# MEDICAL MARIJUANA

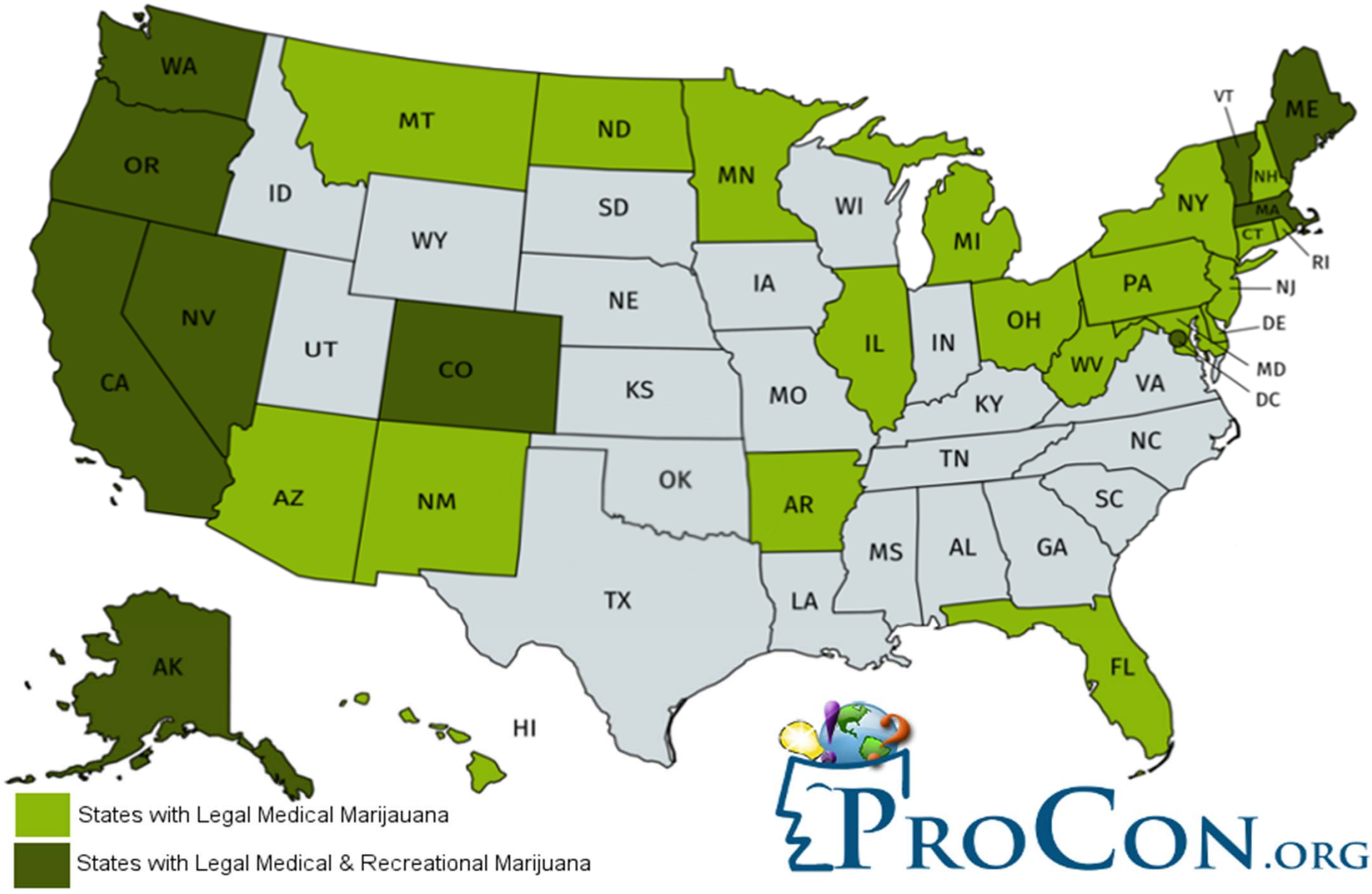
# WHAT IS MEDICAL MARIJUANA?[10]

- "Medical Marijuana refers to using the whole unprocessed marijuana plant or its basic extracts to treat a disease or symptom"
- The FDA has not recognized or approved the marijuana plant as medicine
- The chemicals in marijuana are called cannabinoids

# BACKGROUND[1]

- Marijuana is the female flowers and dried leaves of the hemp plant called *Cannabis sativa*
- 30 states and the District of Columbia have legalized medical marijuana
- All marijuana can be considered medical-grade since it all has some therapeutic effect

# 30 ~~29~~ Legal Medical Marijuana States & DC
# 9 Legal Recreational Marijuana States & DC



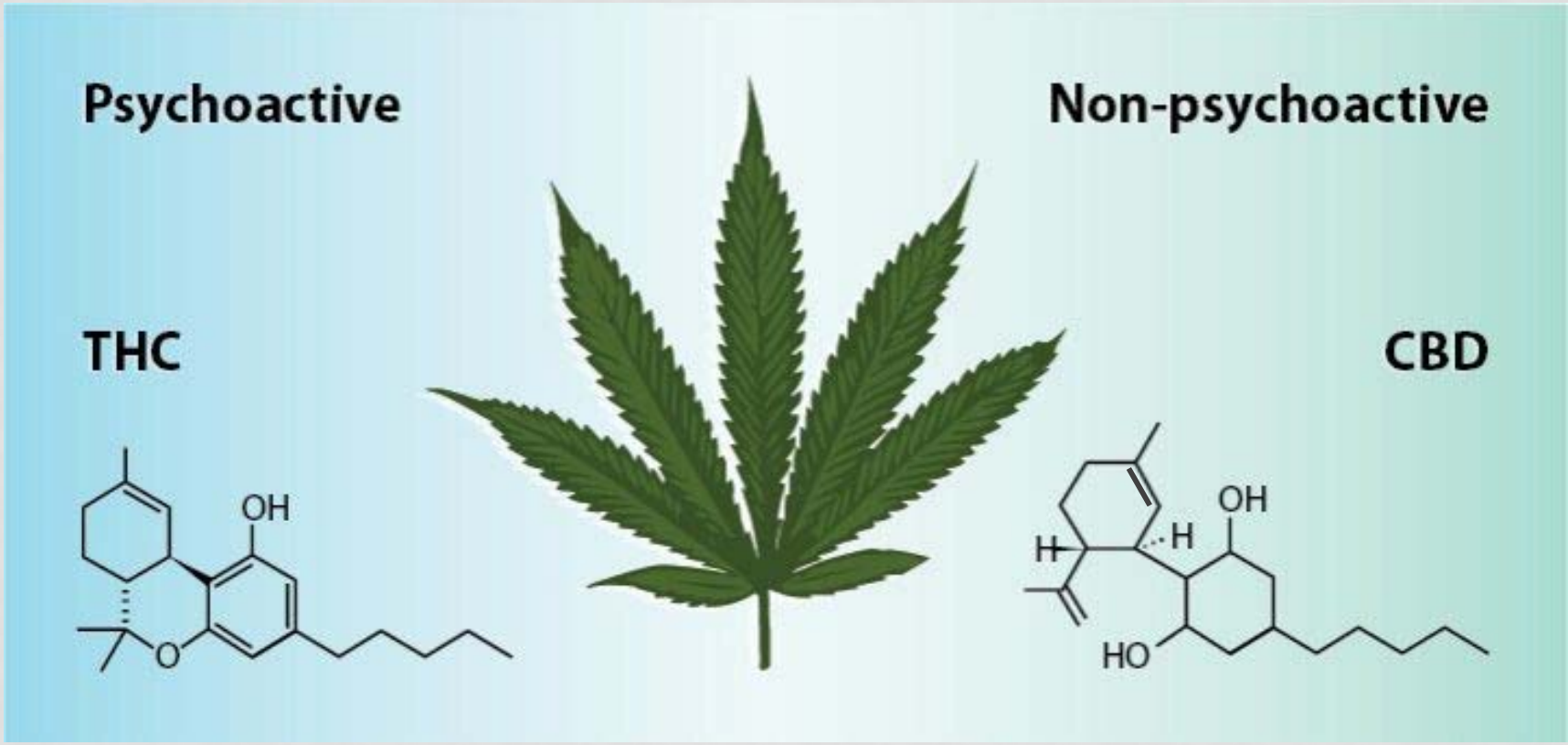
# BACKGROUND[4]

- The potency of marijuana varies from strain to strain
  - As low as 2-3% THC
  - As high as 30% THC
- Higher potency indicates that the patient will need a lower dose

# WHAT ARE CANNABINOIDS?[10]

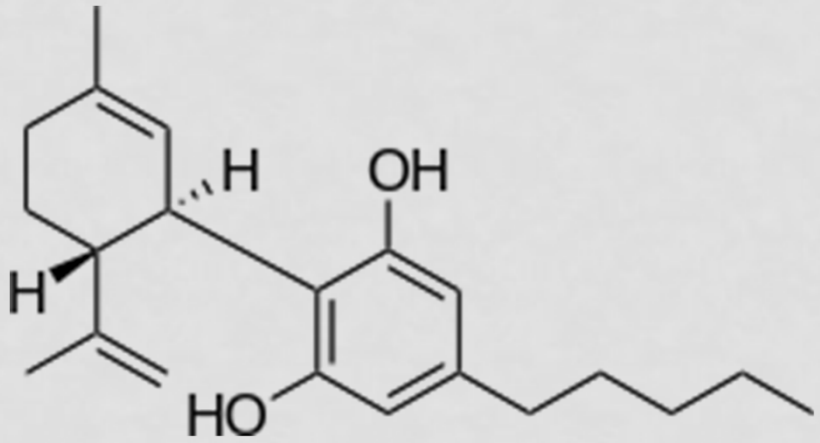
- Cannabinoids are chemicals that are related to the commonly known ingredient in marijuana known as THC (delta-9-tetrahydrocannabinol)
- Another cannabinoid of interest is CBD
- There are over 100 other cannabinoids other than THC that is found in marijuana
- Cannabinoids are similar to flavonoids that are found in chocolate

# WHAT ARE CANNABINOIDS?[10]



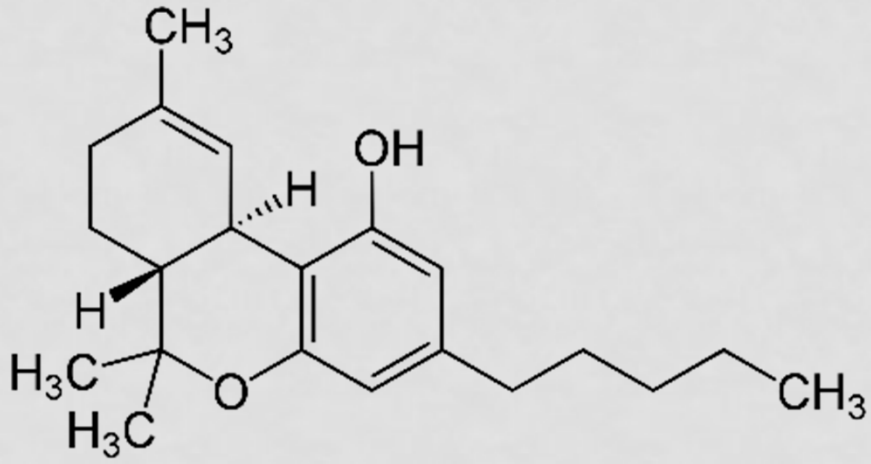
# WHAT IS CBD?[10]

- Cannabidiol (CBD) is a cannabinoid, but it is not psychoactive
- It is useful in reducing pain and inflammation, controlling epilepsy, and possibly treating anxiety and addictions
- Non-CB receptor mechanism



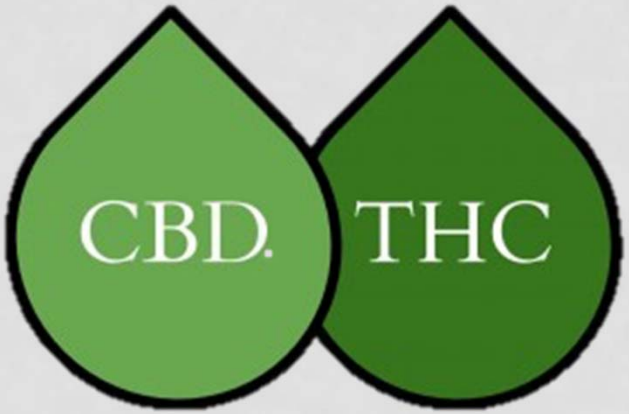
# WHAT IS THC?[10,11,31]

- Δ9-tetrahydrocannabinol (THC) is the psychoactive component of marijuana
- It is a potent antioxidant
- It is a partial agonist for the CB1 and CB2 receptors
- CB1 receptors regulate the release of other neurotransmitters



# WHAT IS THC?[10,11]

- THC increases appetite and reduces nausea
- THC may also decrease pain, inflammation, and muscle control problems
- The FDA has approved the use of synthetic THC for appetite and nausea reduction purposes



# FDA APPROVED CANNABINOIDS

## Dronabinol

**Brand names:** Marinol

**Class:** Synthetic THC


**Approved indications:** Chemotherapy-induced nausea and vomiting in patients who have failed previous treatments;
AIDS – loss of appetite

# FDA APPROVED CANNABINOIDS

## Nabilone

**Brand name:** Cesamet


**Class:** Synthetic THC Analogue

**Approved indications:** Chemotherapy-induced nausea and vomiting in patients who have failed previous treatments

# FDA APPROVED CANNABINOIDS

## Cannabidiol

**Brand name:** Epidiolex

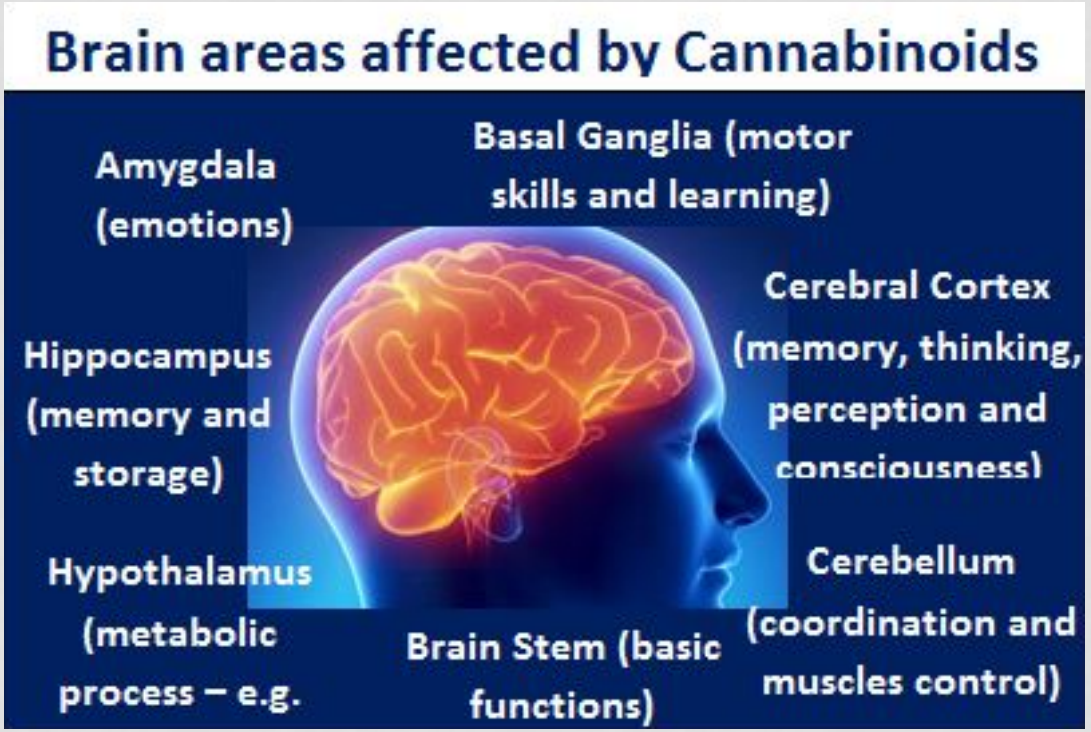
**Class:** Plant-derived CBD


**Approved indications:** Lennox-Gastaut syndrome, Dravet syndrome

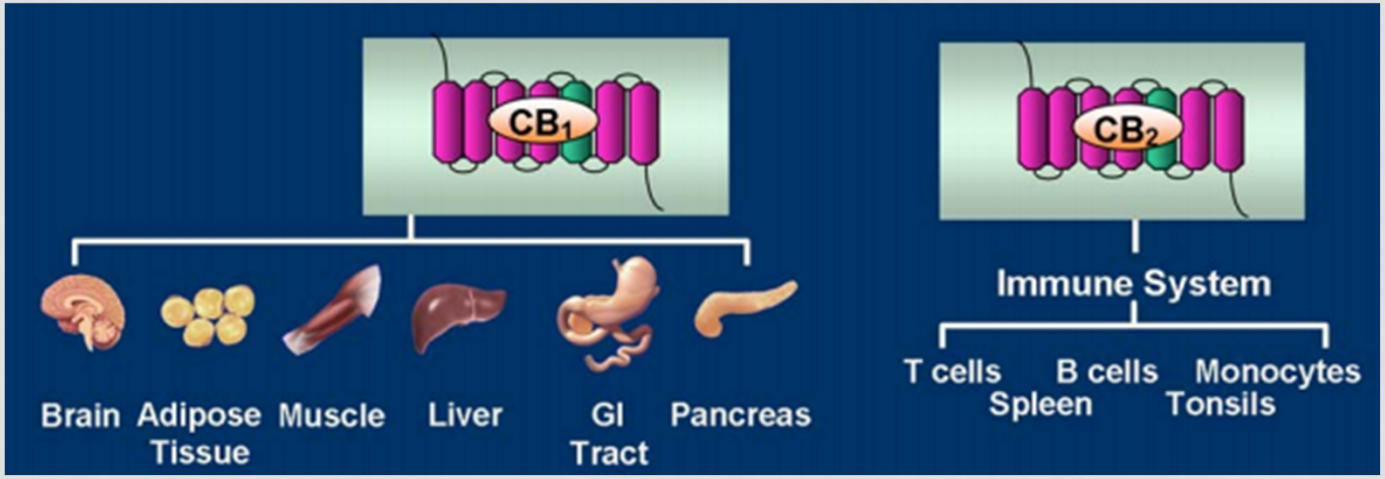
***Approved June, 2018**

# WHAT ARE CANNABINOIDS?[10]

- The body produces its own endocannabinoids that help to regulate the following:
  - Pleasure
  - Memory
  - Thinking
  - Concentration
  - Body movement
  - Awareness of Time
  - Appetite
  - Pain
  - Senses – taste, touch, smell, hearing, and sight



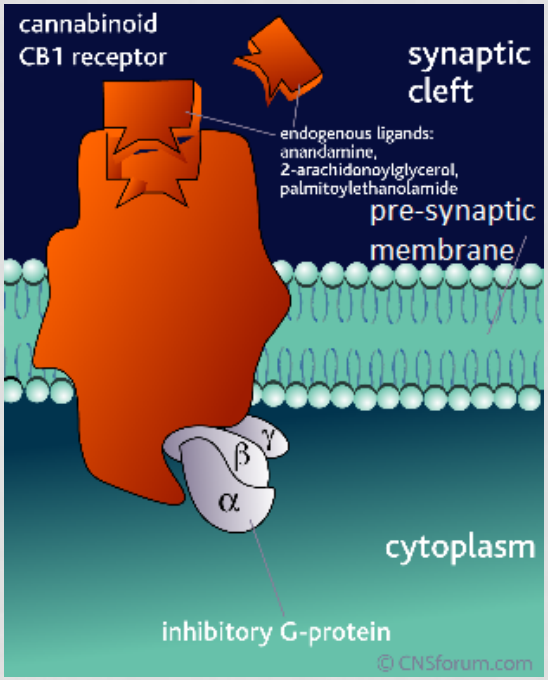
# CANNABINOID RECEPTORS[21-25]




- Receptors are $CB_1$ and $CB_2$
  - $CB_1$ - mostly expressed in the brain, but also found in peripheral nerves, circulating immune cells, adrenal gland, heart, lung, liver, bone marrow, and in reproductive tissues
  - $CB_2$ – mostly expressed in immune tissue
- $G_{i/o}$-protein coupled receptors
- **Only activated by THC – not CBD!**

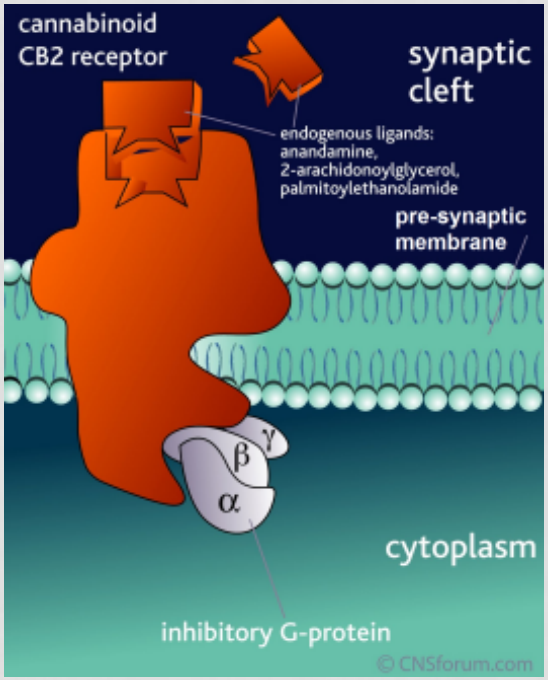
# $CB_1$ RECEPTOR[39]

- Located mainly in central and peripheral nervous system
- Effects of $CB_1$ are neuromodulatory
- Inhibits the release of neurotransmitters
  - Mainly Glutamate, GABA  in the brain
  - Also acetylcholine, norepinephrine, dopamine, serotonin, and D-aspartate



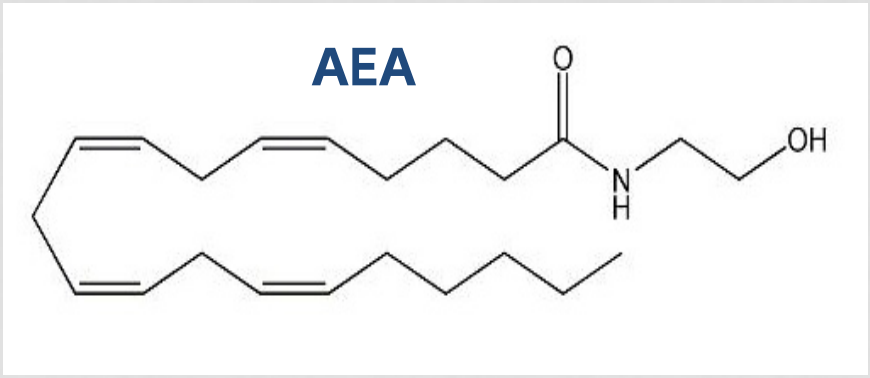
# $CB_2$ RECEPTOR[39]

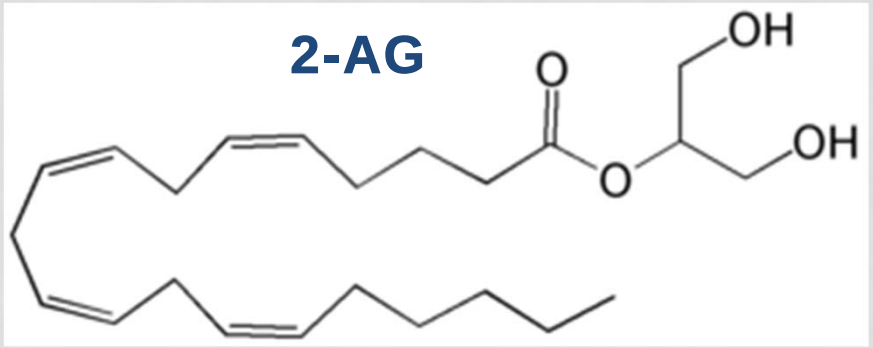
- Present mainly on peripheral tissues and central immune cells
- Activation of this receptor leads to:
  - Immunosuppression
  - Anti-inflammatory effects
  - Anti-nociceptive effects



# ENDOGENOUS CANNABINOIDS

- Ligands for CB1 and CB2
- Arachidonic acid derivatives:
- AEA: Anandamide
  - Relatively low levels in CNS, degraded by FAAH
- 2-AG: 2-arachidonoylglycerol
  - Widespread in the CNS

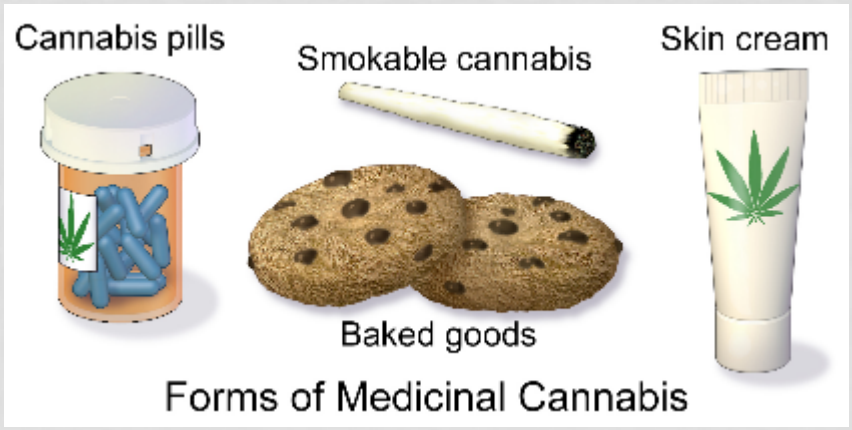


# PHARMACOKINETICS & PHARMACODYNAMICS

# FORMS OF MEDICAL MARIJUANA[2]

- Smoked – most common form
- Capsules
- Vaporization
- Edible form
- Transdermal
- Suppositories
- Liquid to drink



# HOW IS MARIJUANA USED?

| SMOKED | VAPORIZED | EATEN/DRUNK |
|---|---|---|
| Smoked in a pipe, bowl, cigarette | Inhaled through machine that converts active compounds into inhalable form | Consumed as ingredient in baked goods, candies, sodas, pill form |
| Rapid effects | Rapid effects | Takes time to reach brain, so effects are delayed |
| Releases toxins that can cause pulmonary problems | Does not release toxins that cause pulmonary problems | Does not release toxins that cause pulmonary problems |

# PHARMACOKINETICS OF CANNABIS[41]

- Cannabinoids are highly lipophilic and protein bound
- Rapidly distributed into tissues, especially BBB
  - Peak plasma concentration 3 min after smoking
- Volume of distribution (Vd) of THC = 10 L/kg
  - Blood concentrations are therefore not directly related to the drug effect
- The release from the lipid stores along with enterohepatic recirculation accounts for retention of THC

# ONSET AND DURATION OF CANNABIS

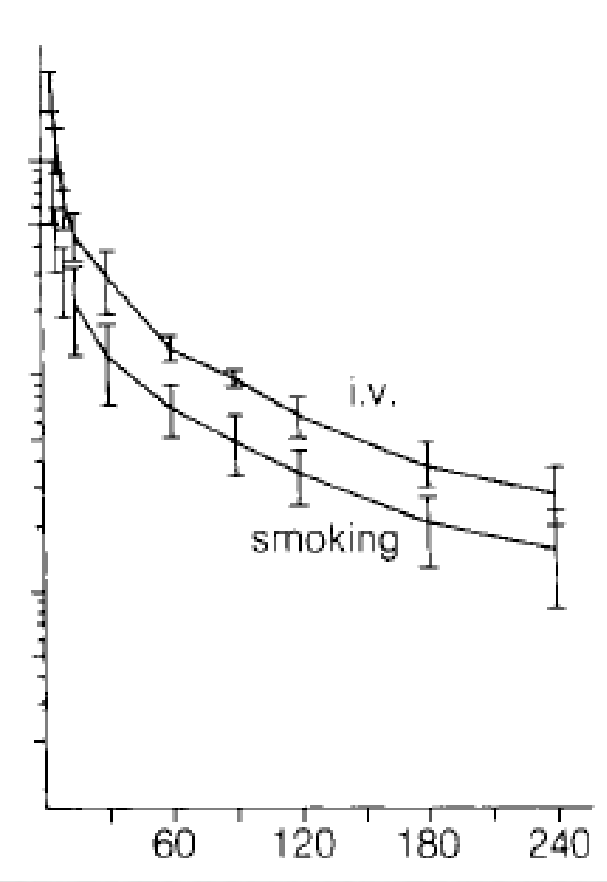
- Physical and psychosocial effects commence within minutes after use
  - Usually within 15 minutes
  - Peak effects occur within 30 minutes to 60 minutes post-smoking and last 2-4 hours
- Psychosocial effects can stay for up to 4 to 8 hours depending upon route of administration
  - Oral has a slower onset, but longer duration

# PSYCHOSOCIAL EFFECTS

- Effects do not depend on blood concentration
  - Depends partially on the dose
- Effects are dose-dependent and route-dependent
  - Lower dose effects: euphoria, relaxation, wide range from exhilaration to introspection, distortion of time and some visual hallucinations, memory distortions (especially short-term memory), hunger
  - Higher dose effects: anxiety, tension, anger, confusion, hallucinations, paranoia, and panic attacks

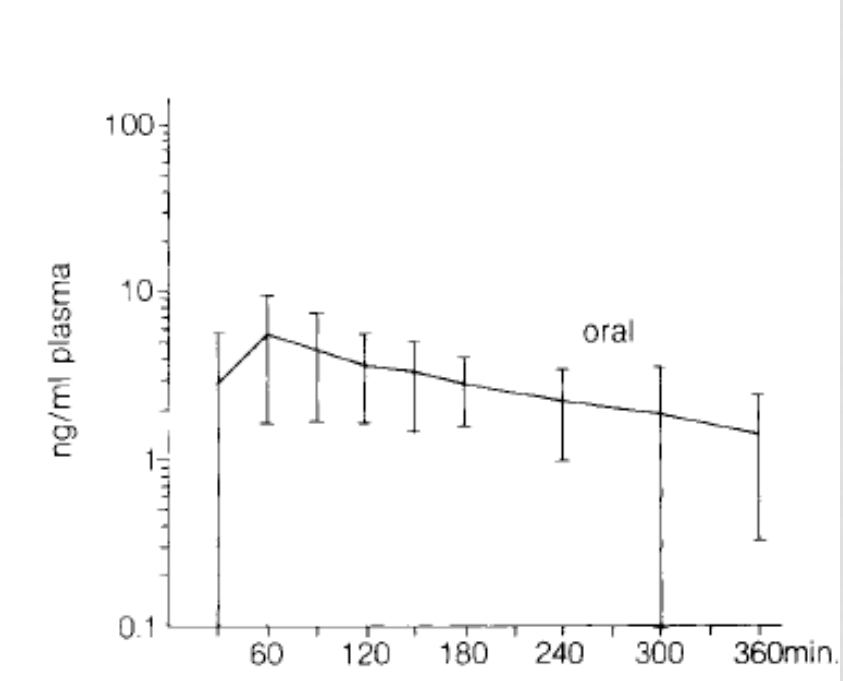
# PHARMACOKINETICS OF SMOKING THC[31]

- Bioavailability: 10-25%
  - 50% of the THC content is delivered into smoke
  - 50% of smoke is exhaled again
    - 60% of inhaled smoke may be metabolized by the lung
- Peak concentrations are reached within 2-10 minutes
- $T_{1/2}$ distribution: 0.5hr
- $T_{1/2}$ elimination: 30hr
- Smoking THC mimics IV



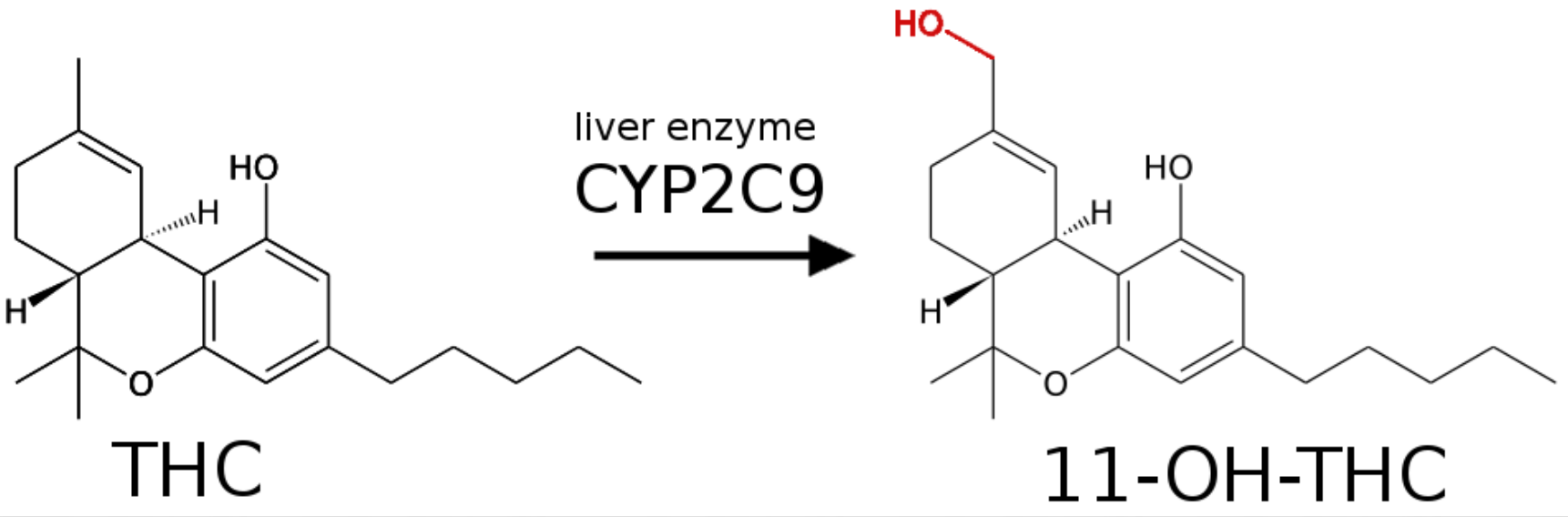
# PHARMACOKINETICS OF ORAL THC[31]

- Bioavailability: 6-20%
  - Usually 1/3 of that smoked due to gastric degradation and extensive first pass metabolism effects
  - High patient variability
    - Can lead to increased toxicities because delayed effect
- Multiple low peak concentrations in 1-6hr
- $T_{1/2}$ absorption: 0.8hr
- $T_{1/2}$ distribution: 3.8hr
- $T_{1/2}$ elimination: 25hr



# METABOLISM OF THC[43]

- 9Δ-THC is converted to 11-OH-THC, a potent psychoactive metabolite
  - Rapid conversion in oral administration via first-pass metabolism



# METABOLISM OF THC[44,45,46]

- THC metabolized by CYP3A4 and CYP2C9
- CBD metabolized by CYP3A4 and CYP2C19

- CBD has been shown to inhibit CYPs 3A4 and 2D6
- THC may induce CYP1A2
  - Only demonstrated *in vitro* - limited clinical data

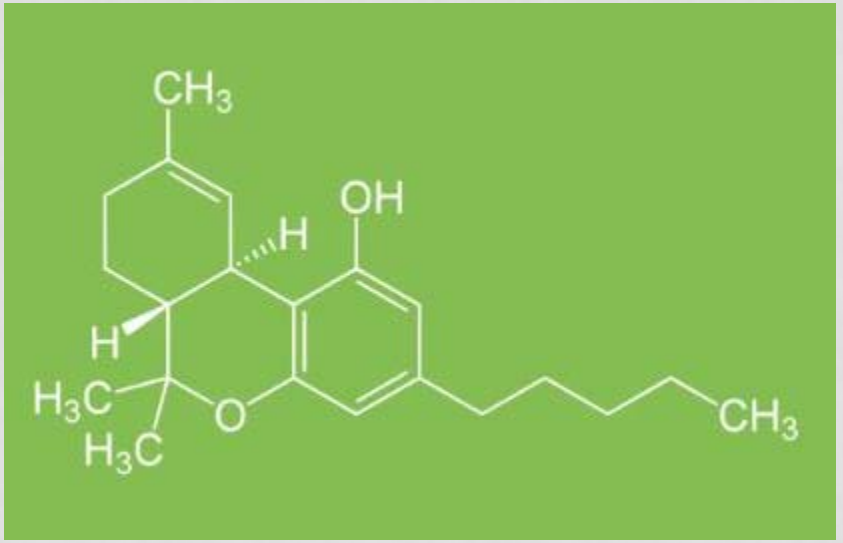
# PHARMACOKINETICS OF CANNABIS

- THC can be detected in urine for days after use
- Terminal half-life up to 4 days in frequent users

- Passive inhalation – "second-hand high" requires very high concentrations of smoke in a small enclosed area
  - Very unlikely

# DOSE OF THC[31]

- Effective dosing of THC
  - Low dose: <7 mg
  - Medium dose: 7-18mg
  - High dose: >18mg
- Tolerance to THC exists via the down-regulation of the CB1 receptors
  - High tolerance occurs with chronic use
  - Low tolerance occurs with intermittent use

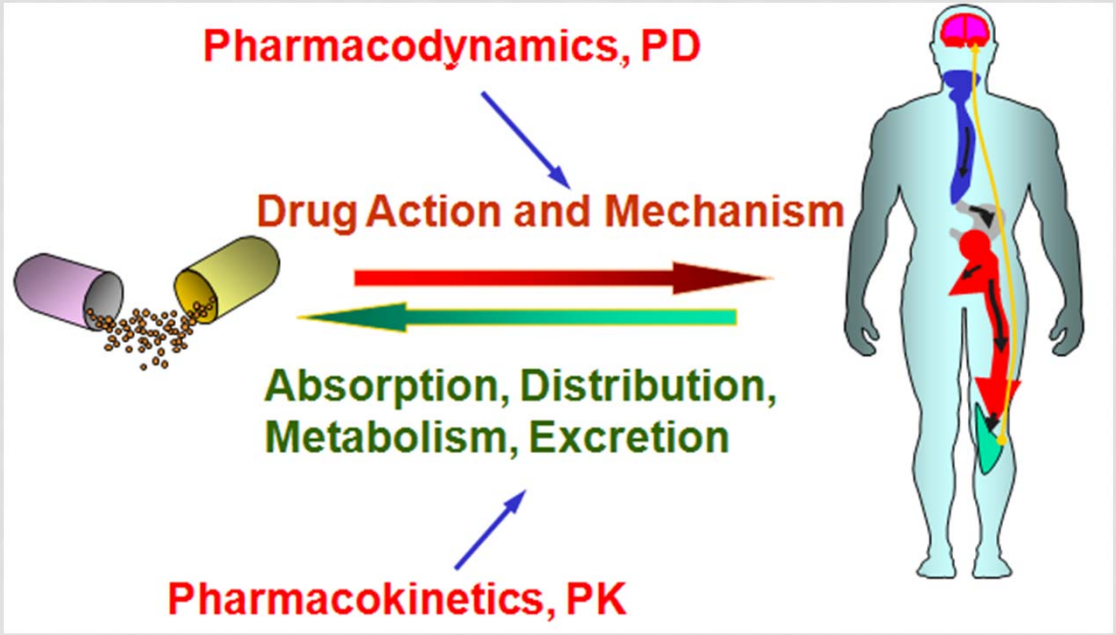


# VAPORIZATION

- Cannabinoids vaporize at a temperature lower than combustion
- Results in lower percent of noxious chemicals

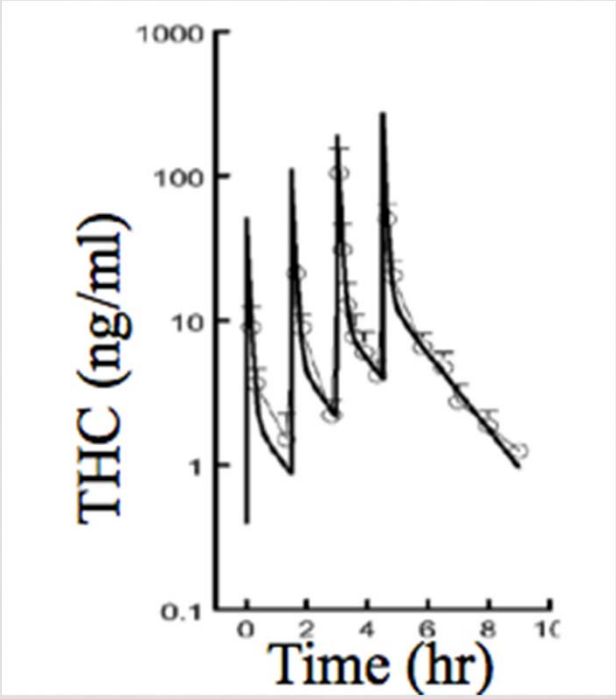
# PHARMACODYNAMICS OF THC[32]

- Elevation in heart rate: average >19bpm
- Increase in subjective feeling high
- Decrease in subjective alertness
- Increase in motor instability – body sway

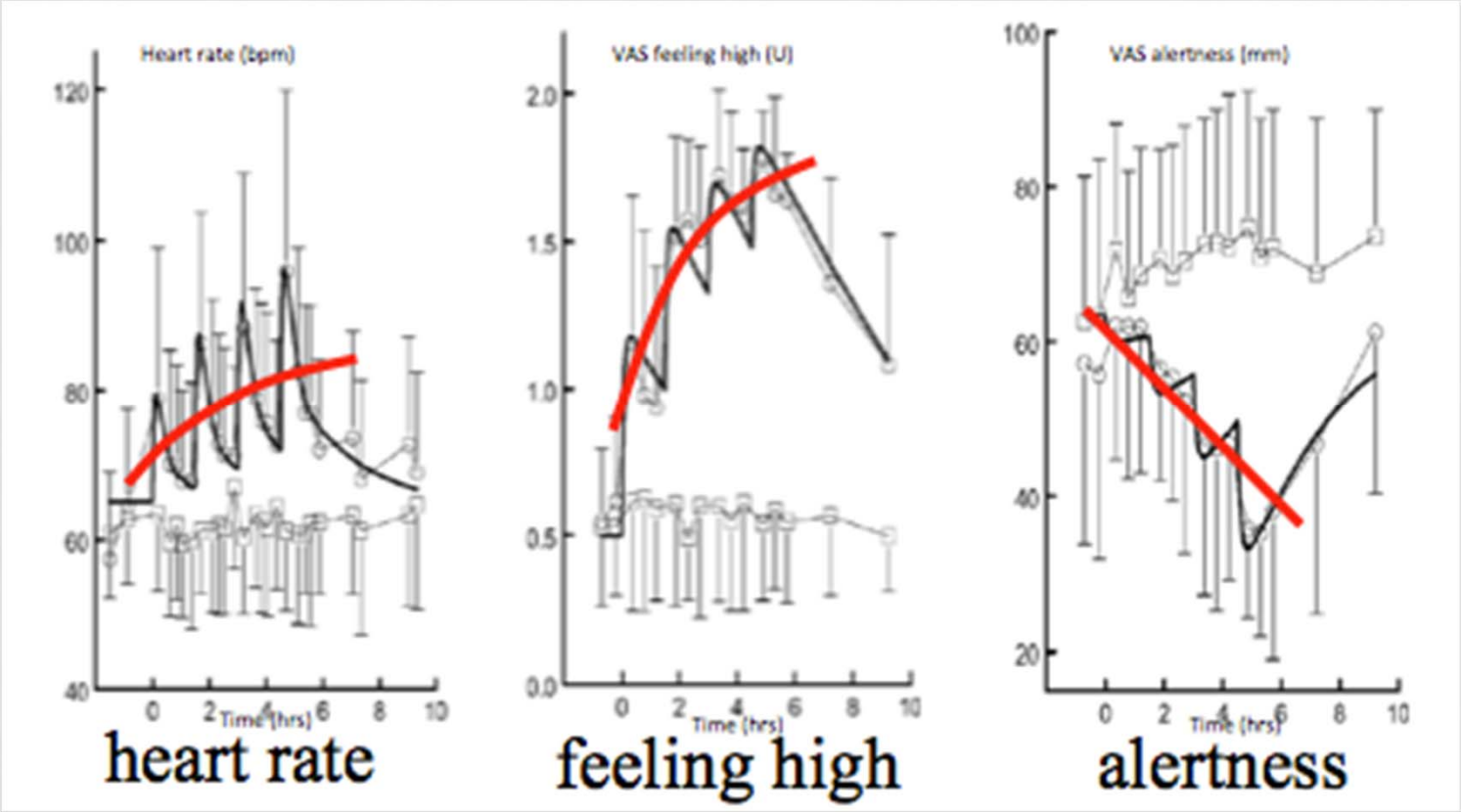


# PK/PD MODEL OF THC[32]

- In study by Zuuman et al, subjects were given increasing doses (2, 4, 6, 8mg) of THC via vaporizer at 1.5hr intervals



# PK/PD MODEL OF THC[32]



# MEDICAL CANNABIS IMPACT ON HORMONES

- Males:
  - Decreases luteinizing hormone (LH)
  - Decreases follicle stimulating hormone (FSH)
  - Decreased Prolactin
  - Decreased growth hormone (GH)

VE SLIDE

- Females: More sensitive than males to THC effects
  - More estrogen suppression

# MARIJUANA EFFECTS ON THE BRAIN

# MARIJUANA EFFECTS ON THE BRAIN

- **Hypothalamus**: increased appetite
- **Brain stem**: nausea relief, lowered blood pressure, drowsiness, decreased pain, decreased spasticity, and decreased tremor
- **Hippocampus**: memory impairment

# MARIJUANA EFFECTS ON THE BRAIN

- **Cerebral cortex**: altered consciousness, perceptual distortions, memory impairment, delusions, hallucinations
- **Cerebellum**: loss of coordination
- **Amygdala**: changes in anxiety, pain attacks, lowered traumatic memories, decreased hostility

# USES OF MEDICAL MARIJUANA

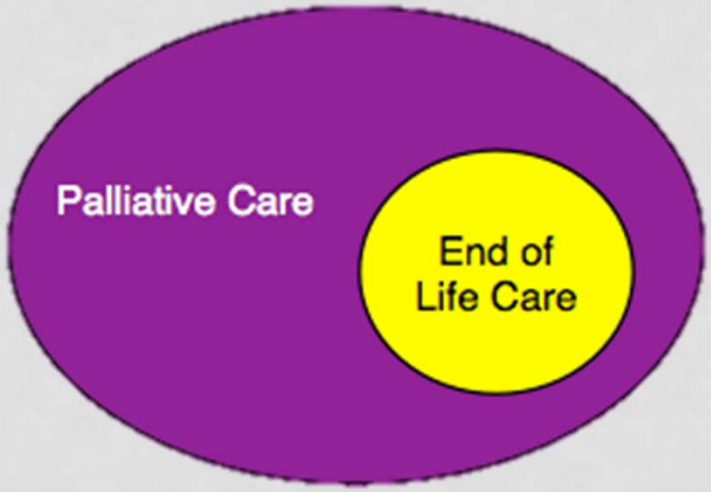
# QUALIFYING MEDICAL CONDITIONS[3]

## Varies by state – e.g. in Michigan:

- **Severe and chronic pain**
- **Severe and persistent muscle spasms**
  - **Ex. MS**
- Alzheimer's Disease
- Amyotrophic lateral sclerosis (ALS)
- Cachexia C
- Crohn's Disease
- Cancer
- Glaucoma
- HIV/AIDs
- Hepatitis C
- Seizures, epilepsy
- Nail-patella syndrome
- PTSD
- Severe nausea

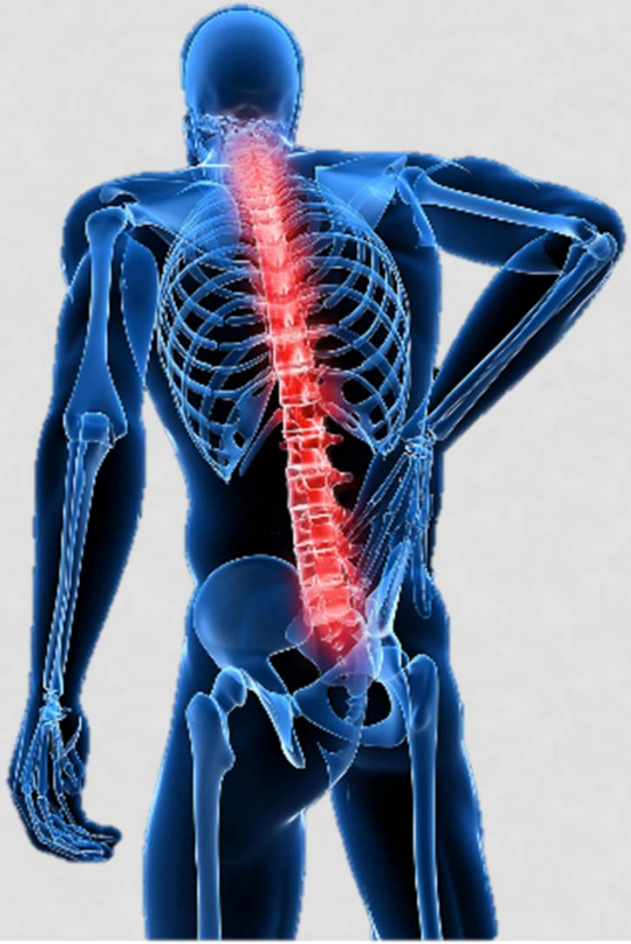
# MEDICAL MARIJUANA AND PALLIATIVE CARE

- Medical marijuana is centered on palliative care — improving quality life of patients and families in order to mitigate suffering



# SEVERE AND CHRONIC PAIN[26]

- Medical marijuana is primarily good at relieving pain
- Components of pain that may respond to cannabis:
  - Neuropathic – burning, piercing
  - Mechanical – dull, aching
  - Inflammatory – acute, sharp



# 2009 META ANALYSIS FOR PAIN[41]

- 18 double-blind RCTs (N=2,838) plant-based preparations or nabilone to placebo in treating any type of chronic pain
- Results: significant reduction in pain
  - Standardized mean difference: **-0.61** (95% CI -.84, -.37)
- Side effects:
  - Mood disturbances (OR 4.11)
  - Alterations in perception (OR 4.51)
  - Affected motor function (OR 3.93)
  - Altered cognitive function (OR 4.46)
- Authors' conclusion: cannabis may offer moderate efficacy for treatment of chronic pain

# 2015 META ANALYSIS FOR PAIN[47]

- 28 double-blind RCTs (N=2,454) comparing any cannabis preparation to placebo in treating any type of chronic pain
- Results: not statistically significant
  - ≥ 30% reduction in pain: **OR 1.41** (95% CI 0.99, 2.00)
  - Mean difference from placebo: **-0.46** (95% CI -.8, -.11) on a numerical 0-10 pain scale
- Authors' conclusion: modest-quality evidence to support the use of cannabinoids to treat chronic pain

- The majority of studies had a high risk of bias

# CHRONIC PAIN CONDITIONS[26]

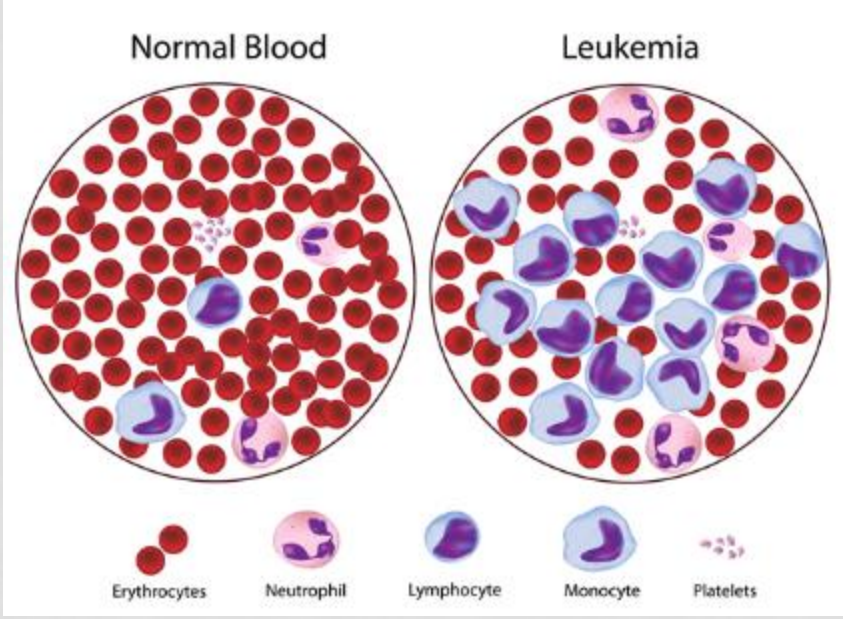
- Some chronic pain conditions that marijuana may help regulate:
  - Myofascial pain syndrome (MPS)
  - Central pain syndrome (CPS)
  - Spinal cord injury
  - Fibromyalgia
  - Osteoarthritis (OA)
  - Rheumatoid Arthritis (RA)
  - HIV Neuropathy

# MIGRAINES[8]

- Marijuana has ability to:
  - Decrease pain signaling nuerotransmitters
  - Modulate serotonergic receptor subtypes
  - Inhibit glutamatergic-mediated toxicities
  - Provide anti-inflammatory activity
  - Provide acute symptomatic and chronic preventative relief

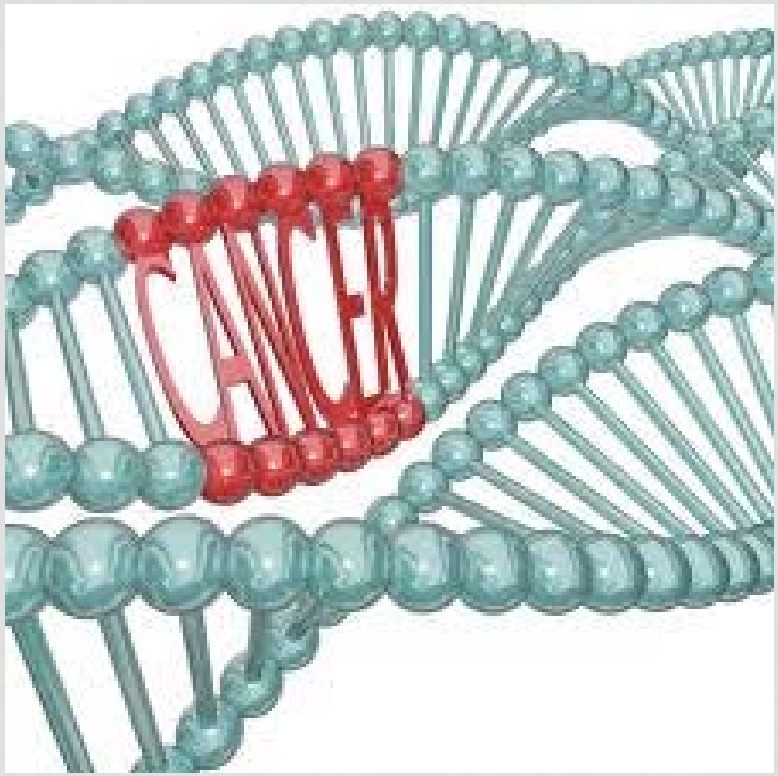
# CANCER[47]

- THC and CBD have anti-tumor properties
  - Preclinical data only
  - Glioblastoma, leukemia, lung, brain, and others
- Exact mechanism of action is unknown
- Proposed mechanisms:
  - CB1 and CB2 agonism modulates ERK, p38 MAPK, and JNK1/2
  - CBD production of ROS, activation of specific receptors



# CANCER[7]

- Benefits
  - Inhibits chemotherapy-induced nausea and vomiting
  - Appetite stimulation
  - Pain inhibition
- Has favorable drug-safety profile and does not produce the conventional side effects of chemotherapy drugs
- No clinical efficacy data for treating cancer in humans



# CANCER ANALGESIA[43]

- Oral THC – two small studies (n=10, n=36)
  - Doses of 10, 15, 20mg were studied
  - 10 and 20mg of THC were equivalent to 60 and 120mg of codeine for analgesia
  - High-dose THC was more sedative than codeine
- THC:CBD oromucosal spray RCT
  - Patients who's pain was not controlled by strong opioids
  - THC:CBD was efficacious in managing cancer pain

# HIV/AIDS

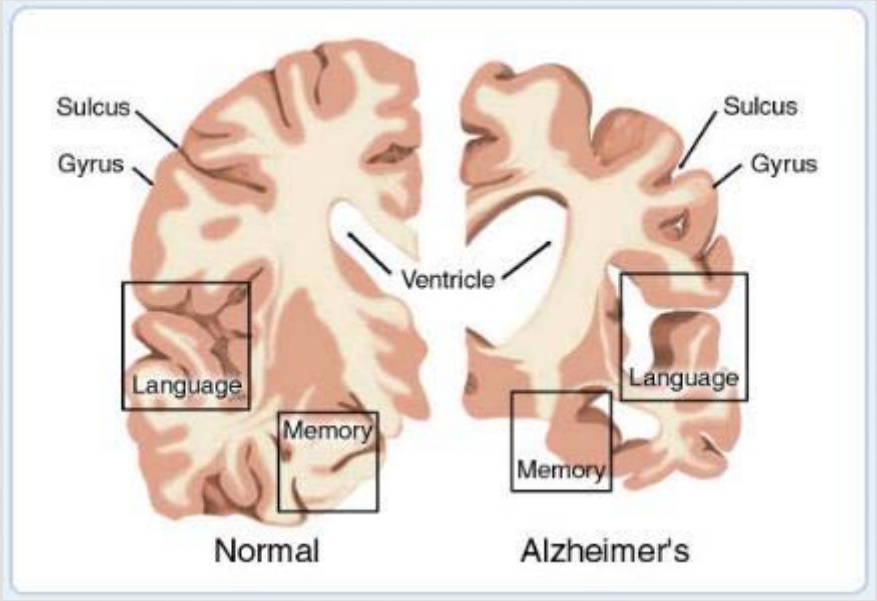
- Marijuana used as an appetite enhancer and pain-relieving medication in HIV-infected patients
- Also can be used for the following in these patients
  - Sleep/relaxation
  - Prevent nausea/vomiting
  - Pain
  - Anxiety/depression
  - Stimulation/energy

# HIV / AIDS[6]

- Study assessed if smoked cannabis is effective as an analgesic in HIV-associated distal sensory polyneuropathy
- It was found that pain relief was greater with cannabis compared to the placebo

# ALZHEIMER'S DISEASE[11]

- CBD reduced neuronal degeneration in rats
- THC can revert memory impairment and of β-amyloid plaque formation in mice
- CBD prevented development of tangles and plaques in mesenchymal  stem cells

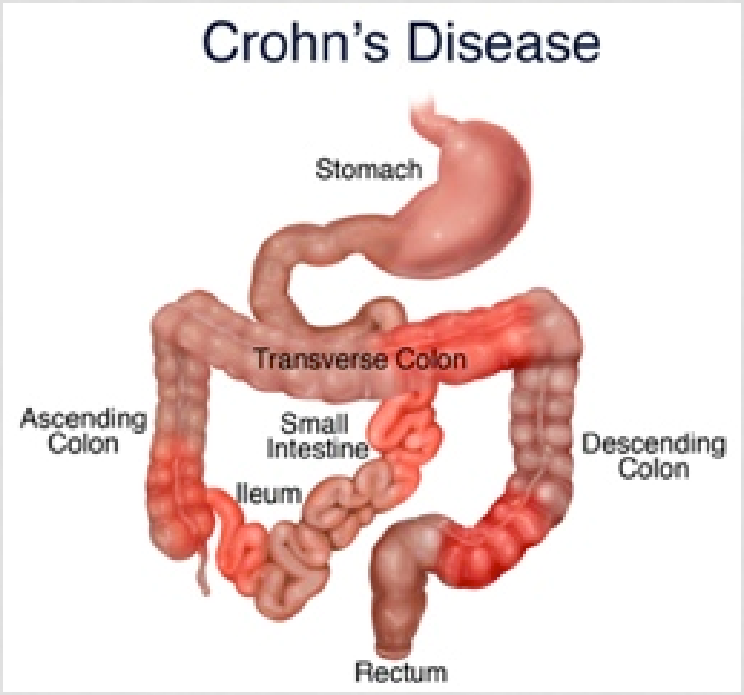


# AMYOTROPHIC LATERAL SCLEROSIS (ALS)[15, 16]

- ALS is a neurodegenerative disease that affects the nerve cells in the brain and the spinal cord
- Medical marijuana helps to manage symptoms of ALS by causing the following:
  - Pain relief
  - Muscle relaxation
  - Dilation of the lungs
  - Improved sleep
  - Appetite stimulation
  - Antioxidant and neuroprotective effects to help prolong neuronal cell survival

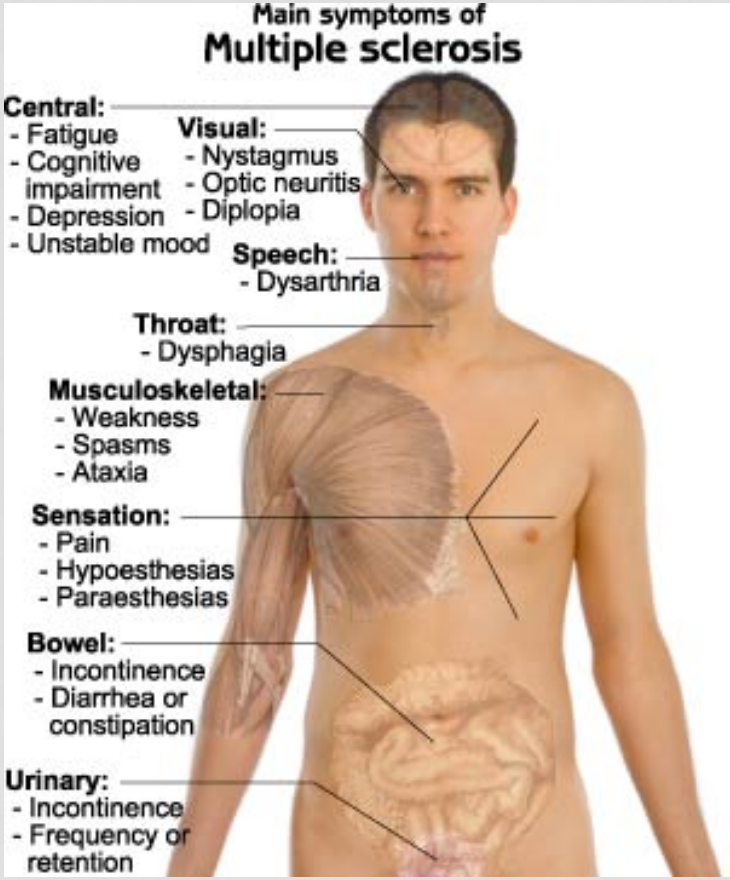
# CROHN'S DISEASE[18]

- Medical marijuana is useful in Crohn's disease for:
  - Easing pain
  - Limiting frequency of diarrhea
  - Helped with weight gain
- Results of a study concluded that more studies need to be conducted with a larger population to further test the result of marijuana as a pharmacotherapy for Crohn's disease



# MULTIPLE SCLEROSIS (MS)[27]

- Cannabinoids probably help to relieve severe and persistent muscle spasms/contractions
- Also may provide neuroprotective and anti-inflammatory effects
- Neuroinflammation reduced through regulation of cytokine levels in microglial cells
- Short-term therapy has been seen to be effective, but further studies need to be conducted to assess long-term treatment



# MULTIPLE SCLEROSIS (MS)[48]

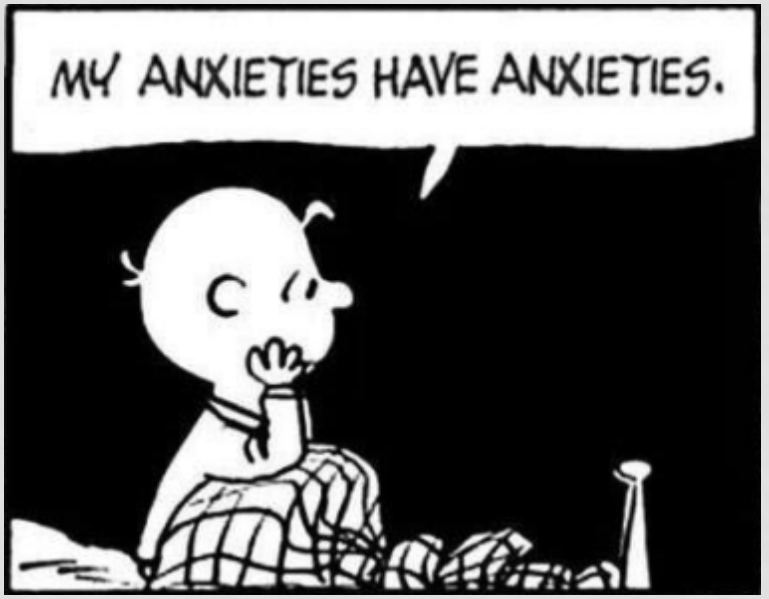
- 2018 Review by Rice J et al.
- Strongest evidence to indicate cannabinoid are beneficial for muscle spasticity and neuropathic pain in MS
- Best dose unknown, but most studies used 20-40mg THC in divided doses
- Need more high quality studies!!!

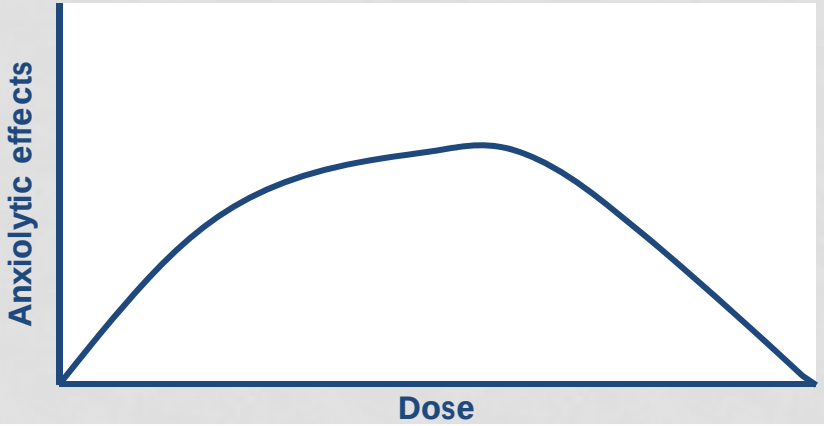
# ANXIETY

- Natural endocannabinoid system regulates anxiety
  - Inhibits excitatory signals that involve glutamate and NMDA
- Chronic and acute stress results in the reduction of endocannabinoids and the responsiveness of the receptors
  - Treatment with medical marijuana helps to increase these levels to relieve the anxiety due to stress

# ANXIETY[48]

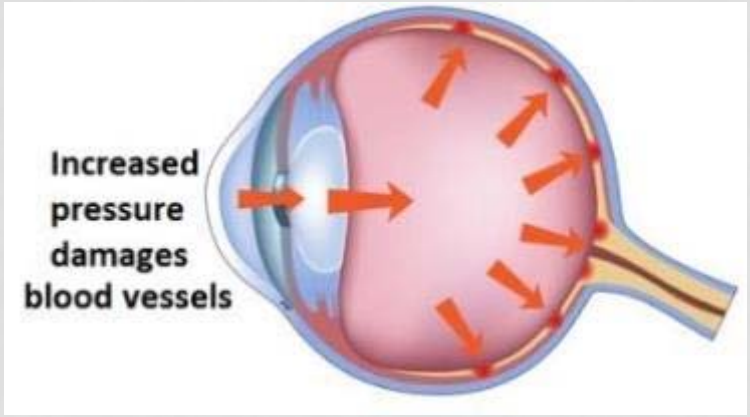
- Human and animal studies have shown that CB1 receptor agonists are:
- Anxiolytic at low doses
  - Also produce euphoria, relaxation, heightened perception, sociability and creativity
- Anxiety-inducing at high doses
  - Also elicit phobia, agitation, panic, dysphoria, psychotic manifestations and cognitive impairments
- Inverse U dose-response



# GLAUCOMA[49]

- CB1 and CB2 receptors are found in the retina and multiple other eye tissues
- 2-AG and AEA are found at high levels in the eye
- THC & nabilone lower IOP
- Neuromudulatory effect of CB1 and CB2 activation may decrease IOP, neuroprotective properties may help with optic nerve



# GLAUCOMA[50]

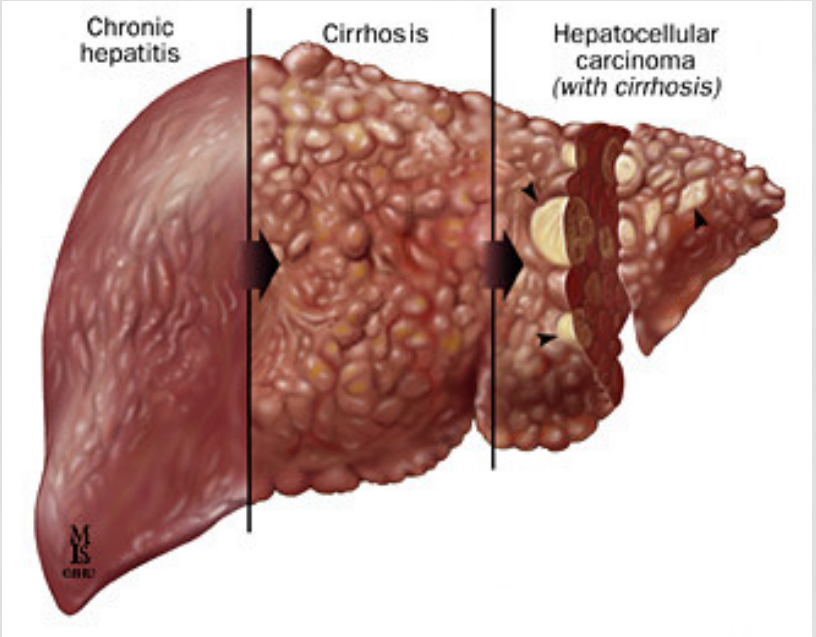
- Problems:
  - Effects are transient, requiring frequent dosing
  - Tolerance to effects after repeat dosing
  - Lack of recent, well-controlled human clinical studies

# GLAUCOMA[19]

- A topical formulation would be the ideal form of application
  - Difficult because eye drop form only results in <5% of penetration of the drug according to a study
  - Delivery of medication needs to be refined

# HEPATITIS C[20]

- Medical marijuana used for Hepatitis C patients to for the following:
  - Nausea
  - Moderation of chronic liver disease
  - Reducing inflammation



# EPILEPSY

- https://www-ncbi-nlm-nih-gov.proxy.lib.umich.edu/pubmed/29768152
- https://www-ncbi-nlm-nih-gov.proxy.lib.umich.edu/pubmed/28188044
- https://www-ncbi-nlm-nih-gov.proxy.lib.umich.edu/pubmed/29115760
- https://www-ncbi-nlm-nih-gov.proxy.lib.umich.edu/pubmed/29061872

# CHILDREN[13]

- Children are not the first age group to be considered for medical marijuana
- A use of medical marijuana in children is the treatment of severe seizures
  - The oil of the cannabis is extracted and used for treatment
- The long-term effects of early marijuana use in children is not known

# ADVERSE EVENTS OF MEDICAL MARIJUANA

# ADVERSE EVENTS ASSOCIATED WITH MARIJUANA USE[17]

- Chronically smoking marijuana use may cause the following adverse events:
  - Dependence
  - Withdrawal
    - Irritability, depression, insomnia, nausea, obstructive pulmonary disease (COPD), and lung cancer
- Using a vaporizer opposed to smoking may diminish the level of the more toxic components in marijuana
  - Smoking marijuana contains 4 times more tar and 50% more carcinogens than that of tobacco

# DETRIMENTAL EFFECTS OF SMOKING[34,35]

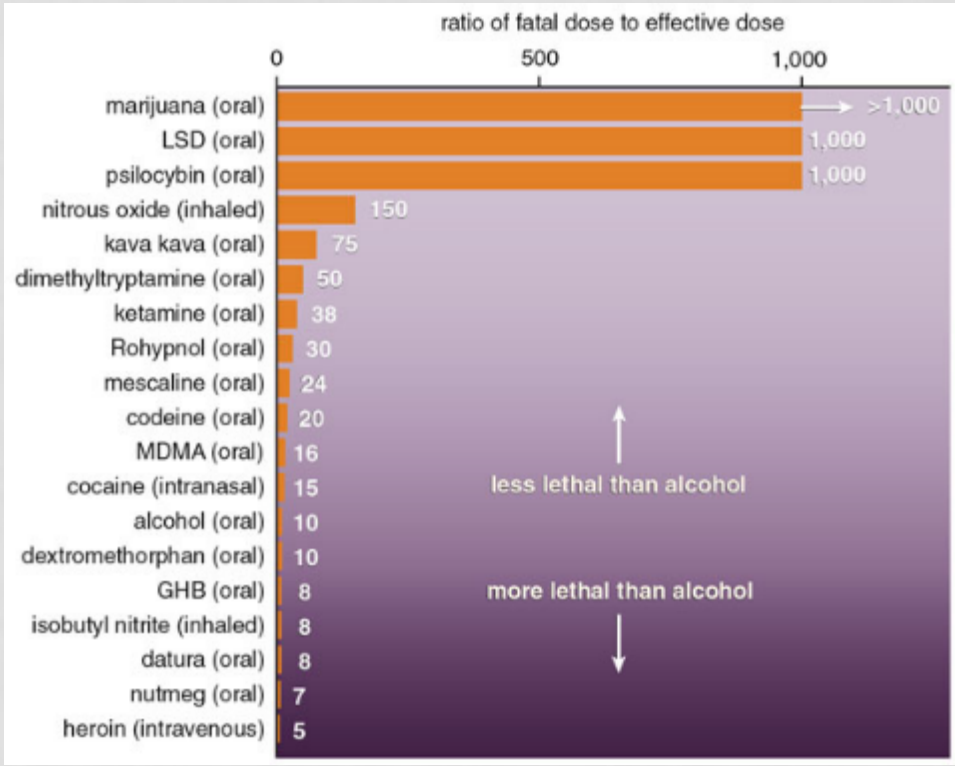
- Can lead to respiratory illness
  - One marijuana cigarette causes as many pulmonary problems as 4-10 tobacco cigarettes
  - Increase risk for bronchitis, emphysema, lung cancer
- Can cause cardiovascular complications
  - Raises blood pressure and heart rate 20-100%
  - 4.8 times risk of hear attack in hour after use

# EFFECTS IN PREGNANCY[36]

- Increasing evidence that prenatal exposure can lead to:
  - Increased risk of motor, social, and cognitive disturbances
  - Higher rate of low birth weight in infants and childhood leukemia
- Marijuana has been found in breast milk
  - Avoid when breastfeeding

# ACUTE TOXICITIES[33]

- Medical marijuana is less lethal than alcohol and many illicit drugs



# TOXICOLOGY OF CANNABIS

- Has wide therapeutic index
- No known direct deaths
  - Implied association with deaths due to underlying health conditions especially arrhythmias/heart attacks
- Fatal dose is unknown, but implied from animal studies that may be 4000 to 40000 times the highest recreational dose

# 2017 NATIONAL ACADEMIES OF SCIENCES REPORT

# 2017 NATIONAL ACADEMIES OF SCIENCES REPORT

- Goal: to develop a comprehensive, in-depth review of existing evidence regarding the health effects (harms and benefits) of cannabis and cannabinoids use
  - Make short and long-term recommendation regarding research agenda to identify the most critical research and advance the cannabis and cannabinoid research agenda

# 2017 NATIONAL ACADEMIES OF SCIENCES REPORT

- Between June and December 2016, a committee held 5 in-person meetings and 1 virtual meeting
- Conducted an extensive search of relevant databases
  - 24,000 articles found
  - Committee considered more than 10,000 abstracts to determine relevance for the report

# 2017 NATIONAL ACADEMIES OF SCIENCES REPORT

- 11 prioritized end-points
  - Therapeutic effects
  - Cancer incidence
  - Cardiometabolic risk
  - Respiratory disease
  - Immune function
  - Injury and death
  - Prenatal, perinatal, and postnatal outcomes
  - Psychosocial outcomes
  - Mental health
  - Problem cannabis use
  - Cannabis use and abuse of other substance

# THERAPEUTICS

- In adults with chemotherapy induced nausea and vomiting, oral cannabinoids are effective antiemetics
- In adults with chronic pain, patients who were treated with cannabis or cannabinoids are more likely to experience clinically significant reduction in pain symptoms

# THERAPEUTICS

- In adults with MS related spasticity, short-term use of oral cannabinoids improves patient-reported spasticity symptoms

- For these condition, the effects of cannabinoids are modest; for all other conditions evaluated there is inadequate information to assess their effects

# RESPIRATORY DISEASE

- Substantial evidence of a statistical association between long-term cannabis smoking and worse respiratory symptoms and more frequent chronic bronchitis episodes

- Moderate evidence of a statistical association between cannabis smoking and improved airway dynamics with acute use, but not with chronic use

# RESPIRATORY DISEASE

- Moderate evidence of a statistical association between cannabis smoking and higher forced vital capacity (FVC)
- Moderate evidence of a statistical association between cessation of cannabis smoking and improvements in respiratory symptoms

# RESPIRATORY DISEASE

- Limited evidence of a statistical association between occasional cannabis smoking and an increased risk of COPD when controlled for tobacco use
- Insufficient evidence to support or refute a statistical association between smoking cannabis and hospital admissions for COPD
- Insufficient evidence to support or refute a statistical association between cannabis smoking and asthma development or exacerbation

# INJURY AND DEATH

- Cannabis use prior to driving increases the risk of being involved in a motor vehicle accident
- In states where cannabis is legal, there is increased risk of unintentional cannabis overdose injuries among children
- Unclear whether and how cannabis use is associated with all-cause mortality or with occupational injury

# CANCER

- Moderate evidence of **no** statistical association between cannabis smoking and the incidence of lung cancer
- Moderate evidence of **no** statistical association between cannabis use and the incidence of head and neck cancers
- Limited evidence of a statistical association between current, frequent, or chronic cannabis smoking and non-seminoma-type testicular germ cell tumors

# CANCER

- Insufficient evidence to support or refute a statistical association between cannabis smoking and the incidence of esophageal cancer

- Insufficient evidence to support tor refute a statistical association between cannabis use and the incidence of prostate cancer, cervical cancer, malignant gliomas, non-Hodgkin lymphoma, penile cancer, anal cancer, Kaposi's sarcoma, or bladder cancer

# CANCER

- Insufficient evidence to support or refute a statistical association between parental cannabis use and subsequent risk of developing AML/acute non-acute lymphoblastic leukemia, ALL, rhabdomyosarcoma, astrocytoma, or neuroblastoma in offspring

# CARDIOMETABOLIC RISK

- Evidence is unclear as to whether and how cannabis use is associated with heart attack, stroke, and diabetes

# IMMUNITY

- There exists a paucity of data on the effects of cannabis or cannabinoid-based therapeutics on the human immune system
- There is insufficient data to draw overarching conclusions concerning the effects of cannabis smoke or cannabinoids on immune competence

# IMMUNITY

- There is limited evidence to suggest that regular exposure to cannabis smoke may have anti-inflammatory activity
- Insufficient evidence to support or refute a statistical association between cannabis or cannabinoid use and adverse effects on immune status in individuals with HIV

# PRENATAL, PERINATAL, AND NEONATAL OUTCOMES

- Smoking cannabis during pregnancy is linked to lower birth weight in the infant
- The relationship between smoking cannabis during pregnancy and other pregnancy and childhood outcomes is unclear

# PSYCHOSOCIAL

- Recent cannabis use impairs the performance in cognitive domains of learning, memory and attention
  - Recent use may be defined as cannabis use within 24 hours of evaluation
- A limited number of studies suggest that there are impairments in cognitive domains of learning, memory, and attention in individuals who have stopped smoking cannabis

# PSYCHOSOCIAL

- Cannabis use during adolescence is related to impairments in subsequent academic achievement and education, employment and income, and social relationship and social roles

# MENTAL HEALTH

- Substantial evidence of a statistical association between cannabis use and the development of schizophrenia or other psychoses, with the highest risk among the most frequent users

- In individuals with schizophrenia and other psychoses, a history of cannabis use may be linked to better performance on learning and memory tasks

# MENTAL HEALTH

- Cannabis use does not appear to increase the likelihood of developing depression, anxiety, and PTSD

- For individuals diagnosed with bipolar disorders, near daily cannabis use may be linked to greater symptoms of bipolar disorder than non-users

# MENTAL HEALTH

- Heavy cannabis users are more likely to report thoughts of suicide than non-users
- Regular cannabis use is likely to increase the risk for developing social anxiety disorder

# PROBLEM CANNABIS USE

- Greater frequency of cannabis use increases the likelihood of developing problem cannabis use
- Initiating cannabis use at younger age increase the likelihood of developing problem cannabis use

# CANNABIS USE AND ABUSE OF OTHER SUBSTANCES

- Limited evidence of a statistical association between cannabis use and the initiation of tobacco use

- Limited evidence of a statistical association between cannabis use and changes in the rates and use pattern of other illicit and illicit substances

# CANNABIS USE AND ABUSE OF OTHER SUBSTANCES

- Moderate evidence of a statistical association between cannabis use and the development of substance dependence and/or a substance abuse disorder for substances including alcohol, tobacco, and other illicity drugs

# CONCLUSIONS

- There are specific regulatory barriers, including the classification of cannabis as Schedule I substance, that impedes the advancement of cannabis and cannabinoid research

- Often difficult for researchers to gain access to the quantity, quality, and type of cannabis product necessary to address specific research questions on the health effects of cannabis use

# CONCLUSIONS

- A diverse network of funders is needed to support cannabis and cannabinoid research that explores the beneficial and harmful health effects of cannabis use

- To develop conclusive evidence for the effects of cannabis use on short and long-term health outcomes, improvements and standardization in research methodology are needed

# REPORT RECOMMENDATIONS

- **Recommendation 1: Address Research Gaps**
  - Develop comprehensive evidence on the short- and long-term health effects of cannabis use (beneficial and harmful)
  - Public agencies, philanthropic and professional organizations, private companies, and clinical and public health research groups should provide funding and support for a national cannabis research agenda that address key gaps in the evidence

# REPORT RECOMMENDATIONS

- **Recommendation 1: Address Research Gaps**
  - Prioritized research streams and objective should include
    - Clinical and observational research
    - Health policy and health economics research
    - Public health and public safety research

# REPORT RECOMMENDATIONS

- **Recommendation 2: Improve research quality**
  - To promote development of conclusive evidence on the short and long-term effects of cannabis use, agencies should jointly fund a workshop to develop a set of research standards and benchmarks to guide and ensure production of high-quality cannabis research
    - US Department of Health and Human Services
    - Centers for Disease Control and Prevention
    - National Institutes of Health

# REPORT RECOMMENDATIONS

- **Recommendation 3: Improve surveillance capacity**
  - To ensure that sufficient data are available to inform research on short and long-term health effects, agencies should fund and support improvements to federal public health surveillance systems and state-based public health surveillance efforts
    - CDC
    - Substance abuse and mental health services administration
    - Association of state and territorial health officials
    - National association of county and city health officials
    - Association of public health laboratories
    - State and local public health departments

# REPORT RECOMMENDATIONS

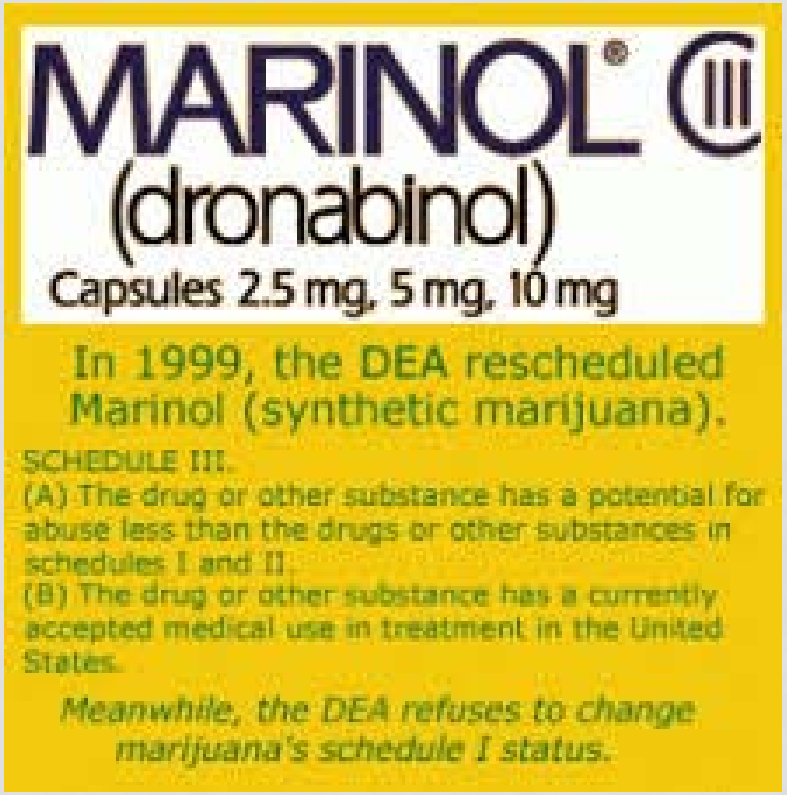
- **Recommendation 4: Address Research Barriers**
  - CDC, NIH, FDA, industry groups, and nongovernmental organizations should fund the convening of a committee of experts tasked to produce an objective and evidence-based report that fully characterizes the impacts of regulatory barriers to cannabis research
    - Propose strategies for supporting development of resources and infrastructure necessary to conduct a comprehensive cannabis research agenda

# PHARMACEUTICAL DRUGS

## CLINICAL USES

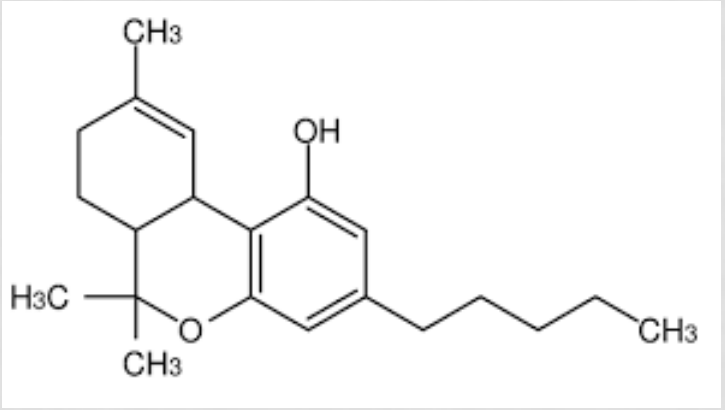
# DRONABINOL

- Also known as marinol
- FDA-approved
- Produced by Unimed Pharmaceuticals
- It is synthetic THC
- Used for treatment of nausea and vomiting in cancer patients
- Also used as an appetite stimulant and as an analgesic to ease neuropathic pain is MS patients



# DRONABINOL

- Can be purchased in states that do not have medical marijuana laws
- Bioavailability: 10-20% of IV
  - High first pass metabolism
- Half-life: 60 hours
- Side effects: sedation, mood altered (laughing, elation), confusion



# NABILONE

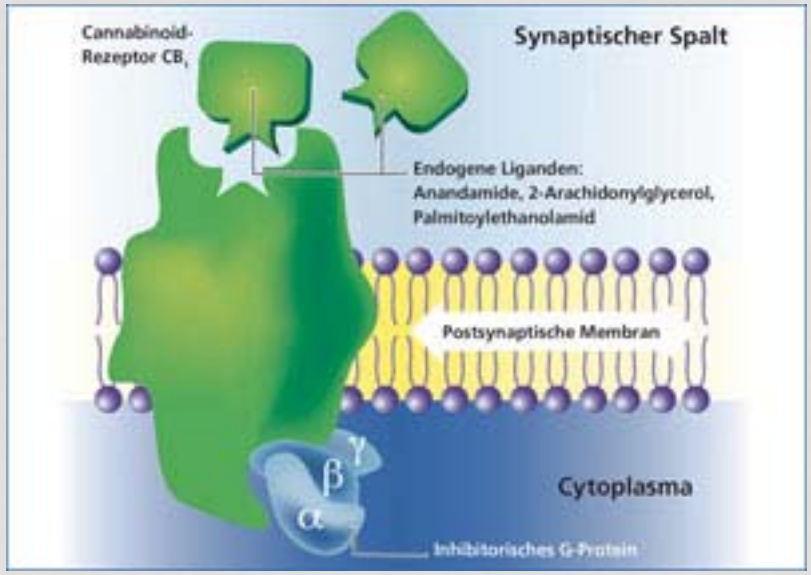
- Also known as Cesamet
- Produced by Valeant Pharmaceuticals International
- Its suggested use is for nausea and vomiting in patients undergoing cancer treatment

# SATIVEX

- Sativex is produced by GW Pharmaceuticals
  - Generic is Nabiximols
  - Approved in UK in June of 2010, not approved in the US
  - Not available in US
- This is a combination of THC and cannabidiol

# SATIVEX

- Formulations: mouth spray or cigarettes
- Uses:
  - Neuropathic pain in patients with Multiple Sclerosis (MS)
  - Adjunct analgesic therapy for cancer patients who have moderate to severe pain and who have already reached the maximum dose of opioid therapy



# RIMONABANT[37]

- Brand names:
  - Accomplia®
  - Zimulti®
- Not available in the US
- It is a cannabinoid recepto 1 blocker
- Used for the treatment of obesity and nicotine dependence

# ROLE OF PHARMACISTS IN MEDICINAL CANNABIS[26]

- Pharmacists need to be involved
  - Educate patients in proper use
  - Counsel the patient and family
- Potential in compounding
  - Ointments, inhalers, capsules, etc.
- Pharmacist can help regulate dosing and help improve efficacy of treatment

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