Medical Marijuana: State of Affairs

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Presenter Disclosure

I have nothing to disclose concerning possible financial or personal relationships with commercial entities (or their competitors) that may be referenced in this presentation.

Educational Objectives

- Analyze the controversies between state and federal law as it applies to medical marijuana and the historical context of regulations
- List the potential therapeutic uses of marijuana
- Discuss the different approaches states have taken to permit marijuana to be used for medical purposes
- Present medical marijuana’s current state of affairs in Florida
- Review the legal issues related to medical marijuana use and the implications to the pharmacist
“Marijuana”
What Do You Think?

- What comes to mind?
- What kind of people come to mind?
- Are your thoughts positive, negative, or mixed?

Who Uses Marijuana?

Kim (22 years old)
Sofia & Terry (46 and 48 years old)
Maria (82 years old)

Marijuana History Timeline

- 2727 BC: Earliest known record of use
- 1545: Introduced to the West by Spaniards
- 1619: Jamestown law required colonists to grow hemp
- 1850: Cannabis extract sold in pharmacies
Marijuana History Timeline

1906
- US restrictions began; tagged as "poison"

1910
- Influx of Mexican immigrants
- Recreational use of marijuana spread among minorities
- Regulations as a drug in most states were placed

1929-1936
- Marijuana Tax Act
- Imposed registration, reporting requirements and a tax

1937
- CSA: Controlled Substances Act

1941
- Removed from the USP

1952
- Boggs Act

1956
- Narcotics Control Act

1970
- CSA classifies cannabis as a Schedule I drug

1978
- Use of cannabis was approved through the Compassionate IND of the FDA to be obtained from the NIDA

1985
- Marinol® approved by the FDA

1996
- California becomes first state to legalize MMJ

Prog Med Chem. 1987;24:159-207.

IND: Investigational New Drug
FDA: Food and Drug Administration
NIDA: National Institute on Drug Abuse
MMJ: Medical Marijuana
Current Marijuana Laws

- 23 states, the District of Columbia, and Guam allow for comprehensive MMJ programs.
- 17 states allow use of "low THC, high CBD" products in limited situations.
- Washington and Colorado allow recreational use.

Past-Month Use of Selected Illicit Drugs

Past-Month Illicit Drug Use 2013

- Illicit Drugs: 24.4
- Marijuana: 13.8
- Prescription Drugs: 6.5
- Cocaine: 4.5
- Hallucinogens: 1.1
- Inhalants: 0.5
- Heroin: 0.2

Past-Month Use of Selected Illicit Drugs 2013

- Number in Millions
State Medical Marijuana Programs Increase Drug Use?

Passage of state MMJ laws does not appear to lead to greater use by adolescents overall. However, states with MMJ programs had an increased use.

Cannabis

- Cannabis sativa or Cannabis indica plant
  - Over 400 chemicals
  - Over 70 cannabinoids
- Most abundant cannabinoids
  - Delta-9-tetrahydrocannabinol (THC)
  - Cannabidiol (CBD)

Endocannabinoid System

Endocannabinoids are substances our bodies make naturally to stimulate cannabinoid (CB) receptors.

- Anandamide
- 2-arachidonoylglycerol (2-AG)
Endocannabinoid System

**CB₁ receptor**
- Cerebellum: Coordination and muscle control
- Hippocampus: Memory storage and recall
- Cerebral cortex: Perceptual awareness/consciousness
- Hypothalamus: Metabolic processes (appetite)
- Amygdala: Emotions
- Brain stem: Arousal, vomiting reflex, heart rate, and pain

*References*

Endocannabinoid System

**CB₂ receptor**
- Immunologic cells: B lymphocytes and natural killer cells
- Brain: Role not well established

*References*

**Potential Physiologic Responses**
- Improves sleep
- Anti-seizure effects
- Reduces anxiety
- Prevents nausea and stimulates appetite
- Reduces intraocular pressure
- Bronchodilator
- Anti-inflammatory
- Anti-proliferative
- Anti-viral
- Relaxes muscles and reduces muscle spasms
- Relieves pain (especially neuropathic)
Potential Adverse Effects

Visual disturbances
Lethargy and sedation
Impaired coordination
Slowed reaction time
Impaired memory formation
Coughing and sputum production
Wheezing
Tachycardia
Palpitations and arrhythmias
Hypertension/Hypotension

Adverse Effects of Marijuana

Acute
- Impaired short term memory
- Altered judgment
- Impaired motor coordination
- Motor vehicle accidents
- Paranoia, hallucination, and psychosis

Chronic
- Altered brain development*
- Cognitive impairment*
- Diminished life satisfaction and achievement*
- Increased risk of psychotic disorders
- Increases risk for respiratory illnesses
- Abuse and dependence

*Effect is strongly associated with initial marijuana use early in adolescence

Specific Ilicit Drug Dependence or Abuse in 2013

<table>
<thead>
<tr>
<th>Drug</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana</td>
<td>4,174</td>
</tr>
<tr>
<td>Painkillers</td>
<td>1,887</td>
</tr>
<tr>
<td>Cocaine</td>
<td>605</td>
</tr>
<tr>
<td>Meth</td>
<td>151</td>
</tr>
<tr>
<td>Heroin</td>
<td>60</td>
</tr>
<tr>
<td>Phencyclidine</td>
<td>603</td>
</tr>
<tr>
<td>Ecstasy</td>
<td>43</td>
</tr>
<tr>
<td>Inhalants</td>
<td>110</td>
</tr>
<tr>
<td>Sedatives</td>
<td>95</td>
</tr>
</tbody>
</table>

Increasing Potency of Marijuana

Pharmacokinetics

Drug Interactions

Metabolism primarily by CYP-450 2C9, 3A4 and 2C19

These INHIBITORS may increase the pharmacological effect and duration of THC
- Macrolide antibiotics
- Oral contraceptives
- Proconvulsive, fluoxetine
- Proton pump inhibitors
- Antifungals

These INDUCERS may decrease the pharmacological effect and duration of THC
- Carbamazepine
- Rifampin
- Phenytoin
- Ritonavir
- St. John's Wort

Increase THC effects

Decrease THC effects

Institute of Medicine, 1999:33-82.
Am J Health Sys Pharm. 2007;64:1037-1044.

Vaporized or smoked
Oral ingestion
Topical Application

Lungs
Gut
Skin

Routes of Administration

Inhbitors may increase the pharmacological effect and duration of THC

Inducers may decrease the pharmacological effect and duration of THC
Drug Interactions

- THC is a CYP1A2 inducer
  - Theophylline
  - Clozapine
  - Chlorpromazine
  - Tricyclic antidepressants

- CBD is a powerful inhibitor of CYP3A4 and CYP2D6
  - Antihistamines
  - Haloperidol
  - Sildenafil
  - Calcium channel blockers
  - Macrolide antibiotics

Drug Interactions

- Anticholinergics
- Phenobarbital
- Benzodiazepines
- Alcohol
- Opiates

Impact of Medical Marijuana on Opioid Use

- Cannabinoids can lead to greater cumulative relief of pain and potential reduction in opiate use
- As an analgesic, it has activity comparable to codeine
  - 20 mg THC is more effective than 120 mg codeine
- Potentially less dangerous than opiates
- Estimated Relative Risk of Death from Illicit Drugs

<table>
<thead>
<tr>
<th>Opioids</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cocaine</td>
<td>4.7-7.6</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>6.2</td>
</tr>
<tr>
<td>Cannabis</td>
<td>1</td>
</tr>
</tbody>
</table>

Note: Cannabis deaths likely underestimated (e.g., motor vehicle accidents and respiratory diseases)
Marijuana’s Medical Potential: Research Evidence

- Appetite stimulant in HIV/AIDS
- Antiemetic
- Pain
- Antispasmodic for MS
- Glaucoma
- Anxiety
- Insomnia

Marijuana’s Medical Potential: Ongoing Clinical Trials

- Knee Osteoarthritis Pain
- Sickle Cell Disease Pain
- Cancer-Related Pain
- Spinal Cord Injury Pain
- Painful Diabetic Neuropathy
- Painful HIV Neuropathy
- Inflammatory Bowel Disease
- Attention Deficit Hyperactivity Disorder
- Schizophrenia
- Post Traumatic Stress Disorder
- Refractory Epilepsy
- Tinnitus

Legalization vs. Prohibition
Before FDA approves a drug as medicine, testing is done to:

- Determine the benefits and risks of the drug
- Determine how it may interact with other drugs
- Assure standardization of the drug
- Determine the appropriate dosage levels
- Identify and monitor side effects
- Identify safe drug administration

FDA’s Role in the Drug Approval Process

Different Kinds of Marijuana-Based Medicine

Single molecule pharmaceuticals - Synthetic THC

- **Dronabinol (Marinol®)**
  - For anorexia associated with weight loss in patients with AIDS
  - For nausea and vomiting associated with chemotherapy

- **Nabilone (Cesamet®)**
  - For nausea associated with chemotherapy

Liquid extract from *Cannabis sativa*

- **Nabiximols (Sativex®)**
  - Approved in UK and exported to a total of 28 countries to date
  - For spasticity due to MS
  - US Phase III trials to alleviate pain due to cancer

- **Cannabidiol (Epidiolex®)**
  - Orphan drug designation granted in Dravet and Lennox-Gastaut syndromes by FDA
Current FDA’s Conclusions and Statements on Marijuana

- FDA has NOT approved marijuana as a safe and effective drug for any indication.
- No animal or human data from scientific studies supported the safety or efficacy of marijuana for general medical use.
- Alternative FDA-approved medications exist to treat many of the proposed uses of smoked marijuana.

Florida Compassionate Use of Low-THC Cannabis

Florida Department Health Office of Compassionate Use

Definitions

Low-THC cannabis
- Mean of the genus Cannabis, flowers, seeds, or any preparation
- Has 0.8% or less of THC and more than 10% of CBD w/w

Medical use
- Administration of ordered amount
- Does not include possession, use, or administration by smoking
- Does not include transfer to another person

Qualified patient
- Resident of FL added to the compassionate use registry by a physician

Smoking
- Inhaling a substance and inhaling the smoke
- Smoking does not include the use of a vaporizer
Before ordering low-THC cannabis the **ordering physician** shall successfully complete an 8-hour CME course and examination
- CME course shall be offered at least **annually**

In addition, the **medical director of the dispensing organization** shall successfully complete a 2-hour CME course and examination

These CME courses and examinations are required each time the ordering physician or/and the medical director of the dispensing organization renew her/his license.

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**Physician Education**

**Florida Compassionate Medical Cannabis CME courses**

- Florida Medical Association
  - [http://www.fmedical.org/Cannabis_Course.aspx](http://www.fmedical.org/Cannabis_Course.aspx)

- Florida Osteopathic Medical Association
  - [http://www.foma.org/low-tch-cannabis-course-for-physicians.html](http://www.foma.org/low-tch-cannabis-course-for-physicians.html)

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**Physician Ordering**

Effective **January 1, 2015**, a physician may order for the patient’s medical use low-THC cannabis if a patient is suffering from:

- **Cancer**
- Medical condition that chronically produces **seizures**
- Severe and persistent **muscle spasms**
**Physician Ordering**

The following conditions are **ALL** required to qualify:

- Permanent resident of Florida
- Potential benefits of low-THC cannabis outweighs the risks
- 2nd physician evaluation for patients <18 years of age
- Physician is registered as the orderer for that patient on the registry and he/she updates the contents of the order
- Voluntary informed consent to treatment is obtained from the patient or the patient’s legal guardian
- Physician maintains a **patient treatment plan**
- Physician must deactivate the patient’s registration when treatment is discontinued

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**Treatment Plan**

- Submit **quarterly** to the University of Florida College of Pharmacy
- Information will be used for research on the safety and efficacy of low-THC cannabis
- Template Treatment Plan Forms that physicians must use to order low-THC cannabis can be found at:
  - [http://pharmacy.ufl.edu/mmtp/](http://pharmacy.ufl.edu/mmtp/)

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**Key Parts of Treatment Plan**

Once low-THC cannabis has been ordered, the physician must maintain a treatment plan that includes the following:

- Patient identifier
- Clinical history and condition
- Dose and type of administration
- Planned duration of therapy
- Monitoring of patients symptoms
- Other indicators of tolerance or reaction to low-THC cannabis

- Initial vs Follow-up Treatment Plan
### Initial Treatment Plan

**Clinical History and Condition**
- Patient's chief complaint that led to the evaluation for cannabis treatment
- Symptoms description in terms of type, frequency, severity, and duration
- Prior treatment(s), duration, and the outcomes
- Patient's social history, comorbidities, and current medications

### Monitoring Plan and Severity of Illness
- Plan for managing the patient by stating the treatment goals
- Monitoring plan and patient follow-up
- Description of how ill the patient is at the time

#### Patient information
- Name of 2nd physician if patient <18 years old
- Cannabis order as entered in the registry

#### Ordering physician information
- Name of ordering physician
- Date of order
- Type of administration

#### Initial Treatment Plan
- Monitoring Plan of Intense 1
- Intensive Letter according to date
- Monitoring Plan of Intense 2
- Monitoring Plan of Intense 3
- Monitoring Plan of Intense 4
- Monitoring Plan of Intense 5
- Description of how ill the patient is at the time

#### Clinical History and Condition
- Patient's chief complaint that led to the evaluation for cannabis treatment
- Symptoms description in terms of type, frequency, severity, and duration
- Prior treatment(s), duration, and the outcomes
- Patient's social history, comorbidities, and current medications

#### Monitoring Plan and Severity of Illness
- Plan for managing the patient by stating the treatment goals
- Monitoring plan and patient follow-up
- Description of how ill the patient is at the time
Every 3 months a follow-up treatment plan must be prepared and submitted

Changes in the cannabis order and reasoning

Changes in the chief complaint, symptoms, co-morbidities, and current medications

Reactions to Cannabis and Outcomes

Description of any problems the patient have experienced with the use of low-THC cannabis

Whether the patient discontinued cannabis during the past quarter

Changes to the treatment goals and the monitoring plan

Comparison of patient’s condition at initiation of cannabis treatment

Penalties

Misdemeanor of first degree, if:

- Physician orders low-THC cannabis for a patient without any indicated condition indicated to be used for
- A person fraudulently claims as having cancer or seizures or severe and persistent muscle spasms for the purpose of being ordered low-THC cannabis
Dispensing Organization

An organization approved by the department to cultivate, process, and dispense low-THC cannabis

➢ Before dispensing cannabis to a qualified patient, the dispensing organization shall verify that the:
   • Patient is active in the Compassionate Use Registry
   • Order presented matches the order contents in the registry
   • Order has not already been filled

➢ Upon dispensing the cannabis, the dispensing organization shall:
   • Record in the registry the date, time, quantity, and form of low-THC cannabis dispensed

Medical Marijuana and the Role of a Pharmacist

Pharmacists should be able to assess patients’ medication and health status and counsel them on:

➢ Its effects on cognition; the risks associated with inhaled carcinogens; and respiratory conditions
➢ Other adverse effects which may include psychological dysfunction and cardiac adverse effects
➢ Drug-drug interactions with other medications

Currently, Connecticut is the only state at which pharmacists are allowed to dispense cannabis for medical use

Summary of Key Concepts

➢ Marijuana use for medical purposes can be traced back to years
➢ There is limited peer-reviewed, published literature on the therapeutic use of inhaled cannabis
➢ CSA lists marijuana as a Schedule I substance
➢ Conflicting federal and state law creates a scenario in which pharmacists can be acting lawfully under state law while simultaneously being at risk of federal prosecution
➢ Marijuana may be less dangerous than other opiates, however, there is still the risk of adverse effects
➢ Smoking marijuana will remain illegal in FL even for MMJ patients
➢ Pharmacists need to stay abreast of several emerging trends: evolving state laws and the development of synthetic cannabinoid analogues
1. When evaluated as an analgesic, marijuana has activity comparable to codeine.  
**TRUE**

2. The Marijuana Tax Act prohibited the use of marijuana for medical purposes.  
**FALSE**

3. Cannabis was listed in the USP as a medicinal agent until 1941.  
**TRUE**

References


References


Robbe H. Marijuana's impairing effects on driving are moderate when taken alone but severe when combined with alcohol: a review of empirical research. Hum Psychopharmacol Clin Exp. 1998;13(S2):S70-S78. DOI: 10.1002/(SICI)1099-1077(1998110)13:2+<S70::AID-HUP50>3.0.CO;2-R.


References


References

THANK YOU FOR YOUR TIME!

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Miami VA Healthcare System

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