Clinical Cannabis: A Pharmacist’s Perspective
Megan Saraceni, PharmD
Clinical Oncology Pharmacist
Oregon Health & Science University
saraceni@ohsu.edu

Statement of disclosure

I have no relevant financial relationships with commercial interests pertaining to the content presented in this program.

Objectives

▪ Describe how natural substances, such as cannabis, are developed into more predictable pharmaceuticals
▪ Describe the clinical pharmacology and pharmacokinetics of clinical cannabis and its active components
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- Describe the clinical pharmacology and pharmacokinetics of clinical cannabis and its active components

Drug development and approval

- Drug companies conduct research in the areas of drug quality, safety, and effectiveness
- Laboratory studies first (pre-clinical studies)
- Must submit an Investigational New Drug (IND) application before conducting human studies
- Human studies conducted in phases (I through III)
- Submit a new drug application (NDA) to the FDA’s Center for Drug Evaluation and Research (CDER)
- Team of CDER physicians, statisticians, chemists, pharmacologists, and other scientists reviews the sponsor’s NDA containing the data and proposed labeling

Drug development and approval

THE STAGES OF DRUG DEVELOPMENT
**History of clinical cannabis**


Western Medicine  Marihuana Tax Act  Narcotic  Schedule 1  Compassionate Use  Synthetic Drugs  Medical Use

**Objectives**
- Describe how natural substances, such as cannabis, are developed into more predictable pharmaceuticals
- Describe the clinical pharmacology and pharmacokinetics of clinical cannabis and its active components

**What is marijuana?**
- Cannabis - a genus of flowering plants indigenous to Asia
- Three main components
  1. **Terpenoids**
     - Aromatic chemicals also found in pine trees, citrus flora, and other odoriferous plants
     - Produce the unique aroma and flavor of cannabis
  2. **Flavonoids**
     - Chemicals common to most plant life
     - Many considered to have anti-inflammatory and antioxidant properties
  3. **Cannabinoids**
     - Highest concentration found in female flowers
Cannabinoids

Cannabinoids in marijuana

• Unique chemical structures found in the cannabis plant

• Over 80 identified in nature; more synthesized chemically

CBD, cannabidiol; CBDA, cannabidiolic acid; CBG, cannabigerol; CBGA, cannabigerolic acid; CBC, cannabichromene; CBCA, cannabichrome carboxylic acid; ∆9-THCA, delta-9-tetrahydrocannabinolic acid; ∆9-THC, delta-9-tetrahydrocannabinol; ∆8-THC, delta-8-tetrahydrocannabinol; THCV, tetrahydrocannabivarin

Cannabinoids

Delta-9-tetrahydrocannabinol (THC)
• Major psychoactive component in cannabis
• Naturally occurs in concentrations anywhere from 0.5 – 20% depending on cannabis strain

Cannabidiol (CBD)
• Lacks any noticeable psychoactive affects
• Does not directly interact with the body’s cannabinoid receptors
• Increases the action of/exposure to THC

Cannabinol (CBN)
• Responsible for the sedative effects of cannabis
• May also have antibacterial, bone growth stimulation, and skin healing effects

Decarboxylation:

HEAT (burned, cooked)

Proposed metabolism of cannabis
Cannabinoid receptors

Two cannabinoid receptors

1. CB1 - identified in 1988
   • Located in central nervous system and peripheral neurons
   • Activation produces classic marijuana-like effects on psyche and circulation

2. CB2 - identified in 1993
   • Located on B lymphocytes and natural killer cells
   • Possible role in immunity?

Endogenous cannabinoid system

• Endocannabinoids = substances produced naturally by cell membranes in our bodies to stimulate CB receptors
  • Anandamide
  • 2-arachidonoylglycerol (2-AG)

• Endorphin-like effect lasting a few brief minutes
• Also found in milk (human and bovine) and chocolate
• May have a role in “runner’s high”
QUIZ QUESTION

CB2 receptors are located mainly in/on...

A. Immune cells, such as B lymphocytes and natural killer cells
B. The central nervous system and peripheral neurons
C. Both of these
D. Neither of these

Cannabinoid effects

Activation of cannabinoid system causes four groups of psychological effects

- Affective: euphoria and easy laughter
- Sensory: temporal and spatial perception alterations and disorientation
- Somatic: drowsiness, dizziness, and motor incoordination
- Cognitive: confusion, memory lapses, and difficulty concentrating
QUIZ QUESTION

Which of the following regarding cannabinoids is true?

A. They are unique chemical structures found in the cannabis plant
B. There are approximately 25 known cannabinoids
C. The potential medical effects of cannabinoids are well understood
D. Cannabidiol is the cannabinoid most responsible for the psychiatric effects of marijuana

Mechanism of analgesia

- Has supraspinal, spinal, and peripheral modes of action, acting on both ascending and descending pain pathways
- CB1 receptor found in both CNS and peripheral nerve terminals
  - Increased levels of the CB1 receptor are found in regions of the brain that regulate nociceptive processing
- Anti-inflammatory mechanism (CB2 effect); cannabinoids acting on:
  - Mast cell receptors to attenuate the release of inflammatory agents, such as histamine and serotonin
  - Keratinocytes to enhance the release of analgesic opioids

Formulations

- Single molecule pharmaceuticals
  - Dronabinol (Marinol®) – schedule III
  - Nabilone (Cesamet®) – schedule II
- Liquid extract: nabiximols (Sativex®)
  - Approved in 8 countries; in phase III trials in USA
- Phytocannabinoid-dense botanicals
  - Cannabis sativa (medical plant) – schedule I
Cannabis pharmaceuticals

Dronabinol (Marinol®)
- Synthetic Δ9-THC in sesame oil
- Activates cannabinoid receptors CB1 and CB2; has approximately equal affinity for each, but efficacy is less at CB2 receptors

Nabilone (Cesamet®)
- Mimics THC; synthetic cannabinoid receptor agonist that binds both CB1 and CB2 receptors

Nabiximols (Sativex®)
- THC and CBD mixture; stimulates both cannabinoid receptors CB1 and CB2

Not available in the USA

Comparison

<table>
<thead>
<tr>
<th></th>
<th>Dronabinol</th>
<th>Nabilone</th>
<th>Nabiximols</th>
<th>MMJ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand name</td>
<td>Marinol®</td>
<td>Cesamet®</td>
<td>Sativex®</td>
<td>---</td>
</tr>
<tr>
<td>Source</td>
<td>Synthetic</td>
<td>Synthetic</td>
<td>Synthetic</td>
<td>Natural</td>
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<tr>
<td>Route of administration</td>
<td>Capsule</td>
<td>Capsule</td>
<td>Oromucosal spray</td>
<td>Inhalation, oral, topical</td>
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<td>Approved indications</td>
<td>CINV; appetite stimulant in AIDS patients</td>
<td>CINV</td>
<td>Symptomatic relief of muscle spasms</td>
<td>---</td>
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<tr>
<td>Onset of action</td>
<td>30-60 min</td>
<td>60-90 min</td>
<td>30-150 min</td>
<td>INH: 2-30 minutes, PO: 2-3 hours</td>
</tr>
<tr>
<td>Duration of action</td>
<td>4-6 hours</td>
<td>8-12 hours</td>
<td>Variable</td>
<td>INH: 2-3 hours, PO: 5-8 hours</td>
</tr>
</tbody>
</table>

QUIZ QUESTION

- Edible marijuana products...
  A. Commonly have accurate labeling of THC content
  B. Require the same dose as inhaled marijuana to achieve the same effects
  C. Have an onset of action of less than 30 minutes
  D. Have a duration of action of 5-8 hours
Product issues

- Purity (herbicides, pesticides, solvents)
- Potency (THC content)
  - Recent Oregonian project and JAMA article showed only 13% and 17% of products, respectively are within 10% of stated amount
  - Appropriate dosing for each medical condition?
  - All medical marijuana used in US research is supplied by FDA and is grown on a single plot in Mississippi
  - Greater than 700 strains currently cultivated outside this plot
  - Dosing is dependent on strain and route

Edibles

- 75 products analyzed for labeling accuracy with respect to THC and CBD content
  - 17% were accurately labeled
  - 23% were underlabeled
  - 60% were overlabeled
  - Median THC:CBD ratio of products with detectable CBD was 36:1
  - 7 had ratios of <10:1
  - 1 had a 1:1 ratio

Bioavailability

- Bioavailability
  - Oral THC 4-12%
  - Oral CBD 15-59%
  - Inhaled (both) ~36%
  - Generally 2-3 mg smoked for average “high”
  - Oral dose must be 3-5 times the inhaled dose due to stomach acid effects and hepatic first pass metabolism
  - Proposed potency categories (oral) based on THC content
    - Low <7 mg/dose
    - Medium 7-18 mg/dose
    - High >18 mg/dose
Metabolism

- Liver metabolism primarily by CYP2C
- Delta-9-THC metabolized in liver to 11-OH-THC, a potent psychoactive metabolite
- Greater generation of metabolite when ingested versus when inhaled
- Eliminated in feces > urine

Drug Interactions

May have additive sedative effects with other CNS depressants

<table>
<thead>
<tr>
<th>Cannabinoids</th>
<th>CYP450 Isoforms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1A1 1A2 1B1 2C8 2C9 2C19 2D6 2E1 3A4 3A5</td>
</tr>
<tr>
<td>Δ9-THC</td>
<td>↓↓↓ S S* S S S↓ S* S↓ S↓ S↓</td>
</tr>
<tr>
<td>CBD</td>
<td>↓↓↓ S S* S S S S S S S* S S</td>
</tr>
<tr>
<td>CBN</td>
<td>↓↓↓ S S S S S S S S</td>
</tr>
<tr>
<td>Smoked cannabis</td>
<td>↑↑↑ S S* S S S S</td>
</tr>
<tr>
<td>Dronabinol</td>
<td>S S S S</td>
</tr>
<tr>
<td>Nabilone</td>
<td>S S S S</td>
</tr>
<tr>
<td>Nabiximols</td>
<td>S S S</td>
</tr>
</tbody>
</table>

S substrate with highest predicted significance in vivo; S* potential substrate; ↓↓↓ induces; ↓↓ inhibits following in vivo experiments

Adopted from www.theanswerpage.com

Drug Interactions

- Pharmacodynamic interactions
  - Anticholinergics
  - Central nervous system depressants
  - Sympathomimetics

- Interactions with CYP450 system
  - CBD inactivates CYP3A4
  - Repeated doses may induce P450 isoforms

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Megan Saraceni, PharmD
Clinical Oncology Pharmacist
Oregon Health & Science University
saraceni@ohsu.edu

Clinical Cannabis for Chronic Pain: A Nurse Practitioner’s Perspective
Kim Dupree Jones PhD, FNP-BC, FAAN
joneskim@ohsu.edu

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Objectives

- Discuss the potential medical uses of cannabis for the treatment of chronic pain

- Identify adverse effects, psychiatric implications, and potential drug interactions that may occur with the use of cannabis

- List patient diagnosis that may present a red flag for using cannabis
Potential Medical Uses for Cannabis

- Pain
- Nausea/vomiting
- Neuropathy
- Seizures
- Anorexia/cachexia
- Muscle spasms
- Cancer
- Glaucoma
- Depression and anxiety
- Insomnia
- Post traumatic stress disorder
- Agitation related to Alzheimer’s disease


QUIZ QUESTION

- What is the most common reason for medical marijuana use in the United States?
  
A. Glaucoma
B. Nausea
C. Muscle spasms
D. Pain

Contemporary Approach to Classifying Pain

Peripheral (nociceptive)
- Inflammation or mechanical damage in tissues
- NSAID, opioid responsive
- Responds to procedures
- Classic examples: Acute pain due to injury, osteoarthritis, rheumatoid arthritis, cancer pain

Peripheral Neuropathic
- Damage or dysfunction of peripheral nerves
- Responds to both peripheral (NSAIDs, opioids, Na channel blockers) and central (TCA’s, neuroactive compounds) pharmacological therapy
- Classic examples: Neuropathic pain

Centralized Pain / Sensory Hypersensitivity
- Characterized by central disturbance in pain processing (diffuse hyperalgesia/allodynia)
- Responsive to neuroactive compounds altering levels of neurotransmitters involved in pain transmission
- Classic examples: Fibromyalgia, irritable bowel syndrome, TMD, tension headache

Mixed Pain States
Evidence: Systematic Reviews to Anecdote

Levels of Evidence

Randomized Controlled Trials (RCTs)

- High evidence
- Moderate evidence
- Low evidence
- Very low evidence

22 of 29 RCT's demonstrated significant analgesic effect

Modest treatment effects

Mean duration of treatment was 2.8 weeks

Cannabinoids for treatment of chronic non-cancer pain: a systematic review of randomized trials

Mary B. Lynch* & Neur Campbell†

Department of Pharmacy, Trinity College Dublin, Ireland, and Department of Anesthesiology, University of British Columbia, Vancouver, Canada

Cannabis for the Treatment of Chronic Non-Cancer Pain: An Updated Systematic Review of Randomized Controlled Trials

Published online: 22 March 2015

All Cannabinoids for Non-cancer Pain

- 22 of 29 RCT's demonstrated significant analgesic effect
- Modest treatment effects
- Mean duration of treatment was 2.8 weeks

to moderate, transient and generally well tolerated. The findings of the current review extend and are consistent with those from the previous review (Lynch and Campbell 2011) such that combined there are a total of 22 of 29 RCTs demonstrating that cannabinoids demonstrate a modest analgesic effect and are safe in the management of chronic pain.
Efficacy and adverse effects of medical marijuana for chronic noncancer pain
Systematic review of randomized controlled trials

- 6 studies—all were inhaled cannabis
- 5 were cross-over design
- Average of 2 weeks exposure of 0% or 3.5% or 9.4% THC

Results—Small to moderate improvements in pain, mostly neuropathic. Multiple transient neurocognitive side effects; no serious adverse events. Likely safe even as adjunct medication.

Efficacy of Cannabis: Summary

- For most qualifying conditions, approval has relied on low-quality scientific evidence, anecdotal reports, individual testimonials, legislative initiatives, and public opinion
- Fewer than 20 trials evaluating smoked cannabis for all possible uses
- Results of studies with individual cannabinoids (e.g., THC or CBD) cannot be extrapolated to marijuana and vice versa
- Meta-analysis including 79 randomized controlled trials of cannabis across a broad range of conditions
  - Most evaluated oral cannabinoids (dronabinol, nabilone, nabiximols)
  - Moderate-quality evidence to suggest that cannabinoids (including smoked THC) may be beneficial for the treatment of chronic neuropathic or cancer pain

QUIZ QUESTION

- Which of the following is true regarding efficacy of cannabis?
  A. Cannabis has undergone the same rigorous approval process as other US pharmaceuticals
  B. A majority of clinical trials involves the oral cannabinoids (dronabinol, nabilone)
  C. There are hundreds of randomized clinical trials among a variety of indications
  D. Results from oral cannabinoid trials can be extrapolated to inhaled cannabis
Objectives

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Potential Harms: Safety and Adverse Events

▪ Cancer

▪ Heart Disease

▪ Mental Health (addiction, dependence, psychosis, schizophrenia)

▪ Accidents

▪ Serious Adverse Events

Cardiac Effects

▪ Acute dosing associated with
  ↑ heart rate  ↑ cardiac output  ↑ blood pressure

▪ Case reports of sudden cardiac death with synthetic cannabinoids

▪ Discuss risks vs benefits in patients with angina, arrhythmia or CVD

Cancer

64k CA Kaiser Permanente patients ages 15-49 years followed 8.6 years:

- In the never smoked group there were 2 cases of lung cancer, in the 50,000 person-years of follow-up of marijuana only
- There were no documented cases of lung cancer, but increased risk of respiratory infection
- Marijuana use was not associated with tobacco-related cancers
- Slightly increased risk of prostate cancer


More recent lung cancer findings:

- Retrospective case-control study in New Zealand assessed the risk of lung cancer as it relates to joint-years and other variables
- Risk of lung cancer increased 8% for each joint-year of cannabis smoking and 7% for each pack-year of cigarette smoking


Respiratory Effects

- Vaporizers have advantage of delivering active components directly to lungs without byproducts of smoking, such as tar
- Inhalation of smoke or vaporized cannabis increases risk of pulmonary infections
  - Most common bacteria = Enterobacteriaceae
  - Most common mold = Aspergillus
- Danger is primarily to the immunocompromised host
  - Dry buds more dangerous than oil
- Numerous medical case reports; fatal outcome in some
- Sterilization techniques exist, but not routine in the USA

Psychosis

Early use of cannabis = increased risk.

Vulnerable groups:
• Adolescent users
• Previous psychotic episodes
• At risk for developing schizophrenia

Schizophrenia

Cannabis in Adolescents

• Endocannabinoid system critical in brain development and maturational processes
  • Axon elongation, neurogenesis, neural maturation and specification, glia formation, neuronal migration, synaptic pruning

• Adolescent exposure causes long-lasting alterations in the endocannabinoid system and other neurotransmitter systems
  • Linked to affective, behavioral, cognitive, and neurochemical consequences lasting into adulthood

• Brain development continues until age 25 years
  • Legal sales to persons aged 21 years or older
Addiction and Dependence

- Not generally considered to be addictive; brain develops a tolerance to cannabinoids
- Dependence develops in 9-10% of cannabis users
- Risk much lower than nicotine, heroin, cocaine, and alcohol, and equivalent to anxiolytics

Withdrawal

Like all substances that affect the CNS, withdrawal is possible
- Usually mild symptoms if any; dissipate after a few days
- Irritability, insomnia with sleep EEG disturbance, restlessness, hot flashes, nausea, and cramping
- Stored in adipose tissue and excreted at a low rate (half life approximately 1-3 days)

Overdose on Inhaled Cannabis?

Overdose
- Cannabinoid receptors not located in brainstem areas controlling respiration; lethal overdoses due to respiratory depression do not occur
- LD₅₀ estimated to be 1500 pounds smoked in 15 minutes
Potential Reproductive Harms

- Reproductive/post-natal effects
  - Animal studies show growth retardation and fetal malformations
  - Most human studies confounded by concomitant tobacco, alcohol, or other illicit drug use
  - Appears to result in lower birth weight at the very least
  - Delayed visual system development, increased tremors
  - Lower scores in memory and verbal outcomes seen along with increased rates of delinquency and problem behaviors at age >10

COMPASS trial

- Most common serious adverse events (SAEs) in cannabis group were abdominal pain, intestinal obstruction, and nephrolithiasis
- Most common non-SEAs in cannabis group somnolence, anorexia, cough, nausea, dizziness, euphoric mood, hyperhidrosis, and paranoia
- Sensory component of pain, physical function, total symptom distress score, and total mood disturbance scale all improved for cannabis users compared to controls

<table>
<thead>
<tr>
<th></th>
<th>Cannabis group</th>
<th>Control group</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least 1 SAE</td>
<td>28 patients (13%)</td>
<td>42 patients (19%)</td>
<td>0.64</td>
<td>0.38-1.04</td>
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<tr>
<td>Incidence rate</td>
<td>4.81 events/person-year</td>
<td>2.85 events/person-year</td>
<td>1.64</td>
<td>1.35-1.99</td>
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<tr>
<td>Reduction in</td>
<td>0.92</td>
<td>0.18</td>
<td></td>
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<tr>
<td>average pain</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Incidence rate of non-SEAs

- 4.61 events/person-year
- 2.85 events/person-year
- IRR = 1.64
- 95% CI 1.35-1.99

Reduction in average pain

- 0.92 vs 0.18

QUIZ QUESTION

- Which of the following is true regarding safety of cannabis?
  A. Serious adverse events are commonly reported
  B. Cannabinoids have linked to affective, behavioral, cognitive, and neurochemical consequences lasting into adulthood
  C. There are hundreds of randomized clinical trials among a variety of indications
  D. Mothers using cannabis are more likely to seek antenatal care compared to non-cannabis users
Objectives

▪ Discuss the potential medical uses of cannabis for the treatment of chronic pain
▪ Identify adverse effects, psychiatric implications, and potential drug interactions that may occur with the use of cannabis
▪ List patient diagnosis that may present a red flag for using cannabis

Red Flags

Although most adverse effects are minor, there is a real (but low) risk of
- psychosis
- schizophrenia
- dependence (~9%)
PMH or Family history of addiction
Pregnant women
Adolescents
Uncontrolled HTN
Unstable CV disease
Immunosuppression, particularly for inhaled cannabis

Cannabis is currently framed as 3rd line not 1st line

An appropriate candidate should have:
1. A debilitating medical condition that data from RCTs suggest would respond to medical marijuana pharmacotherapy (e.g., N/V associated with cancer chemotherapy, anorexia from wasting illnesses like AIDS, chronic pain, neuropathic pain, or spasticity associated with multiple sclerosis)
2. Multiple failed trials of first and second line pharmacotherapies for these conditions
3. A failed trial of an US FDA approved cannabinoid (dronabinol or nabilone)
4. No active substance use disorder or psychotic disorder or no unstable mood disorder or anxiety disorder. Warn about anxiety
5. Residence in a state with medical nurse practice act and medical marijuana laws and meets requirement of these laws

Adapted from JAMA. 2015;313(24):2456-2473
NP Provider Resources

- Published literature from Canada, Israel, Germany
- YouTube:
  - The Arthritis Society (Canada)
  - CNN Documentary- Weeds: Sanjay Gupta MD
- Books: Stoned by D Cararett MD
- Cannabis and Cannabinoids PDQ-Health Professional NIH
- www.cancer.gov/about-cancer/treatment/cannabis

Provider Resources

Take Home Points

- In the eyes of the federal government, cannabis remains an illegal, schedule 1 drug
- Cannabinoids act as synaptic breaks
- Cannabinoids are not recommended for long term treatment of neuropathic pain because of lack of long term data
- For many types of pain cannabinoids have a modest effect
- Although most adverse effects are minor, there is a real (but low) risk of psychosis, schizophrenia and dependence (~9%) particularly in adolescents
- The future will bring other formulations, routes of delivery and longer-term trials
Summary

▪ Current literature regarding efficacy of non-synthetic clinical cannabis is lacking, but is likely to improve significantly in next 5-10 years
  ▪ Will continue to see more research done for both smoked cannabis and cannabinoid products.
▪ Current commercial products are not regulated in a meaningful manner, production is non-standardized, and exact dosage is unknown. Seed-to-sale may change this.
  ▪ Serious complications of smoked cannabis use include acute psychotic reactions, invasive Aspergillus infections, CV events, and unaccounted for drug interactions.
▪ Legalization of marijuana in Oregon does not change OHSU policy.
  ▪ Federally, still a class I controlled substance.

Clinical Cannabis for Chronic Pain: A Nurse Practitioner’s Perspective
Kim Dupree Jones PhD, FNP-BC, FAAN
joneskim@ohsu.edu

Clinical Cannabis: An Oregon Patient Advocacy Perspective
Stephanie Truex RN BSN
PhD Student Oregon Health & Science University
truex@ohsu.edu
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Objectives

▪ Discuss state and federal legislative issues that affect patient’s use of medical/clinical cannabis
▪ Identify the different products available to patients
▪ Describe what patients should expect from a cannabis dispensary
Federal Prohibition

- Cannabis has been federally prohibited since 1937 under the Marijuana Tax Act
- Mandatory sentences for drug offenses under the Boggs Act of 1952
- Currently prohibited under the Controlled Substances Act of 1970

Schedule 1 Drugs

- Cannabis is currently classified as a Schedule 1 Drug, a classification reserved for drugs where:
  - The drug or other substance has a high potential for abuse.
  - The drug or other substance has no currently accepted medical treatment use in the U.S.
  - There is a lack of accepted safety for use of the drug or substance under medical supervision.

- Titled Cannabinoids as Antioxidants and Neuroprotectants
- Held by the US federal government since 2003
### US Medical Cannabis Laws

- 25 states and the District of Columbia have legalized medical cannabis
- 43 states have some form of medical marijuana law
- First medical use law passed in California in 1996
- Oregon went second in 1998 but didn’t license dispensaries until 2014

### The Oregon Medical Marijuana Program (OMMP)

- Patients may possess up to 1.5 pounds (24 oz) of cannabis
- Patients may grow up to six mature plants (and unlimited immature plants)
- Patients may designate a caregiver who may possess and administer cannabis
- Patients may designate a grower to grow their allotted plants
- Patients may purchase cannabis tax free at medical or recreational cannabis stores

### Recreational Cannabis

- Colorado and Washington passed laws allowing recreational use in 2012 and began sales in 2014
- Oregon, Alaska and Washington D.C. passed rec laws in 2014
- Cannabis became legal for all adults in Oregon in July 2015
- Limited retail adult use sales began in Oregon in October 2015
Recreational Cannabis in Oregon

- Oregon adults may possess up to 8 oz. dried cannabis at home and up to 1 oz. in public
- Each Oregon household can grow up to four plants
- Smoking in public is prohibited (a parked car is not considered "in public")

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Forms of Cannabis

- Flower
- Concentrates/Extracts
- Edibles
- Topicals
Cannabis Flower

THC and CBD

- Most flower is high THC, but we have high CBD strains as well
- As one goes up, the other goes down
- In THC strains, THC content typically ranges from 15%-30% with CBD typically less than 1%
- We also have strains with a variety of CBD:THC Ratios
  - 1:1 strains have equal concentrations (typically 8%-12% of each)
  - 2:1 strains have twice as much CBD as THC (typically 8%-16% CBD and 5%-8% THC)
  - High CBD strains can have ratios of 30+1, with CBD concentrations up to 25% and THC less than 1%

Concentrates and Extracts
Edibles

Topicals and Transdermals

Topicals
- Refers to lotions and salves applied topically
- Patients say they help with minor aches and pains, inflammation and rashes
- Non-psychoactive—these cannot get you high

Transdermals
- Not really a topical but sometimes grouped with them
- THC and CBD versions
- The THC version will get you high

Objectives

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Portland, Oregon Cannabis Dispensary

Cannabis is Cash Only

Economics

Cost is as high as $3000 per pound (tobacco leaves ~$2 per pound)

<table>
<thead>
<tr>
<th>Product</th>
<th>Cost Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flower</td>
<td>$5-$20 per gram</td>
</tr>
<tr>
<td>Concentrate</td>
<td>$20-$60 per gram</td>
</tr>
<tr>
<td>Edibles</td>
<td>$3-$10 per dose</td>
</tr>
<tr>
<td>Tinctures</td>
<td>$15-$80 per bottle</td>
</tr>
<tr>
<td>MMJ recommendation</td>
<td>$80-$200 for new patients</td>
</tr>
<tr>
<td>Smoking paraphernalia</td>
<td>$2 rolling papers, $20+ glass pipe, $50-$300 water pipe, $100-$700 vaporizers</td>
</tr>
</tbody>
</table>
Budtenders/sales associates

Patient factors to consider
- Many strains of marijuana each with different potencies and plant properties
- Dosing and response varies greatly between patients
- Pharmacokinetics will differ depending on formulation and administration
- Drug interactions
- Employees at dispensary helping patient choose product
- Patient-provider relationship may be absent
- Create safe environment for patients to discuss all drug use, including MMJ

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