

Maryland Medical Marijuana

It's current status and projected future



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HUMAN HISTORY SHOWS COMMON USE OF PSYCHOACTIVE OR ANALGESIC DRUGS FROM PLANTS



Importance

- cultural
- economic
- medicinal-pharmacological
- recreational-addiction

Wide spread sources of natural drugs exist that alter perception

Near Eastern

- + ergot (LSD)
- + cannabis-Marijuana
- + opium-*Papaver*
- + *Amanita muscaria*



South America

- + coca-Erythroxylum



Mexico

- + peyote
- + *Psilocybe*

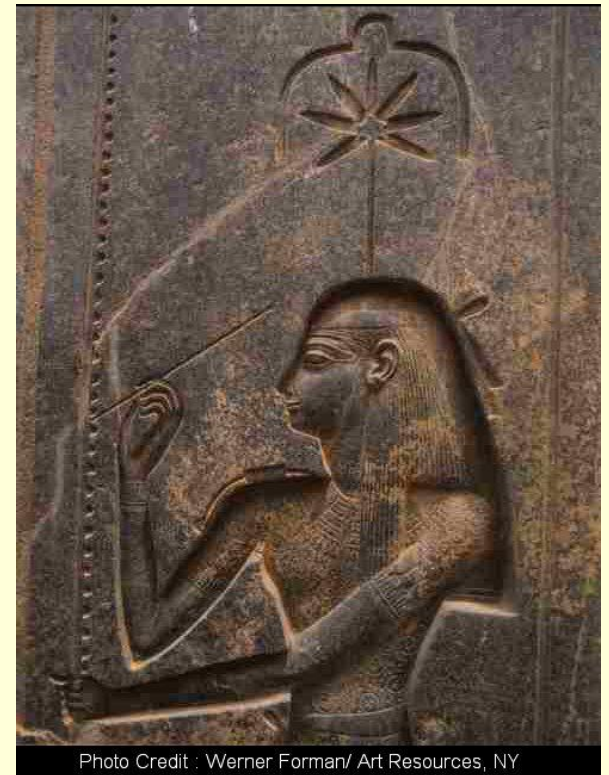


- Many plant-derived compounds alter perceptions of reality. They may produce feelings of tranquility, invigoration, or dream states. These compounds can be used medicinally, to escape from reality, or for religious or ceremonial events.
- Toxicity and hallucinogenic properties are interrelated based on dosage and individual user tolerance.

What is the right dosage?



- Marijuana and Hemp are a source of fiber. Seed oils from cannabis are used in many cultures. The plant has also been used medicinally and for its psychoactive properties. According to some sources, cannabis is the number one cash crop in the U.S. today.
- Cannabis is found in ancient Chinese writings as well as in ancient texts from Egypt and India.



First medicinal report of Marijuana

Ebers Papyrus (ca. 1550 BC) in Ancient Egypt describes medical cannabis. Egyptians used Cannabis in suppositories for pain relief of hemorrhoids as well as sore eyes.

Chinese surgeon Hua Tuo (c. 140-208) is credited with recording personal use of *Cannabis* as an anesthetic. He reduced the plant to powder and mixed it with wine for administration prior to conducting surgery.

[de Crespigny, Rafe (2007)]

[Pain, Stephanie (15 December 2007)]

Smoking plant products was developed by Native Americans and introduced into Europe in the 1500's. Cannabis was brought to the New World by the Europeans to establish a fiber crop for ropes. The plant has become naturalized and widespread in many areas. Most of the wild cannabis has little psychoactive material in it.

Cannabis resin (Hashish) was originally eaten and is commonly used today in India and many other places. Marco Polo reported the use of hashish during his travels in the East.



Cannabis sativa
Marijuana,
Cannabaceae

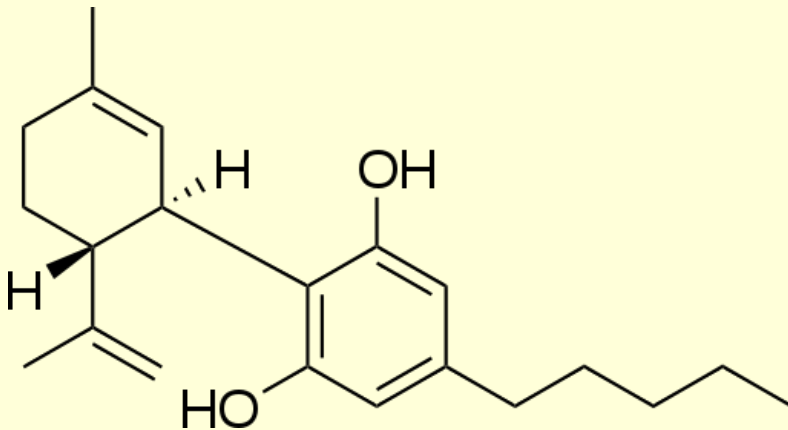
The resinous alkaloidal monoterpenes of *Cannabis sativa* (Cannabaceae) have been used in China for thousands of years. Cannabis is probably native to central Asia.

As shown here it was often cultivated with other tall crops to escape detection.

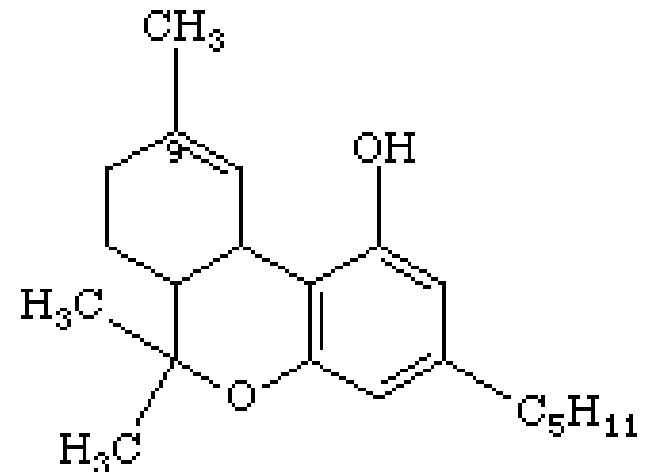


- Most psychoactive compounds contain nitrogen and many are alkaloids. The best known **exception** are the cannabinoids which lack nitrogen but are the active ingredients of marijuana.
- The compounds are can be taken orally, injected, or absorbed through mucous membranes as in the mouth or nose. Many are absorbed through the lungs.

cannabidiol

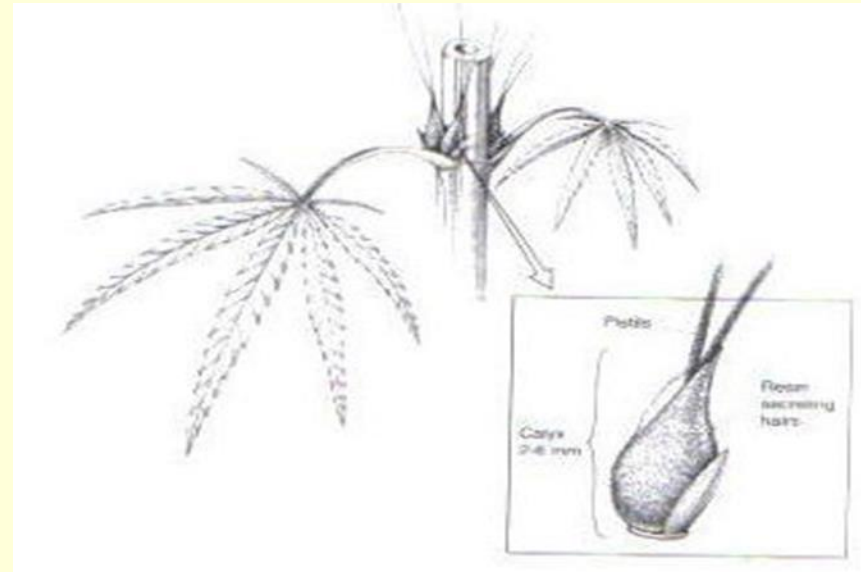


tetrahydrocannabinol



Cannabinoid Chemistry

- Marijuana plants are either male or female.
- Many Cannabinoids, such as THC and CBD, are found throughout the plant but in trace levels.
- The exception is high concentrations in the female flora parts.



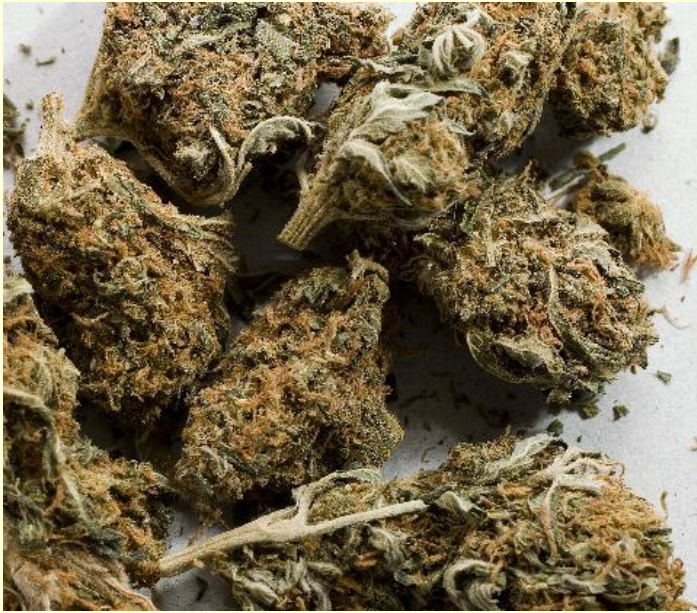
Each small, petal-less flower is enclosed by a calyx, with tiny, resin-secreting hairs.

High concentrations of cannabinoids are found in the resin, which tends to collect in the top of the flower.

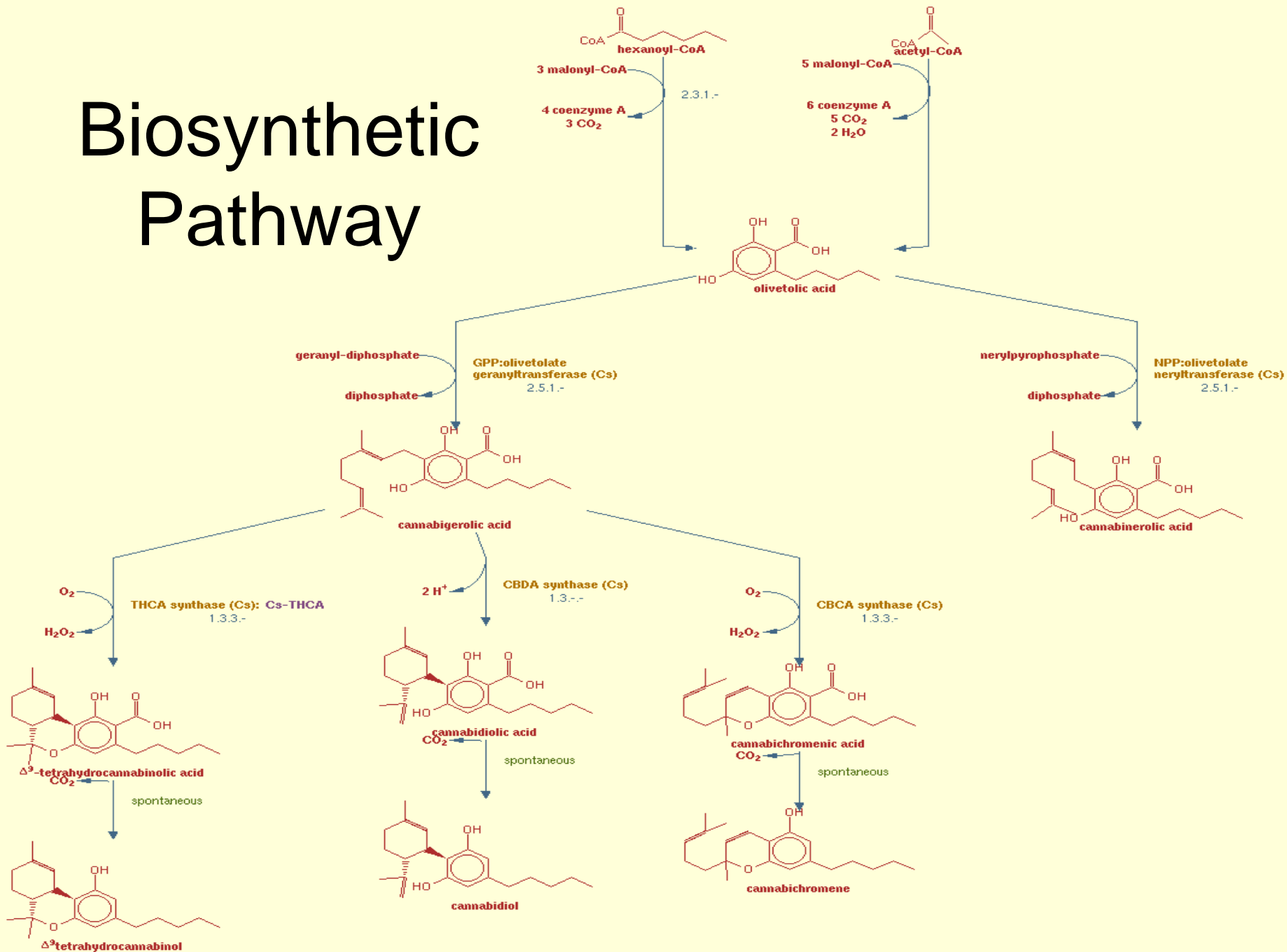
Male (left) and female (right) flowers of *Cannabis sativa*



The inflorescence of Marijuana



Biosynthetic Pathway

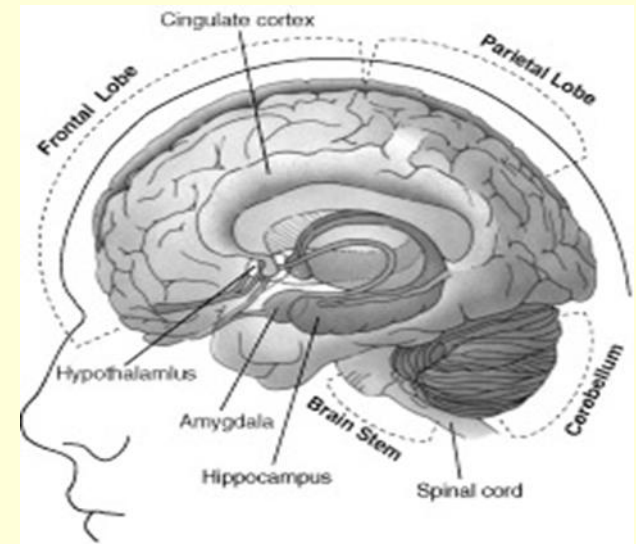


Pharmacology & Cannabinoid Receptors

- The behavioral effects of THC are receptor mediated.
- Cannabinoid receptors are members of the G- protein-coupled receptors.
- Cannabinoid receptors ligands bind reversibly and are stereoselective.

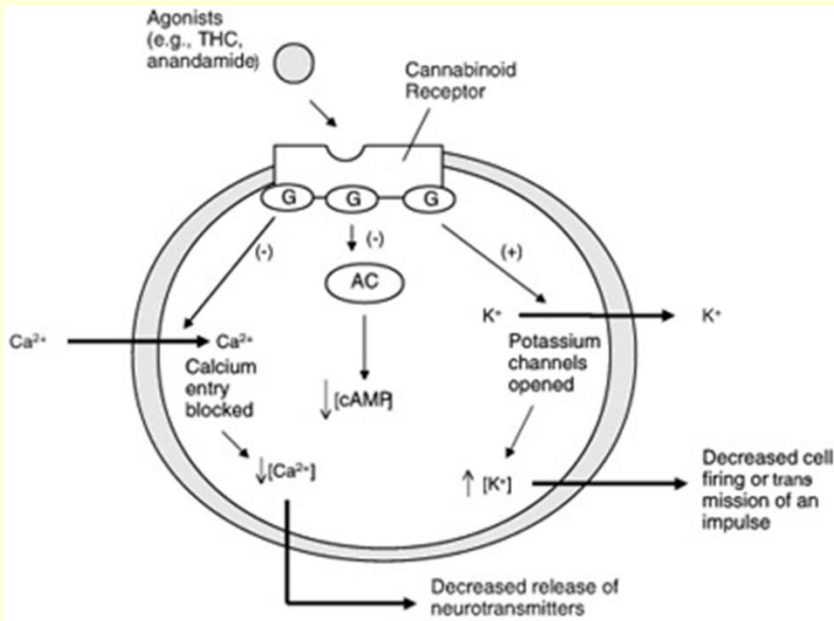
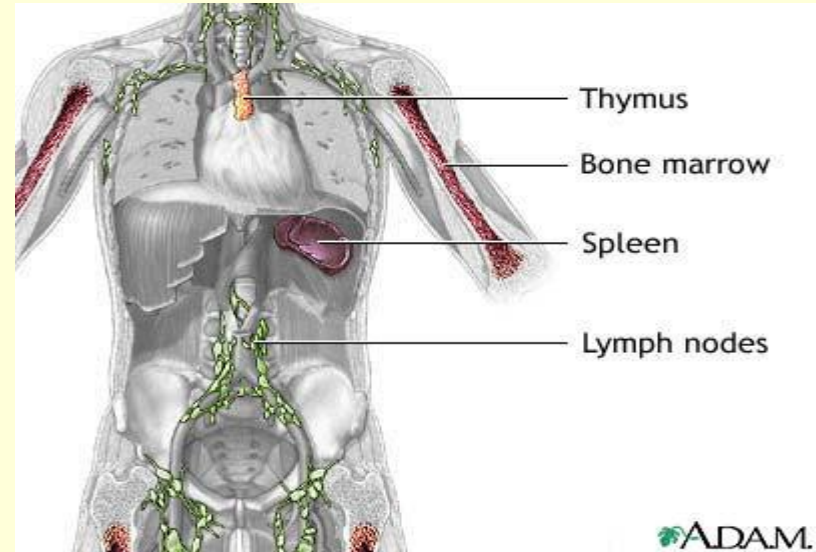
In the 1980's, cannabinoid receptors, CB1 & CB2, were discovered.

CB1 are found in the brain including the hippocampus, cerebral cortex, basal ganglia, and cerebellum.



CB2 Receptors

CB₂ receptors are also found in the brain, but expressed mainly in the immune system.



Marijuana: What's It reported to Do?

- Marijuana is a mild hallucinogen, classified as a depressant
- THC (TetrahydroCannabinol) and other Cannabinoids can be ingested, inhaled or absorbed.
- Marijuana effects may include dry mouth, increased heart rate, impaired coordination and balance, delayed reaction time and short term memory loss. These short term effects wear off within two-three hours

Marijuana's Impact on the Body

- Chronic Marijuana smokers are subject to chest colds, bronchitis, emphysema and bronchial asthma
- Smoking exposes you to carcinogens and toxins similar to those in cigarette smoke
- Marijuana is reported to:
 - Delay of onset in puberty in men
 - Abnormal menstrual cycles and inhibited ovulation in women
 - Smaller birth weights in infants from prenatal smoking mothers.

<http://www.acde.org/common/Marijana.htm>



Does Medical Marijuana have identifiable medical uses?

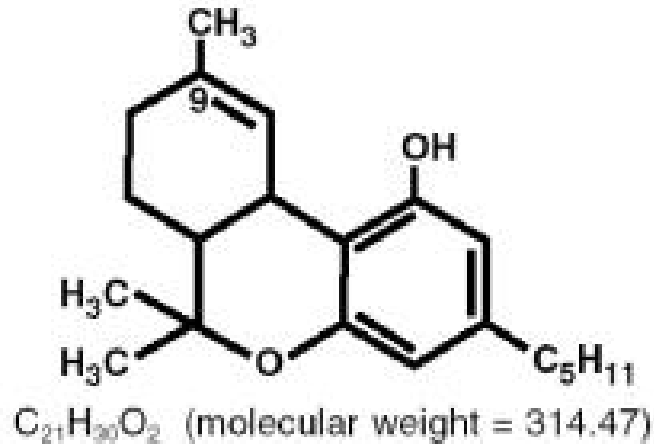
List of potentially prescribed uses for Marijuana in Maryland

- epilepsy/spasms
- autism
- Crohn's disease
- PTSD
- muscular dystrophy
- Nausea
- HIV/AIDS
- Pain relieve
- cancer
- depression/anxiety
- Parkinson's disease
- Schizophrenia
- multiple sclerosis
- Sleep Disorders
- sickle cell anemia
- Inflammation
- alcoholism
- diabetes

Best Evidence for Medical Marijuana uses?

- Marijuana has been implicated in alleviating multiple sclerosis neurological effects?
- Marijuana has been implicated for pain relief.
- Marijuana has been implicated for Nausea relief.
- Marijuana has been implicated for appetite enhancement.

Synthetic Marijuana Marinol®



- Active ingredient is dronabinol
- Dronabinol is a synthetic derivative of Delta 9-THC.
- Stimulates appetite and reduces nausea and vomiting

MARINOL® 
(dronabinol)
Capsules 2.5 mg, 5 mg, 10 mg

In 1999, the DEA rescheduled
Marinol (synthetic marijuana).

SCHEDULE III.
(A) The drug or other substance has a potential for
abuse less than the drugs or other substances in
schedules I and II.
(B) The drug or other substance has a currently
accepted medical use in treatment in the United
States.

*Meanwhile, the DEA refuses to change
marijuana's schedule I status.*

Wasting Syndrome and Appetite Stimulation

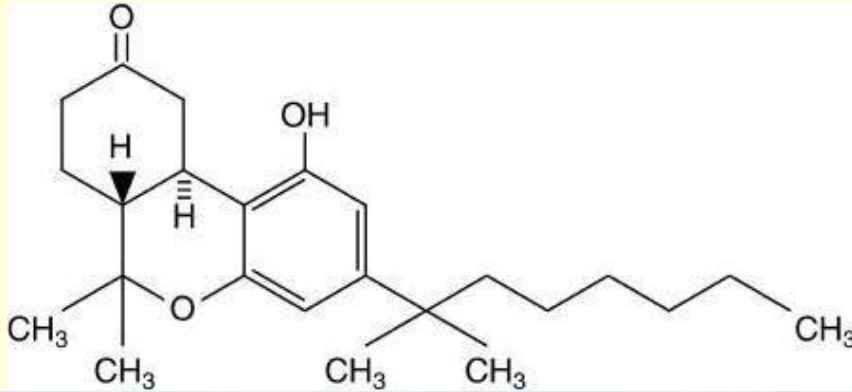
- Small amount of literature published in this area.
- THC (Dronabinol) was studied for effectiveness of cannabinoids in appetite stimulation.
- A six week and one-year therapy program with dronabinol was associated with a gain in weight and increased appetite in a significant number of patients.



Nausea and Vomiting

- Cannabinoids are semi-effective in preventing emesis.
- New York State Study
 - 56 cancer patients who were unresponsive to conventional antiemetic drugs.
 - 34% of patients rated marijuana as being effective.
 - Results were inconclusive because there was no control group.
- Canadian Oncology Study
 - A double blind, placebo-controlled study compared smoked marijuana vs. THC in liquid oral dosages.
 - 25% of patients achieved control of emesis with either treatment.

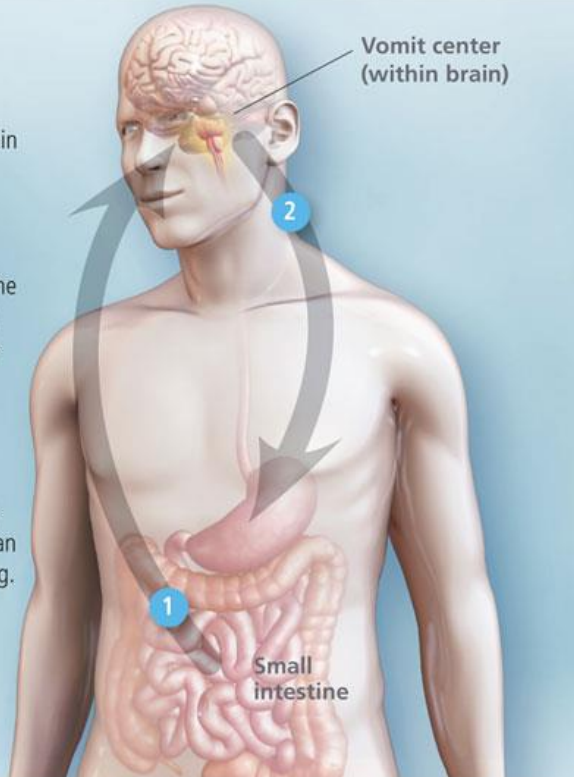
Cesamet (Nausea)



1) When chemotherapy reaches cells in the small intestine, these cells send signals to a part of the brain called the vomit center

2) The vomit center sends out its own signals to the stomach. This can cause the feeling of nausea and can cause muscle contractions in the abdomen, which leads to vomiting

The vomit center is like a control center. It coordinates many different signals that can cause nausea and/or vomiting.



- Active ingredient is nabilone.
- Synthetic derivative of Delta-9-THC.
- Used in treating nausea and vomiting

Analgesic Benefits

- Cannabinoids can be useful as analgesics.
- 3 types of research studied the effects of cannabinoids on pain.
 - Experimentally Induced Acute Pain
 - Post-Surgical Acute Pain
 - Chronic Pain

The results of these studies suggest that small doses of smoked cannabis may improve pain, mood and sleep in some patients with chronic pain

Neurological Disorders

- Marijuana may relieve symptoms but not cure in 3 types of neurological disorders:
 - Muscle Spasticity (Multiple Sclerosis)
 - Movement Disorders (Parkinson's Disease)
 - Epilepsy
- Cannabis has 480 different compounds, including over 66 cannabinoids and around 200 terpenes. Synergistic effects for interactions between the cannabinoids and the terpenes may be more important than studying a single counterparts.
- Cannabis Literature is skewed towards non-Scientists. For example this phrase is commonly found:

Not only is the research limited, but the research that is done remains obscured with scientific jargon and hidden in Medical journals that often require the public to pay in order to view them.

Epilepsy

- Individual testimonies that marijuana is effective abound, but clear hard evidence is often empirical.
 - Ng Case-Controlled Study
 - 308 patients in experimental group; 294 in control group.
 - Marijuana is a protective factor for first-time seizure for men, but not women.
- The American Epilepsy Society takes the position that robust evidence is lacking and the risk/benefit ratio does not warrant use of Marijuana for Epilepsy at this time (2015).

Muscle Spasticity

- Marijuana is reported as reducing muscle spasticity in MS patients.
 - Mail Survey
 - 112 MS patients reported that smoked marijuana reduced muscle spasticity and associated pain.
 - Double-Blind Placebo-Controlled Study
 - 10 MS patients & 10 healthy patients
 - Patients reported that marijuana impaired posture and balance.

Glaucoma

- Smoked marijuana has shown to reduce intraocular pressure (IOP) by 25%.
- Similar effects were also found when given in oral and intravenous forms.
- Topical treatments, such as eye drops, were not effective in reducing IOP.
- Not as effective as conventional treatments currently in use (Becker, 2016 personal communication).

Does Medical Marijuana cause harm?

-Does Marijuana Harm The Brain?

In studies on Brain Development and Function: Cannabis Use and Cognitive Impairment were correlated.

Populations for the study were self selected and IQ's measured at young age and again after more than a decade of Marijuana use. IQ's declined at least 5 points in users vs non users, however no dosage or frequency controls and population IQ's were different at the start of study.

-Univ. California and Univ. Arizona

Conclusions

- Marijuana has been seen to be effective in stimulating appetites, preventing emesis, and as a pain reliever.
- However, clinical studies are small and inconclusive.
- Oral or intravenous application are less toxic than inhalation method.
- More studies are needed.

What happened in Maryland?

HOUSE BILL 302

By: Delegates Glenn, Anderson, Carter, Oaks, and B. Robinson
Introduced and read first time: January 24, 2013, Passed in
modified form March 23, 2013.

- Assigned to: Health and Government Operations and
Judiciary

"A BILL ENTITLED AN ACT concerning Maryland Medical
Marijuana Act

- FOR the purpose of authorizing the medical use of marijuana
under certain circumstances; repealing certain criminal
provisions that allow the imposition of a certain fine or the
use of an affirmative defense for use or possession of
marijuana...".

Saunders USDA/ARS Drug Crops Program

Completed Projects

- Developed DNA fingerprinting of drug crops.
 - Coca
 - Opium Poppy
 - Marijuana
- Developed chemical herbicide for drug crops
 - Coca
 - Opium Poppy
 - Marijuana
- Developed biological control for drug crops
 - Coca
 - Opium Poppy

USDA-ARS, Beltsville Secure Greenhouse Facilities



USDA Drug Crops Field



Determining male
from female
plants of Marijuana
using AFLP DNA
genotyping.

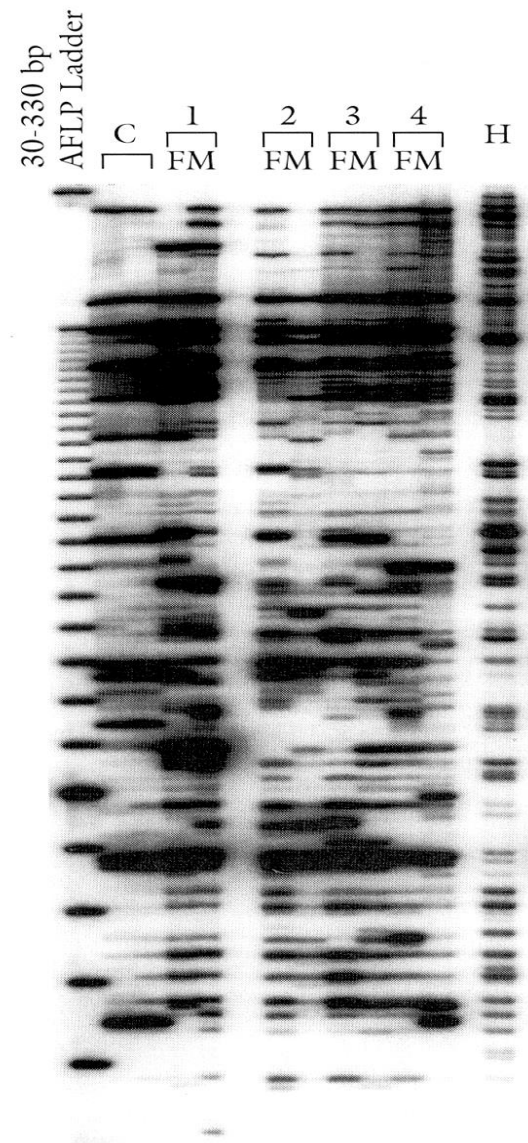


FIGURE 1. AFLP DNA analysis of several male and female plants of cultivars of *Cannabis sativa*. AFLP reactions were electrophoresed on a denaturing 6% (w/v) polyacrylamide sequencing gel. Female (F) and Male (M) samples were analyzed from cultivars of *Cannabis sativa* from the following locations: Lane 1. Hawaii, Lane 2. Afghanistan, Lane 3. Kentucky, Lane 4. Mexico, Lane C. Control from a common population collected before flowering, and Lane H. Hemp sample.

Approached to provide scientific guidance on advisory boards for several Grower Applicants in 2015

Grower Licenses (15):

Received 146

Each Grower application was 115 questions relating to Cannabis horticulture. For example: Question 56: **Please describe how as soon as is practical, the Applicant will, for each plant, (1) create a unique identifier for each plant, (2) assign each plant to a batch, (3) enter information regarding the plant into the inventory control system, (4) create a tag with the unique identifier and batch number, and (5) securely attach the tag to a plant container or plant.**

Maryland Marijuana Commission

Overview of Regulations

Three types of Licenses due November 6, 2015:

- 1) Grower Licenses (15) \$2000 each application
- 2) Processor Licenses (no limit) \$2000 / application
- 3) Dispensary Licenses (94) plus additional 15

Two per senatorial district (47 x 2) plus an additional 15 for companies which get grower licenses \$1000/ application

Maryland Marijuana Commission Response from Application solicitation 11/6/2015

Grower Licenses (15):	Received 146
Processor Licenses no limit:	Received 124
Dispensary License 94:	Received 811
Total applications received	1081

Total application fees collected \$1,351,000

Provisions of the Medical Marijuana laws

- No Marijuana or its constituents can be transported across Maryland state borders.
 - Immaculate conception of growing stocks.
- All Marijuana grown in Maryland will be tested by State certified labs for cannabinoid content, contamination by pesticides, and other chemical constituents.
 - No state certified labs exist nor are the criteria for testing established.

Provisions of the Medical Marijuana laws

It is prohibited on any Federal Property:

1. Fort Meade
2. USDA
3. Fort Detrick
4. NIH
5. Aberdeen
6. FDA
7. NASA
8. Interstate Highways (Eisenhower Interstate
Defense Highway 1956)

Maryland Marijuana Commission

Overview of Regulations

- Covers smoking products, tinctures, and extracts. Does not cover edible products identified as Food Products because the regulation of food products is under the authority of the Maryland Office of Food Safety. The Commission has not developed regulations regarding the production of medical cannabis in forms like food. **75% of Colorado cannabis consumption are edibles.**
- All applicants must be associated with Resident of Maryland.

Maryland Marijuana Commission

Overview of Regulations

- Commission established limits of 120 grams of usable cannabis (primarily dried flower) as a 30-day supply. At current costs this represents an annual cost per year for each patient of \$3,370. Cash only due to interstate bank regulations control by Federal Government.
- Commission established limits on medical cannabis-infused products measured by tetrahydrocannabinol limits of 36 grams of THC as a 30-day supply.

Problems with ranking of Applications for Medical Marijuana Commission

1. Numbers of Applications (Growers 15:146) 10%
Dispensary (94:811) 11%
2. Dispensary districts 47: Duplicate applications in every district.(can only receive one)
3. Grower applications: Duplicate applications in different individual names were submitted. (to check for identical scoring)
4. Adequate reviewing panels not established prior to application deadline (initial grant system review failed)

Medical Marijuana Commission Policies

Hannah Byron, the commission's executive director, abruptly resigned in January 2016. Patrick Jameson, a former state police officer who advocated eliminating drugs in his 2010 election campaign for county sheriff, was appointed April 2016. One of his first decisions was to restrict processor licenses to 15 to **make it easier for regulators to carry out inspections.**

Charles County First to approve zoning for Medical Marijuana

- Although Maryland State legislature approved medical Marijuana use in the state they left local zoning decisions to regional jurisdictions.
- In March 2016 Charles County commissioners voted 3-1 to approve medical cannabis zoning becoming the first County to eliminate local restrictions.

Provisions of the Medical Marijuana laws

- It must be prescribed by medical authorities.

This was modified in April 2016 to include: dentists, podiatrists, nurse midwives and nurse practitioners in addition to physicians that can provide certifications for medical cannabis.

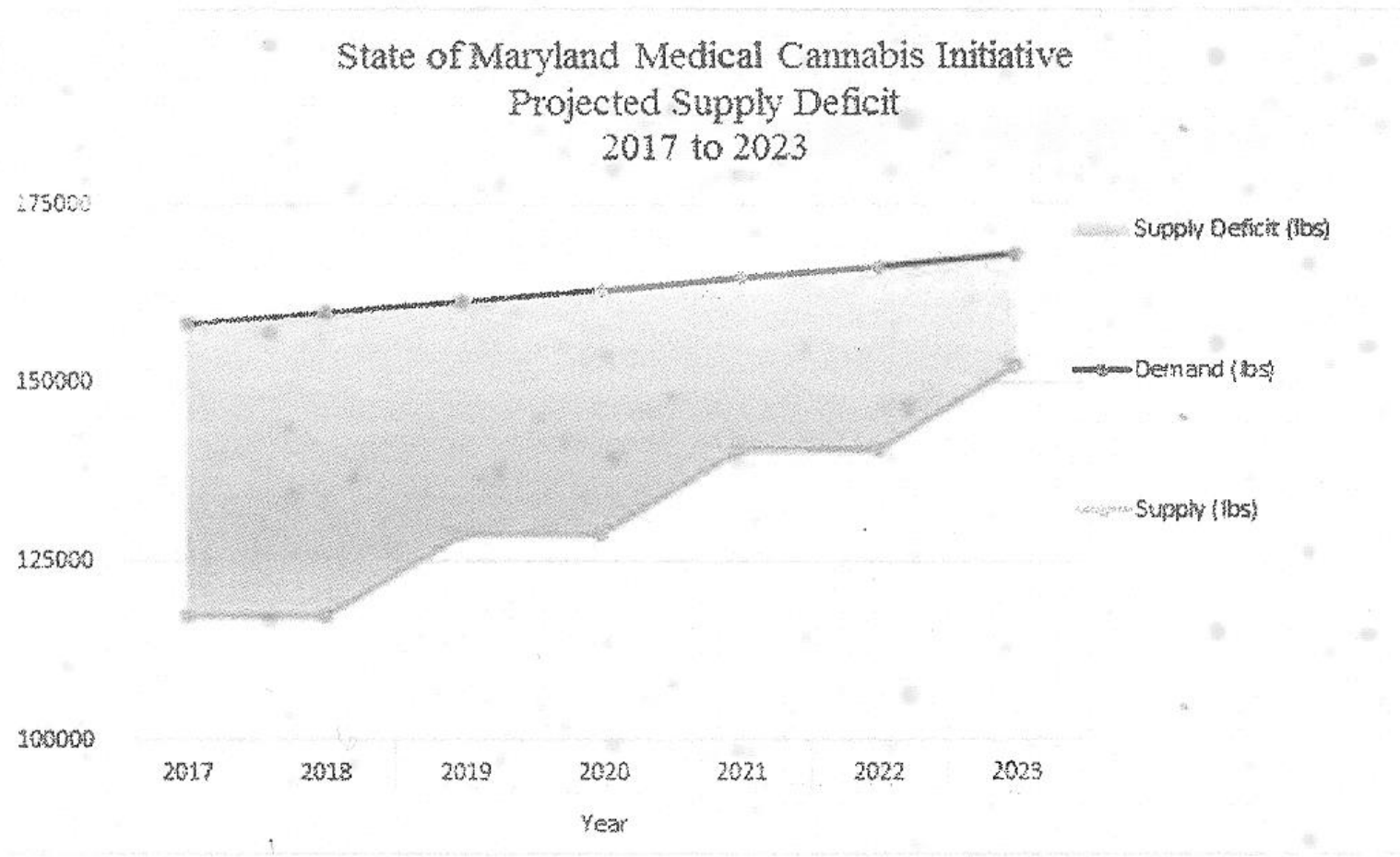
The medical providers must have an active license and a controlled substances . Based on information provided by the Maryland Department of Legislative Services , there are 40,048 health care providers that qualify.

Future of Maryland Medical Marijuana

- Licensing applicants will be announced sometime in summer of 2016.
- They have one year to pay \$50,000 fee, obtain local zoning approval and established they physical business or they will loose license.
- Predicted Maryland population for medical marijuana is 2% of 6 million or 120,000 patients by 2018.
- Predicted Maryland deficit need is for 50,000 lbs by 2018.
- Predicted Maryland income is \$400,000,000 by 2018.

Maryland Medical Marijuana Production Deficit (in lbs) Projected based on Patient growth needs

Table 2. Medical Cannabis Flower Supply Deficit from 2017-2023



Maryland Marijuana Commission

Future action

- Linking with FDA to provide license for edibles which constitute 75% of market in Marijuana use in Colorado.
- Initiate future rounds of applications to increase number of Growers and Processors in Maryland.
- Dealing with inconsistencies in current policies regarding transportation, Importing improved varieties, reciprocal agreements with neighboring States and the District of Columbia Commission established limits on medical for patient usage.
- Clarification of Federal Policies regarding Medical Marijuana use.
- Enhanced funding for critical research.

Maryland Medical Marijuana

It's coming

The United States of Marijuana

