

1 **PHARMACOLOGIC
MECHANISM AND
DRUG INTERACTIONS
OF THC AND CBD**

ALEX ROCK

PHARMD. AAHIVP.

2 **VARIETIES / PRIMARY CHEMICALS**

- Cannabis Sativa and Cannabis Indica
 - Herbal products, polypharmaceutical, up to 108 cannabinoid compounds¹
 -
- Tetrahydrocannabinol (THC) and Cannabidiol (CBD)
-
- Receptors² CB₁ and CB₂
-
-
-
-
-
-

3

4 **TERMINOLOGY / QUANTITIES**

- 1 joint year – a term used to describe someone who smokes 1 joint a day for a year
-
- 1 joint = 0.66 g¹, 0.43 g², 0.32 g³ (average of 0.47 g)
-
- Rolled cannabis is approximately 5-8% THC yielding 23.5-37.6 mg of THC/CBD ratio and concentration depends on the strain.
 - Some dispensaries will sell products up to 30% (141mg)
-
- Dispensaries will often label oral products with an mg content.

5

6

7 **ABSORPTION**

8 **DISTRIBUTION**

9 **METABOLISM**

10 **PREDICTING DRUG INTERACTIONS**

- CYP Inhibitors -> Increase substrate concentrations
- CYP Inducers -> Decrease substrate concentrations
-

11 **CYP 3A4**

1 INDUCER

- 2 • Efavirenz
- Nevirapine
 - Carbamazepine/Oxcarbazepine
 - Glucocorticoids
 - Modafinil
 - Phenobarbital
 - Phenytoin
 - Pioglitazone
 - Rifabutin
 - Rifampin
 - St Johns Wort

•

3 INHIBITOR

- 4 • Indinavir
- Nelfinavir
 - Ritonavir
 - Clarithromycin
 - Itra/Ketoconazole
 - Nefazodone
 - Saquinavir
 - Aprepitant
 - Erythromycin
 - Fluconazole
 - Grapefruit juice
 - Verapamil
 - Diltiazem
 - Cimetidine

•

12  **CYP 2C9**

1 INDUCER

- 2 • Rifampin
- Secobarbital

3 INHIBITOR

- 4 • Fluconazole
- Amiodarone
 - Fenofibrate
 - Fluvastatin
 - Fluvoxamine
 - Isoniazid
 - Lovastatin
 - Phenylbutazone
 - Probenicid

- Sertraline
- Sulfamethoxazole
- Teniposide
- Voriconazole
- Zafirlukast
-

13 **CYP 2C19 (CBD ONLY)**

1 INDUCER

- #### 2 • Carbamazepine
- Norethindrone
 - Prednisone
 - Rifampicin

3 INHIBITOR

- #### 4 • Lansoprazole
- Omeprazole
 - Pantoprazole
 - Rabeprazole
 - Chloramphenicol
 - Cimetidine
 - Felbamate
 - Fluoxetine
 - Fluvoxamine
 - Indomethacin
 - Ketoconazole
 - Modafinil
 - Oxcarbazepine
 - Probenecid
 - Ticlopidine
 - Topiramate
 -

14 **CBD**

1 INDUCER

- #### 2 • None defined

3 INHIBITOR

- #### 4 • UGT2B7 (gemfibrozil, lamotrigine, morphine, lorazepam)
- UGT1A9 (diflunisal, propofol, fenofibrate)
 - CYP2C8 (phenytoin)
 - CYP2C9 (phenytoin)
 - CYP2C19 (diazepam, clobazam)
 - CYP1A2 (theophylline/caffeine)
 - CYP2B6 (bupropion, efavirenz)

15 **SPECIAL POPULATIONS**

- CYP2C9 polymorphism
 - May have increased adverse events associated with medical cannabis due to decreased clearance.

16 **DRONABINOL (MARINOL)**
SYNTHETIC DELTA-9-TETRAHYDROCANNABINOL [DELTA-9-THC]

- MOA: Activates cannabinoid receptors CB₁ and CB₂,
-
- Effects: Affective, sensory, somatic, and cognitive
-
- Kinetics: 97% protein bound, highly lipophilic
-
- Contraindications: Hypersensitivity to dronabinol, sesame oil, alcohol and recent or current exposure to disulfiram- or metronidazole-containing products within 14 days.
-
- Warning/caution: Avoid use in pregnancy/breastfeeding and inform patients to report new and excessive nausea/vomiting
-
-
-

17 **CANNABIDIOL (EPIDIOLEX)**

- MOA: The precise mechanism for the treatment of epilepsy is unclear, the effect does not appear to be through activation of CB receptors
-
- Indication: Indicated for the treatment of seizures associated with Lennox-Gaust syndrome (LGS) and Dravet syndrome (DS) in pts. ≥2 years old
-
- Kinetics: ingestion with a fatty meal increased C_{max} by 5-fold, T_{1/2} is 56-61 hours when at steady state.
-
- Contraindications: Hypersensitivity to CBD, alcohol, sesame seed oil, strawberry flavor, and sucralose
-
- Warning/caution: Moderate/Severe Liver impairment (dose adjustment necessary), can raise creatinine (10%), increased suicidal ideation
-
-
-

18

19 **MEDICAL CANNABIS**
WHO AND HOW?

- Executive Office of Health and Human Services (EOHHS) restrictions:
 - If < 18 years old

- Two MA licensed MD's must diagnose the patient with (one that is BCP(S)) Illness that doesn't respond to other treatments AND
 - Is expected to result in death with in 2 years or if benefits outweigh the risks.
- 18 years old
- MA Drivers license or state ID card
 - OR Passport with proof of MA residency
 - Appropriate medical diagnoses AND provider-patient relationship
-

20

- Patient Registration – Annual renewal
 - <https://www.mass.gov/patients-of-the-medical-use-of-marijuana-program>
 - PIN #, MA ID, Photograph, payment (\$50), or proof of financial hardship.
 - Medical card lasts 3 years

21

- MA licensed MD or DO
 - Active full license with no prescribing restrictions
 - MA Controlled Substance Registration (MCSR)
 - At least one established place of practice in MA
- Completion of 2 continuing professional development credits
- Registration with Cannabis Control Commission (CCC) via Medical Use of Marijuana Online System “MMJ online system”
- Can NOT be associated with a registered medical dispensary

- -
-

22 **RESOURCES**

- International cannabinoid research society
 - <http://www.icrs.co/index.html>
 - International association for cannabinoid medicine
 - <http://www.cannabismed.org>
 - Massachusetts Medical Society
 - <http://www.massmed.org/Continuing-Education-and-Events/>
-
-

-