The Medicinal Application of Marijuana: What’s Legal and What’s Not

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CLINICAL PHARMACIST

Disclosure Statement

I have relevant financial relationships with the product(s) or service(s) described, evaluated, reviewed, or compared in this presentation.

Employed as a Clinical Pharmacist at LeafLine Labs
Today’s Agenda

Historical Overview
The Endocannabinoid System and Phytocannabinoids
Minnesota Medical Cannabis Program Overview
Legal Considerations
LeafLine Labs Overview

2700 BC

EARLY USE
- Commercial purposes (e.g. textiles, clothing)
- Medicinal
- Recreational

ANCIENT TEXT: *Pen Ts’ao* (Translation: *The Herbal*)
- Chinese herbal pharmacological book
- Depicts 350+ medicines derived from minerals, plants and animals

Abrams, “Medical Cannabis and the Endocannabinoid System.”
1800s

Mid-1800s: Cannabis was added to the U.S. Pharmacopeia

**USED TO COMMONLY TREAT:**
- Opiate withdrawal
- Migraine
- Pain
- Leprosy
- Incontinence
- Gout
- Convulsive disorders

1930’s: Anti-Marijuana Propaganda in the U.S.

*Images of vintage anti-marijuana posters.*
1937: First US Legislative Action on Cannabis

SCIENTIFIC FINDINGS
Anslinger wrote to 30 scientific experts. Of those experts, 29/30 wrote back asserting the medical value of cannabis

Anslinger ignored these findings.

OCTOBER 1937: “Marihuana Tax Act”
• Taxed growers, sellers and buyers
• Resulted in significant decline in cannabis prescriptions

NOTE: This tax did NOT make prescribing cannabis illegal.

1970: Shafer Commission Findings

OFFICIAL COMMISSION FINDINGS
“Marijuana DOES NOT lead to physical dependency, although some evidence indicates heavy long-term users may develop psychological dependence on the drug.”

The Shafer Commission, 1970

NIXON RESPONDS
“As you know, there is a Commission that is supposed to make recommendations to me about this subject; in this instance, however, I have such strong views that I will express them. I AM against legalizing marijuana. Even if the Commission does recommend that it be legalized, I WILL NOT follow that recommendation...”

President Nixon, 1970
Today’s Agenda

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CANNABIS PLANT

• C. SATIVA, C. INDICA, C. RUDERALIS

• OVER 60-113 COMPOUNDS CALLED CANNABINOIDS

• MOST COMMON CANNABINOIDs
  • Δ-9-tetrahydrocannabinol (THC)
  • CANNABIDIOL (CBD)
Entourage Effect
• Terpenes
• Terpenoids: Responsible for scent as well as have a broad Spectrum of action
  • Limonene: Citrus - Gastric Reflux, Anti-fungal, Anti-depressant, Anti-anxiety
  • α-Pinene: Pine - Anti-inflammatory, Bronchodilator, Aiding in Memory
  • β-Myrcene: Mango and more - Anti-inflammatory, Analgesic, Anti-tumor, Muscle Relaxant
  • Linalool: Lavender - Anti-anxiety, Sedative (sleep-aid), Analgesic, Anti-convulsant
  • Caryophyllene Oxide: Cloves - Anti-fungus, Anti-tumor, Anti-oxidant, Improved uptake of CBD/CBC
• “Entourage Effect”
• 500 Different Chemical Compounds
• All of these compounds work together

Cannabinoids & The Endocannabinoid System

**ENDOCANNABINOIDS** (found and produced in the human body)

- **Anandamide**
  - N-arachidonoylthanolamine

- **2-AG**
  - 2-Arachidonoylglycerol

**PHYTOCANNABINOIDS** (found and produced in plants)

- **9 THC**
  - Tetrahydrocannabinol

- **CBD**
  - Cannabidiol

References:
Cannabinoids & The Endocannabinoid System

**Endocannabinoids** (found and produced in the human body)
- **2-AG** (2-Arachidonoylglycerol)
- **Anandamide** (N-arachidonylethanolamine)
- **THC** (Tetrahydrocannabinol)
- **CBD** (Cannabidiol)

**Phytocannabinoids** (found and produced in plants)

**Cannabinoids & The Endocannabinoid System**

*Bermudez-Silva et al., "The Endocannabinoid System, Eating Behavior and Energy Homeostasis."

**The Endocannabinoid System (ECS)**

**CB1 & CB2 RECEPTORS**

**CB1 RECEPTORS**
- **Cannabinoid Effects on CB1 Receptors**
  - Decreased pain (analgesia)
  - Decreased nausea and vomiting
  - Increased appetite
  - Increased muscle control
  - Sleep aid
  - Memory suppressant
  - Anti-prolific

**CB2 RECEPTORS**
- **Cannabinoid Effects on CB2 Receptors**
  - Anti-inflammatory
  - Increases immune function
  - Decreased pain (analgesia)
  - Anti-prolific

*Abrams, Medical Cannabis and the Endocannabinoid System*
Phytocannabinoids
ACTIVE CANNABIS COMPONENTS

Some Effects of THC:
• Decrease pain
• Stimulate appetite
• Analgesic
• Anti-emetic
• Sleep aid
• Psychotropic

Some Effects of CBD:
• Mitigation of psychotropic effects of THC
• Analgesic
• Anti-inflammatory
• Anti-epileptic
• Anxiolytic

THC
$\Delta^9$-TETRAHYDROCANNABIDIOL
TARGETS BOTH CB1 & CB2 RECEPTORS

CANNABIDIOL
TARGETS PRIMARILY CB2 RECEPTORS
*modulates other cannabinoids

CB1 Receptor
CB2 Receptor

Terpenes

β-Myrcene
Anti-inflammatory
Anti-tumor
Anti-insomnia
Increase BBB Permeability

Phytol
Anti-Oxidant

Humulene
Anti-tumor
Anti-bacterial
Anti-inflammatory
Appetite suppression

Citronellol
Anti-inflammatory
Immuo-regulating

Linalool
Anti-inflammatory
Anti-Anxiety
Anti-Epileptic

Caryophyllene Oxide
Anti-tumor
Anti-fungal
Anti-inflammatory
Anti-tumor

Beta Caryophyllene
Anti-tumor
Anti-bacterial
Anti-septic

Limonene
Anti-depressant
Treat Gastric Reflux

Terpinolene
Anti-insomnia

α-Pinene
Anti-inflammatory

Synthesis of Vitamin E/K

Appetite suppression
Whole Plant Medicine vs. Synthetic Medicine
WHAT’S THE DIFFERENCE?

Hundreds of various compounds

- Terpenes
- CBC
- CBG

CBD
THC

Medical Cannabis Special Considerations

Psychosis
- Limit use in those with history of psychosis

Use in Children & Adolescents
- Consider higher risks: benefits
- Potential impact on adolescent brain development
- Short term cognitive effects and possible negative academic impacts
- Unclear long term impacts on cognition
Cannabis vs. CBD vs. Hemp Oil

<table>
<thead>
<tr>
<th>Marijuana</th>
<th>Hemp</th>
<th>Hemp seeds (cannabis sativa seed oil)</th>
</tr>
</thead>
<tbody>
<tr>
<td>produces tetrahydrocannabinol (THC) at 20%+ levels (the psychoactive compound that makes a person feel &quot;high.&quot;)</td>
<td>has to be less than 0.3% THC to be sold legally</td>
<td>0% THC, trace amounts of CBD</td>
</tr>
<tr>
<td>produces CBD at 10%+ levels</td>
<td>produces CBD at 20%+</td>
<td>used as food such as hempseed milk, granola, and more</td>
</tr>
<tr>
<td>medicinal and therapeutic uses for chronic pain, mental health, and illnesses</td>
<td>stalks of the hemp plant can produce clothing, rope, paper, fuel, home insulation... (the list goes on and on)</td>
<td>cold-pressed for oil production that can be used in cooking, beauty products, and even in paint</td>
</tr>
</tbody>
</table>

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Minnesota Medical Cannabis Program
SETTING A NEW STANDARD: DIFFERENTIATING FACTORS

01
Healthcare provider must CERTIFY patient eligibility for program

02
1st smoke-free cannabis program

03
Extensive patient registration & reporting process through MDH

04
Personal consultation with specially trained licensed pharmacists

ROLE OF THE HEALTHCARE PRACTITIONER (HCP)

DO
Assess and certify patients’ qualifying conditions

Do NOT
Prescribe, refer or recommend medical cannabis medications

CAN
Coordinate Care with LeafLine Labs care delivery teams

HEALTHCARE PRACTITIONER
Minneapolis Medical Cannabis Program
REGISTRATION PROCESS FOR PATIENTS

1. CONDITION CERTIFICATION
Have your medical condition certified by a healthcare provider

2. REGISTER WITH THE OFFICE OF MEDICAL CANNABIS (OMC)
• Receive certification confirmation email
• Register online
• Annual $200 registration fee, or $50 for those with SSI, SSD, MA, Medicaid or CHAMPVA

3. SCHEDULE YOUR INITIAL CONSULTATION
Call our patient care centers to schedule your initial consultation.

Approved Indications in Minnesota

- Intractable Pain
- Cancer
- HIV/AIDS
- Seizures
- Obstructive Sleep Apnea
- Autism
- PTSD
- Tourette’s Syndrome
- Glaucoma
- ALS
- Muscle Spasms
- Inflammatory Bowel Disease
- Terminal Illness
- Alzheimer’s Disease
What is “Intractable Pain”?

As defined by the state of Minnesota, intractable pain is a pain state where the cause of pain cannot be removed or otherwise treated. It is a state in which no relief or cure of the cause of pain is possible.

Primary causes of such pain include, but are not limited to:

1. Arthritis: rheumatoid
2. Arthritis: osteoarthritis
3. Cancer
4. Complex Regional Pain Syndrome
5. Crohn’s Disease
6. Disc (vertebral) herniation
7. Endometriosis
8. Fibromyalgia syndrome
9. Headache: migraine
10. Headache: other
11. Low back pain
12. Lupus
13. Multiple sclerosis
14. Muscular dystrophy
15. Myofascial pain
16. Myelopathies
17. Neck pain
18. Neuropathy: diabetic
19. Neuropathy: HIV
20. Neuropathy: post-herpetic
21. Neuropathy: OTHER
22. Parkinson’s
23. Phantom limb pain
24. Post-stroke pain
25. Postoperative pain
26. Sciatica
27. Spinal cord injury
28. Spinal stenosis
29. Trauma (including vertebral compression fracture)
30. Trigeminal neuralgia
31. Vascular disease
32. OTHER
# Medical Cannabis Program Update

## Table 5: Breakdown of Registered Health Care Practitioners by Type, as of September 30, 2019

<table>
<thead>
<tr>
<th>Healthcare Practitioner Type</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician</td>
<td>1186 (74%)</td>
</tr>
<tr>
<td>Physician Assistant</td>
<td>121 (8%)</td>
</tr>
<tr>
<td>Advanced Practice RN</td>
<td>305 (19%)</td>
</tr>
<tr>
<td>Total</td>
<td>1,612</td>
</tr>
</tbody>
</table>

## Figure 2. Weekly number of patients enrolled and in active status in registry.

*Minnesota Department of Health, Office of Medical Cannabis. Medical Cannabis Program Update. July 2018*
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THERAPEUTIC RESEARCH ACT; MEDICAL CANNABIS
Subd. 6. MEDICAL CANNABIS

(a) "Medical cannabis" means any species of the genus cannabis plant, or any mixture or preparation of them, including whole plant extracts and resins, and is delivered in the form of:

• (1) liquid, including, but not limited to, oil;
• (2) pill;
• (3) vaporized delivery method with use of liquid or oil but which does not require the use of dried leaves or plant form; or
• (4) any other method, excluding smoking, approved by the commissioner.

(b) This definition includes any part of the genus cannabis plant prior to being processed into a form allowed under paragraph (a), that is possessed by a person while that person is engaged in employment duties necessary to carry out a requirement under sections 152.22 to 152.37 for a registered manufacturer or a laboratory under contract with a registered manufacturer.
THERAPEUTIC RESEARCH ACT; MEDICAL CANNABIS
152.23 LIMITATIONS.

(a) Nothing in sections 152.22 to 152.37 permits any person to engage in and does not prevent the imposition of any civil, criminal, or other penalties for:

1. undertaking any task under the influence of medical cannabis that would constitute negligence or professional malpractice;

2. possessing or engaging in the use of medical cannabis:
   (i) on a school bus or van;
   (ii) on the grounds of any preschool or primary or secondary school;
   (iii) in any correctional facility; or
   (iv) on the grounds of any child care facility or home day care;

3. vaporizing medical cannabis pursuant to section 152.22, subdivision 6:
   (i) on any form of public transportation;
   (ii) where the vapor would be inhaled by a nonpatient minor child; or
   (iii) in any public place, including any indoor or outdoor area used by or open to the general public or a place of employment as defined under section 144.413, subdivision 1b; and

4. operating, navigating, or being in actual physical control of any motor vehicle, aircraft, train, or motorboat, or working on transportation property, equipment, or facilities while under the influence of medical cannabis.

THERAPEUTIC RESEARCH ACT; MEDICAL CANNABIS
152.33 VIOLATIONS.

Subd. 1a. Intentional diversion outside the state; penalties.

(a) In addition to any other applicable penalty in law, the commissioner may levy a fine of $250,000 against a manufacturer and may immediately initiate proceedings to revoke the manufacturer's registration, using the procedure in section 152.25, if:

1. an officer, director, or controlling person of the manufacturer pleads or is found guilty under subdivision 1 of intentionally transferring medical cannabis, while the person was an officer, director, or controlling person of the manufacturer, to a person other than allowed by law; and

2. in intentionally transferring medical cannabis to a person other than allowed by law, the officer, director, or controlling person transported or directed the transport of medical cannabis outside of Minnesota.

(b) All fines collected under this subdivision shall be deposited in the state government special revenue fund.
152.33 VIOLATIONS.

• Subd. 2. **Diversion by patient, registered designated caregiver, or parent; criminal penalty.**
  • In addition to any other applicable penalty in law, a patient, registered designated caregiver or, if listed on the registry verification, a parent or legal guardian of a patient who intentionally sells or otherwise transfers medical cannabis to a person other than a patient, designated registered caregiver or, if listed on the registry verification, a parent or legal guardian of a patient is guilty of a felony punishable by imprisonment for not more than two years or by payment of a fine of not more than $3,000, or both.

THERAPEUTIC RESEARCH ACT; MEDICAL CANNABIS
152.33 VIOLATIONS

• Subd. 3. **False statement; criminal penalty.**
  • A person who intentionally makes a false statement to a law enforcement official about any fact or circumstance relating to the medical use of cannabis to avoid arrest or prosecution is guilty of a misdemeanor punishable by imprisonment for not more than 90 days or by payment of a fine of not more than $1,000, or both. The penalty is in addition to any other penalties that may apply for making a false statement or for the possession, cultivation, or sale of cannabis not protected by sections 152.22 to 152.37. If a person convicted of violating this subdivision is a patient or a registered designated caregiver, the person is disqualified from further participation under sections 152.22 to 152.37.
The CDPHE’s Retail Marijuana Public Health Advisory Committee biennially publishes a comprehensive review of relevant marijuana research. The 2019 report found substantial evidence in the literature to support the following:

- Recent marijuana use increases a driver’s risk of a motor vehicle crash.
- Less-than-weekly marijuana users exhibit meaningful driving impairment with THC levels of 2-5 ng/mL or ingestion of 10 mg or more of THC.
- Combining marijuana and alcohol increases impairment and motor vehicle crash risk more than each alone.
- Delaying driving for a minimum of six hours after smoking or 8 hours after ingesting allows THC-induced impairment to resolve for less-than-weekly users at 18 mg of THC.
- Research is lacking on marijuana and impairment in frequent users.

**Impaired Driving**

- The Delta-9 THC level in blood decreases rapidly in the first hour after use, then gradually thereafter, making prompt testing critical.
• Results from studies that examined Delta-9 THC concentration, subjective high, and performance of subjects show THC concentration peaks early, but the impairing effects on driving-related performance tasks and subjective high appear long after the peak concentration.

• This suggests that there are performance deficits that follow the peak of THC concentration. Furthermore, high THC concentration in blood does not perfectly correspond to impairment.

UCSF Trial Confirms THC in Breath During Window of Peak Impairment

The latest clinical trial results from the University of California – San Francisco (UCSF) confirm that THC is detectable in breath for up to three hours after smoking marijuana. Beyond three hours, THC levels drop to virtually undetectable levels.

The three-hour timeframe is significant because research has shown that this is when people are most likely to be impaired. Other marijuana tests – urine, blood, oral fluid, hair – detect previous use that is well outside the window of peak impairment.
A placebo-controlled study to assess Standardized Field Sobriety Tests performance during alcohol and cannabis intoxication in heavy cannabis users and accuracy of point of collection testing devices for detecting THC in oral fluid.

- Conclusions Standardized Field Sobriety Tests were mildly sensitive to impairment from cannabis in heavy users. Lack of sensitivity might be attributed to tolerance and time of testing. SFST were sensitive to both doses of alcohol. The Dräger Drug Test® 5000 appears to be a promising tool for detecting THC in oral fluid as far as correct THC detection is concerned.

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Horticulture Operations

Laboratory Operations
LeafLine Labs
PATIENTS FIRST. ALWAYS.

Hibbing
St. Cloud
St. Paul
Eagan

Patient Experience at Leafline Labs Patient Care Center
LeafLine Labs Medications

• **Tangerine** → Formulation with higher THC/CBD ratio (>20:1)
  • Beneficial alone or in combination for various pain conditions, glaucoma, Tourette’s, Cachexia, poor appetite, inflammatory bowel disease, muscle spasticity etc.

• **Heather** → Formulation with equal THC/CBD (1:1)
  • Beneficial for various pain conditions, muscle spasticity etc.

• **Cobalt** → Formulation with Higher CBD (CBD/THC >20:1)
  • Beneficial alone or in combination for Seizures, inflammation, potentially much more.

What’s Legal in Minnesota
Minnesota Medical Cannabis Registry Verification Card

Patient Information

Parent, Legal Guardian or Spouse

Date Sold

Registered Caregiver

Product Dispensed

This card is for information purposes only and satisfies MN Statute 152.27 Subd. 6e. All authorized individuals that can possess medical cannabis for a specific approved patient will have their name printed on the medical cannabis container label. The office of Medical Cannabis will not confirm or deny participation in the registry without a valid search warrant.
Cannabis Delivery Methods Available in Minnesota

<table>
<thead>
<tr>
<th>Method</th>
<th>Onset</th>
<th>Peak Concentration</th>
<th>Duration</th>
<th>Bioavailability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaporization</td>
<td>3 to 10 minutes</td>
<td>15 minutes</td>
<td>2 to 4 hours</td>
<td>5% to 20% (varies based on technique)</td>
</tr>
<tr>
<td>Oral Dosage</td>
<td>60 to 90 minutes</td>
<td>1 to 6 hours</td>
<td>8 to 12 hours</td>
<td>10% to 20% (varies based on vehicle)</td>
</tr>
<tr>
<td>Oral Mucosal (Sublingual)</td>
<td>10 to 30 minutes</td>
<td>30 to 90 minutes</td>
<td>2 to 4 hours</td>
<td>20% to 40%</td>
</tr>
<tr>
<td>Topical</td>
<td>15 minutes to 1 hour</td>
<td>30 to 90 minutes</td>
<td>2 to 4 hours</td>
<td>20% to 40% (highly variable)</td>
</tr>
</tbody>
</table>

LeafLine Labs Medications

**DRUG DELIVERY METHODS**

- **Tangerine** (THC > CBD)
- **Heather** (THC = CBD)
- **Cobalt** (THC < CBD)
LeafLine Labs Medications
DRUG DELIVERY METHODS

Tangerine
(THC > CBD)

Heather
(THC = CBD)

LeafLine Labs Medications
DRUG DELIVERY METHODS

Tangerine
(THC > CBD)
LeafLine Labs Medications
DRUG DELIVERY METHODS

Heather
(THC = CBD)

Minnesota Medical Solutions
Minnesota Medical Solutions

Minnesota Medical Solutions
What’s NOT Legal in Minnesota

Plant Material (aka: “flower”/”bud”)
"Other" vape cartridges, Wax, & Shatter

Edibles
Patients first. Always.