suicide	41,149)
149,205 • Injury by Fi	irearms 33,630	6
130,557 • Alcohol-Ind	duced Death 29,00)]
35,369 • Parkinson's	s Disease 25,196	5
84,767 • Homicide	16,12	21
 HIV Diseas 	e 6,955	5
• Cannabis (1	Marijuana) o)

http://www.drugwarfacts.org/cms/causes_of_death#s



WORK THIS OUT ALCOHOL CANNABIS **ADDICTIVE** NON-ADDICTIVE DEPRESSANT ANTI-DEPRESSANT CAUSES CANCER CURES CANCER 1 MILLION DEATHS PER ZERO DEATHS IN ANNUM HISTORY COST POLICE & NHS SAVES POLICE & NHS BILLIONS BILLIONS DEATH VIA OD NO OD DESTROYS BRAIN CELLS GROWS BRAIN CELLS LEGAL ILLEGAL

Do Medical Marijuana Laws Reduce Addictions and Deaths Related to Pain Killers?

David Powell, Rosalie Liccardo Pacula, Mireille Jacobson NBER Working Paper No. 21345 Issued in July 2015

Many medical marijuana patients report using marijuana to alleviate chronic pain from musculoskeletal problems and other sources.

If marijuana is used as a substitute for powerful and addictive pain relievers in medical marijuana states, a potential overlooked positive impact of medical marijuana laws may be a reduction in harms associated with opioid pain relievers, a far more addictive and potentially deadly substance.

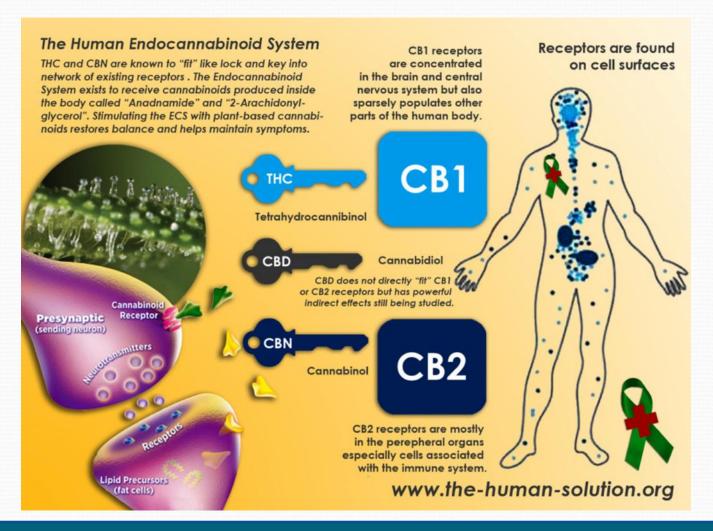
Timeline in USA for Medical Marijuana

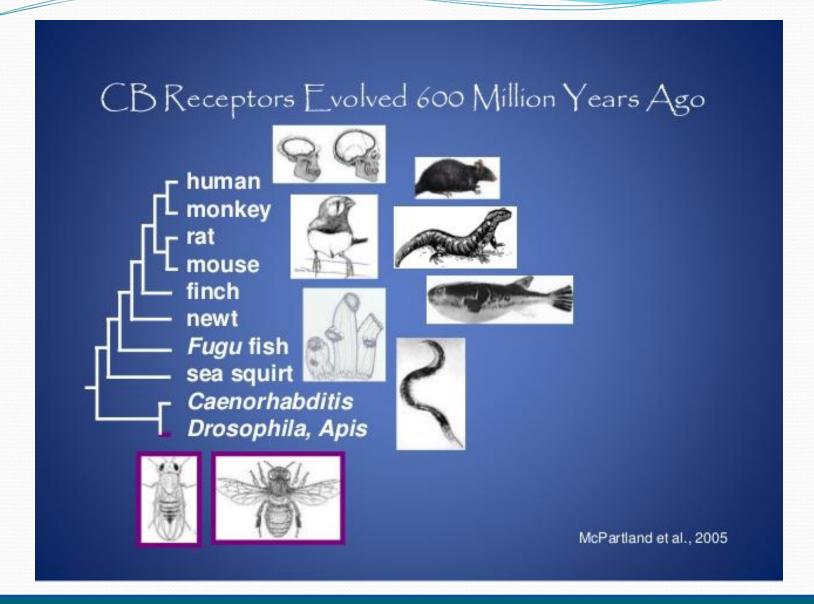
- •1996: California
- •1998: Alaska, Oregon, Washington
- •1999: Maine
- •2000: Colorado, Hawaii, Nevada
- •2004: Montana
- •2006: Rhode Island
- •2007: New Mexico, Vermont
- •2008: Michigan
- •2010: Arizona, New Jersey
- •2011: Delaware, Washington, D.C.
- •2012: Connecticut, Massachusetts
- •2013: New Hampshire, Illinois
- •2014: Maryland, Minnesota, New York

2015

- Marijuana, the most common illicit drug used in the USA
- Federal government considers marijuana a Schedule I substance (having no medicinal use & high risk for abuse)
- 4 states and District of Columbia (DC) have legalized marijuana for adult recreational use,
- 23 states and DC have passed laws allowing its use as a treatment for certain medical conditions

The Endocannabinoid System





Dr. Vincenzo Di Marzo



- 1998 summarized ECS
- The ECS was meant to for us to "Relax, Eat, Sleep, Protect and Forget."

Endocannabinoids

- Crucial to bioregulation.
- Formed from the internal lipid constituents of cellular membrane, making it lipophilic
- Hydrophobic with limited mobility in an aqueous environment
- Their main role is in cell-signaling, and, because they are hydrophobic, their main actions are limited to:
 - paracrine (cell-to-cell) or
 - autocrine (same cell), rather than systemic, effects.

Endocannabinoids

- Retrograde transmission in the brain; travels backward from postsynaptic to presynaptic cells
- Synthesized "on demand" and not stored
- Very short half-life
- Degradation by FAAH may regulate ECs bioactivity

The Principal Catabolic Pathways for both AEA and 2-AG by Fatty Acid Amide Hydrolase (FAAH) and Monoacylglycerol Lipase (MGL), respectively, both producing Arachadonic Acid

These enzymes, FAAH and MGL, have become therapeutic targets for pharmacologic interventions of the ECS. FAAH inhibition has shown the advantages of a lack of abuse potential or physical dependence compared with MGL.

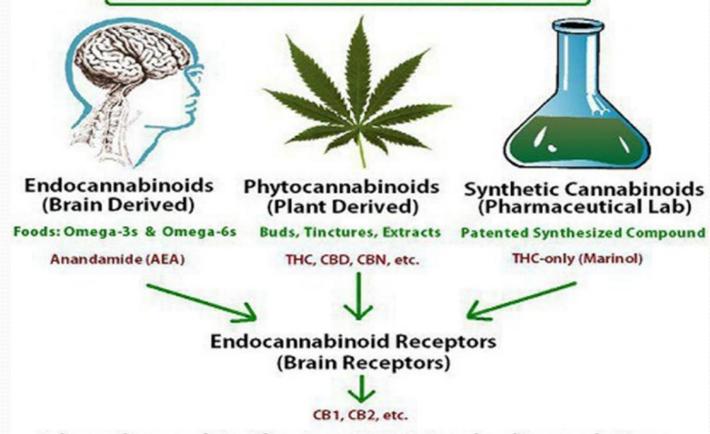
Chemical Structure

- Although the first EC to be identified was AEA, 2-AG is the most abundant in the brain.
- Several other ECs have been identified, but their function and role in ECS physiology remains to be determined.
- Five of the best-known ECs all share the same 19-C backbone structure but differ in the R-group constituents.

The Five-Best known Endocannabinoids Showing the Common 19-C Backbone Structure and specific R-group Constituents

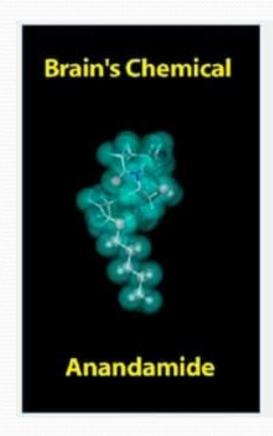
$$\begin{array}{c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$





The endocannabinoid system (ECS) is involved in regulating a variety of physiological processes including appetite, pain and pleasure sensation, immune system, mood, and memory.

Endocannabinoid vs Phytocannabinoid





- THC's chemical structure is similar to the brain chemical anandamide
- Allows drugs to be recognized by the body and to alter normal brain communication

The Endocannabinoid System: Receptors and Ligands



7-member transmembrane G-protein-coupled receptor





Immune System



Brain

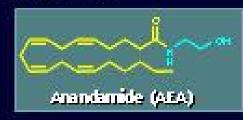
Adipose

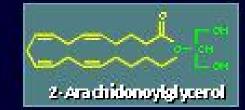
Muscle

Liver GI tract

Pancreas

II. Endogenous Ligands





- Synthesized from membrane-derived phospholipids
- Taken up and degraded rapidly.
- Act as retrograde messengers

CB=cannabinoid.

CB1-R CB2-R Roles in the Body

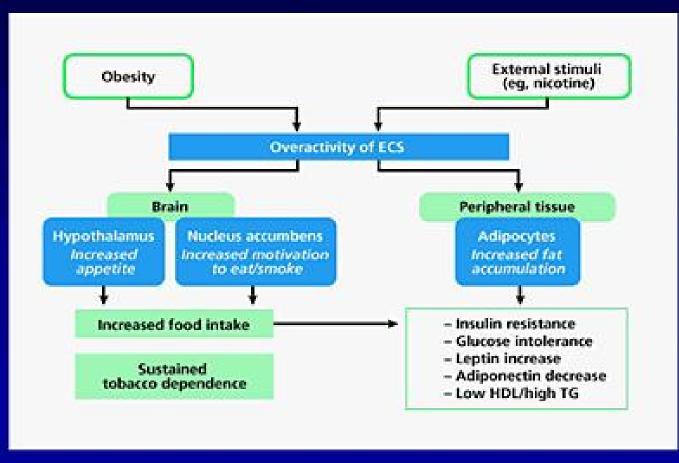
- Chronic stress
- Obesity
- Nervous system
- Pain
- Heart and blood vessels
- Cancer
- Gastrointestinal system
- Liver
- Reproductive system
- Skeletal system

Endocannabinoid Deficiency

- Clinical endocannabinoid deficiency (CECD): can this concept explain therapeutic benefits of cannabis in migraine, fibromyalgia, irritable bowel syndrome and other treatment-resistant conditions?
- CONCLUSION: Migraine, fibromyalgia, IBS and related conditions display common clinical, biochemical and pathophysiological patterns that suggest an underlying clinical endocannabinoid deficiency that may be suitably treated with cannabinoid medicines.

Neuro Endocrinol Lett. 2008 Apr;29(2):192-200. Russo EB

Effects of Endocannabinoid System Overactivity



Synthetic Cannabinoids

- MarinolTM
- CesametTM
- Acomplia[™]
- EpidiolexTM

Marinol™

- Dronabinol (synthetic THC)
- Control of nausea and vomiting caused by chemotherapeutic agents used in the treatment of cancer
- Stimulate appetite in AIDS patients.
- In 1999 placed in Schedule III of the CSA.



Cesamet™

- Nabilone: contains a synthetic cannabinoid similar to THC and is used for the same purposes as Marinol®
- It was approved by the FDA in 1985, began marketing in the US in 2006.
- Schedule II of the CSA.



Acomplia™

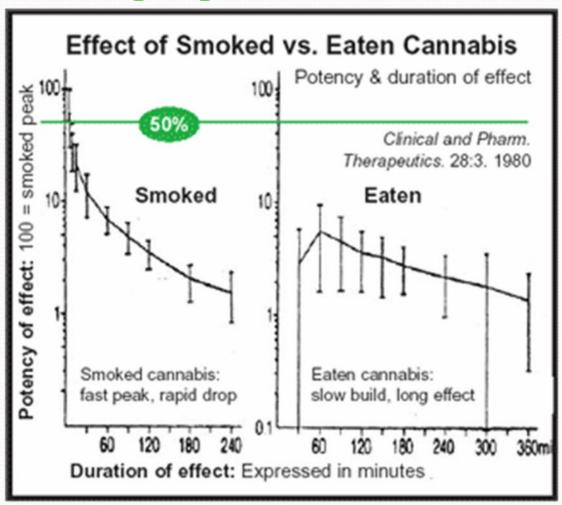
- Rimonabant (SR141716) 1st CB1 receptor blocker1. Its main effect is reduction in appetite. anorectic antiobesity drug
- June 2006 approved in Europe and other countries, but never approved in the United States.
- January 2009 withdrawn from the market due to potentially serious side effects.



Epidiolex™

- Clinical trials to establish its effectiveness and safety (necessary to obtain FDA approval) a CBD-based drug
- Created to treat certain forms of childhood epilepsy.
- Some parents of children with a severe form of epilepsy called Dravet Syndrome have reported success in using a high-CBD strain of marijuana to control seizures in their children.

Delivery Systems & Effects



Consumption of Cannabis

- Inhalation
- Ingestion
- Topical
- Other

GHHS. LLC 2015

Inhalation







Ingestion







Topicals







Other





Sativa vs. Indica Medical Effects



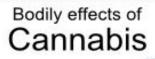
Sativa/Indica Hybrid strains will have a mixture of effects

Mind Dominant

Anti-Anxiety
Anti-Depressant
Activating
Uplifting
Increase Alertness
Increase Energy
Enhance Creativity

Body Dominant

Sedating
Relaxing
Muscle Relaxant
Treats Acute Pain
Reduces Nausea
Increases Appetite
Increases Dopamine



Eyes: -

- Reddening
- Decreased intra-ocular pressure

Mouth: -

- Dryness

Skin: -

 Sensation of heat or cold

Heart: -

 Increased heart rate

Muscles: -

- Relaxation

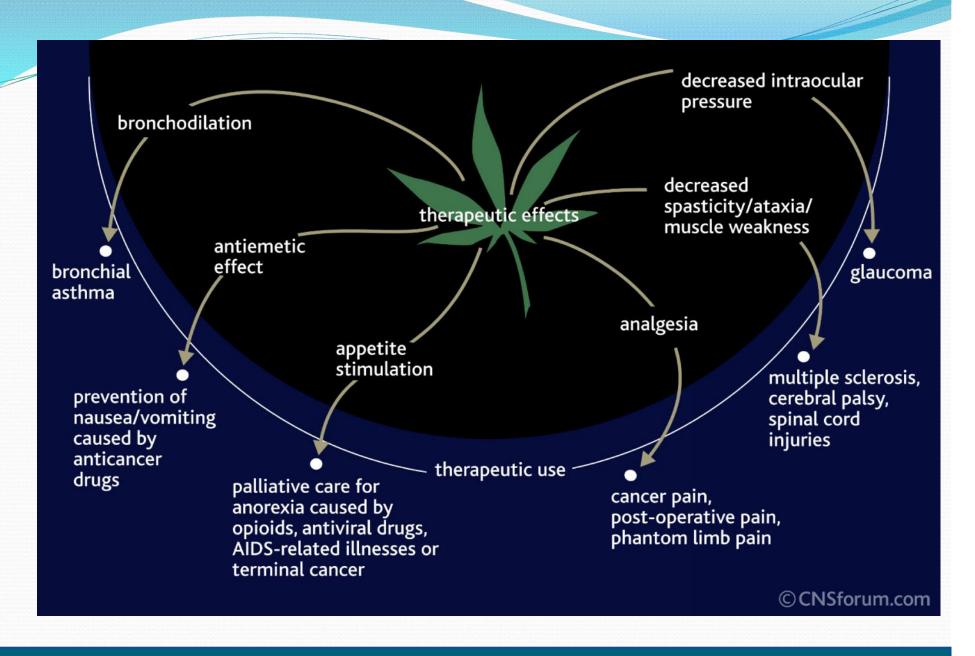
Hyperemesis

- Increased Vomiting Paranoia

Anxiety

Overwhelmed

Relaxed





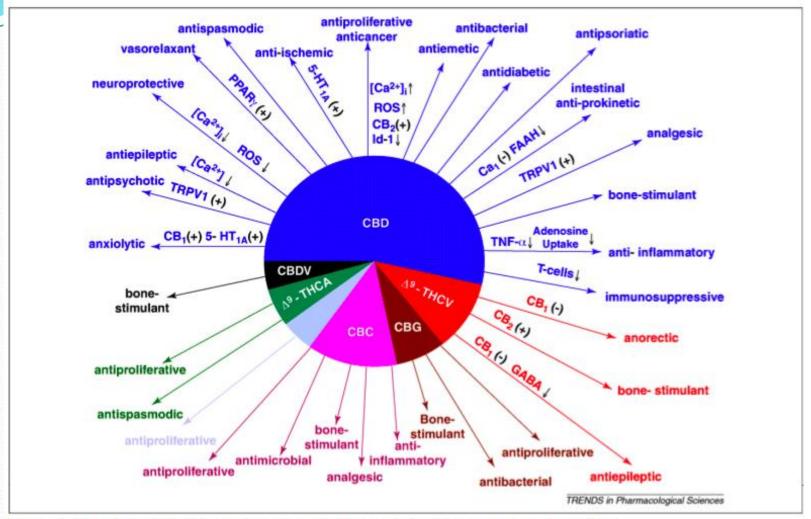
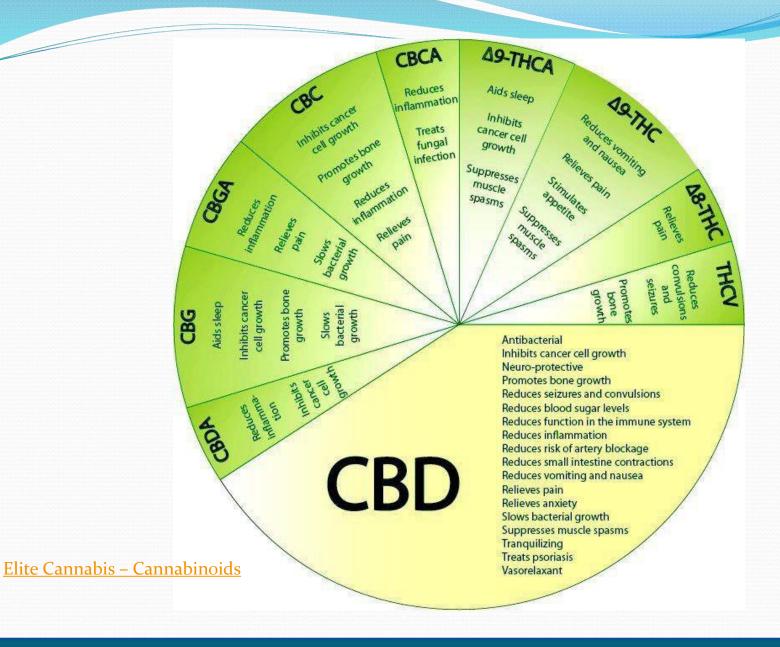


Figure 1. Pharmacological actions of non-psychotropic cannabinoids (with the indication of the proposed mechanisms of action).

Abbreviations: Δ⁹-THC, Δ⁹-tetrahydrocannabinol; Δ⁸-THC, Δ⁸-tetrahydrocannabinol; CBN, cannabidiol; CBD, cannabidiol; Δ⁹-THCV, Δ⁹-tetrahydrocannabivarin; CBC, cannabichromene; CBG, cannabigerol; Δ⁹-THCA, Δ⁹-tetrahydrocannabinolic acid; CBDA, cannabidiolic acid; TRPV1, transient receptor potential vanilloid type 1; PPARγ, peroxisome proliferator-activated receptor γ; ROS, reactive oxygen species; 5-HT_{1A}, 5-hydroxytryptamine receptor subtype 1A; FAAH, fatty acid amide hydrolase.

(+), direct or indirect activation; ↑, increase; ↓, decrease.



Reported Medical Applications for Cannabis

- ADHD
- AIDS
- Anorexia
- Anxiety
- Arthritis
- Bipolar Disorder
- Cancer
- Chron's Disease
- Depression
- Epilepsy/Seizures
- Fibromyalgia
- Glaucoma

- Irritable Bowel
- Meniere's Disease
- Multiple Sclerosis
- Nausea/Emesis
- Neuropathic Pain
- OCD
- Parkinson's
- PTSD
- Psychosis
- Schizophrenia
- Rheumatism
- Sleep Disorders

Cannabis and Cancer

- Antiproliferative
- Antimetastatic
- Antiangiogenic
- Apoptosis

Patients – Cannabis

- NEVER used Cannabis
- Prior user > 20 Years Ago
- Present user Self Medicating

Healthcare Providers - Cannabis

- NO Knowledge
- Some Knowledge
- Curious
- Alienate/Discharge Patient from Practice
- Ignore/Tolerate Patient use of Cannabis
- Accept/Engage Patients use of Cannabis

Impact On Patients

- Exit from Pharmaceuticals and Narcotics
- Improvement in Quality Of Life
 - SELF Care
 - Mindful
 - Return to Work
 - Relationships: START having them Significant others, Children, etc
 - Activities: Return to hobbies, Recreation, Lose weight
 - Engaged Empowered
 - Brings Generations Together
 - Improves Sex, Spirituality, Sanity
 - NEW NORMAL

SUMMARY

- Cannabis A PLANT Medicine
- Cannabis has killed NOBODY!
- Cannabis is in Schedule I (Heroin, LSD, Ecstasy)
- POLITICS NOT Evidence Based Medicine Prohibition of Cannabis
- The ENDOCANNABINOID System Homeostasis: LIFE
 - RELAX EAT SLEEP FORGET PROTECT
- Cannabis was Prescribed by Doctors is USA Pharmacopeia: 1850 to 1942
- EDUCATE! EMBRACE! EMPOWER!
- TotalHealthCareTHC.com

GHHS. LLC 2016

"Cannabis is not an entrance drug, it is an exit drug from pharmaceuticals & narcotics."

Dr. Uma Dhanabalan

CANNABIS...Marijuana MADNESS OR MEDICINE?

References

- National Institute on Drug Abuse. Marijuana Retrieved from http://www.drugabuse.gov/publications/drugfacts/marijuana on February 3, 2015"
- Retrieved 2014-12-16. https://news.vice.com/article/new-york-is-about-to-allow-medical-marijuana-but-you-cant-smoke-it
- "Congress Quietly Ends Ban on Medical Marijuana". The L.A. Times. 2014-12-16. Retrieved 2014-12-16.
- United States. Department of Health (DPH). Medical Use of Marijuana Program. Patient Guidance: Registering with the Medical Use of Marijuana Program. Mass. Gov. Web. Retrieved from http://www.mass.gov/eohhs/docs/dph/quality/medical-marijuana/patient-guidance-for-registration.pdf on 31 Mar. 2016.

GHHS. LLC 2016