# CANNABIS & HIDRADENITIS SUPPURATIVA

1


2

# CANNABINOIDS – OVERVIEW

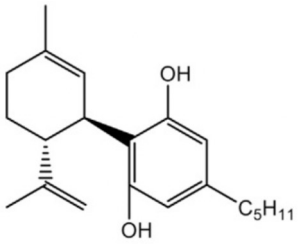
- CLASS OF BIOLOGICAL COMPOUNDS THAT BIND TO CANNABINOID RECEPTORS
- MARIJUANA CONSISTS OF MORE THAN 421 COMPONENTS AND 60 PHARMACOLOGICALLY ACTIVE CANNABINOIDS
  - THE TWO BEST-DESCRIBED CANNABINOIDS ARE DELTA9-TETRAHYDROCANNABINOL (THC) AND CANNABIDIOL (CBD)
  - MOST OF THE OTHER COMPOUNDS ARE NOT YET UNDERSTOOD AND THEIR MENTAL AND PHYSICAL EFFECTS ARE UNKNOWN
- CANNABIS GENUS
  - *C. SATIVA, C. INDICA, AND C. RUDERALIS*

Sheikh NK, Dua A. Cannabinoids. StatPearls. 2025: Jan-Feb.

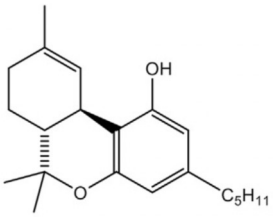
3

# CANNABINOIDS – MOA

- HIGHLY LIPOPHILIC
  - STORAGE IN ADIPOSE TISSUE, LIVER, MUSCLE AND SPLEEN
  - REDISTRIBUTION INTO THE BLOOD STREAM LONG AFTER INGESTION
  - THE HALF-LIFE OF INFREQUENT USERS IS 1.3 DAYS, 5-13 DAYS FOR FREQUENT USES
- METABOLISM
  - A MAJOR FRACTION OF THC IS DESTROYED BY PYROLYSIS
    - CAUSES VARIANCE IN SYSTEMIC BIOAVAILABILITY BETWEEN HEAVY AND OCCASIONAL USERS
  - MORE THAN 2000 COMPOUNDS ARE PRODUCED BY PYROLYSIS
    - MOST OF THESE ARE UNKNOWN IN THEIR CLINICAL STRUCTURE AND PHYSICAL AND MENTAL EFFECTS
  - CYTOCHROMES INVOLVED IN THE OXIDATION OF THC ARE CYP450
    - THC INDUCES CYP1A2
    - CBD INHIBITS CYP3A4, CYP2D6



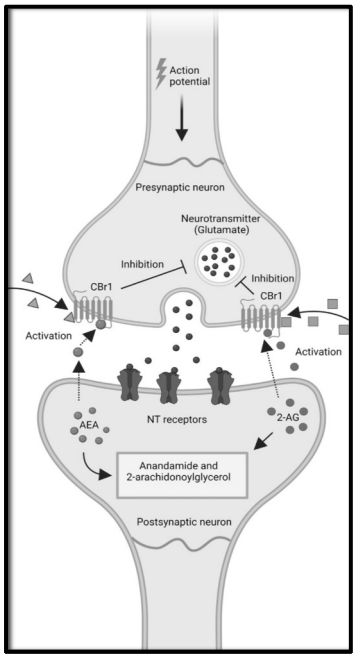

**CBD**




**THC**

Sheikh NK, Dua A. Cannabinoids. StatPearls. 2025: Jan-Feb.

4



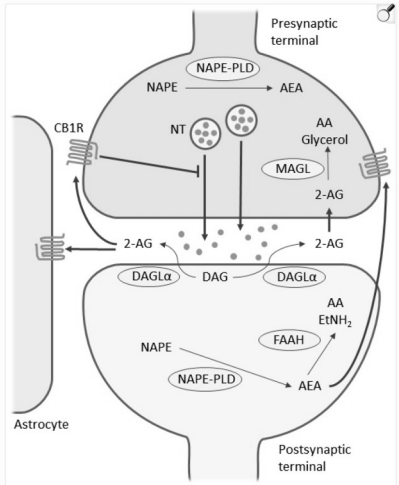

# CANNABINOIDS – MOA

- BINDS TO TWO TYPES OF G-PROTEIN-COUPLED RECEPTORS, CB1 AND CB2
  - CB1 = BRAIN AND THE SPINAL CORD
  - CB2 = IMMUNE SYSTEM
- ENDOGENOUS PRODUCTION
  - 2-ARACHIDONOLGLYCEROL (2-AG) IS BIOSYNTHESIZED FROM DIACYLGLYCEROL (DAG) BY DIACYLGLYCEROL LIPASE-A (DAGLA)
  - ANANDAMIDE (AEA) IS SYNTHESIZED FROM N-ACYL-PHOSPHATIDYLETHANOLAMINE (NAPE) BY NAPE-SPECIFIC PHOSPHOLIPASE D (NAPE-PLD)

Sheikh NK, Dua A. Cannabinoids. StatPearls. 2025: Jan-Feb.

5

# CANNABINOIDS – MOA




- CANNABINOID RECEPTORS ARE PREDOMINANTLY LOCATED ON PRESYNAPTIC NEURONS
- RETROGRADE DIFFUSION FROM POST → PRE
  - AGONIST AT CB1R
  - ACTIVATION INHIBITS THE RELEASE OF THE NEUROTRANSMITTERS ACETYLCHOLINE AND GLUTAMATE FROM THE PRESYNAPTIC NEURON
    - ON THE ASTROCYTE, IT CAUSES RELEASE OF GLUTAMATE
  - INDIRECTLY AFFECTS Y-AMINOBUTYRIC ACID, N-METHYL-D-ASPARTATE, OPIOID AND SEROTONIN RECEPTORS

Zou S, Kumar K. Cannabinoid receptors and the endocannabinoid system: Signaling and function in the central nervous system. *Int J Mol Sci*. 2018 Mar 13;19(3):833.

6

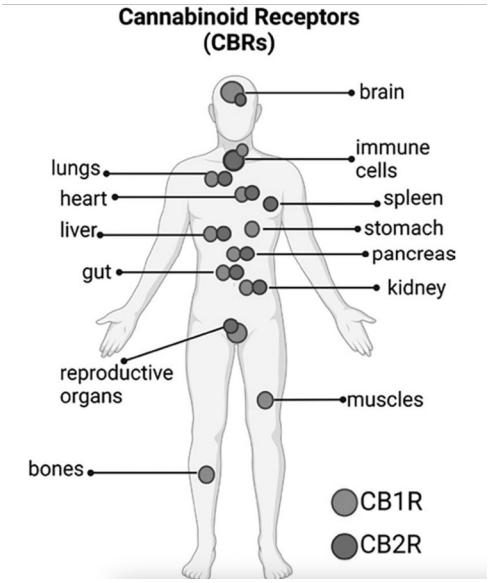
# CANNABINOIDS – MOA

## CB1

- HIPPOCAMPUS: IMPAIRMENT OF SHORT-TERM MEMORY
- NEOCORTEX: IMPAIRMENT OF JUDGMENT AND SENSATION
- BASAL GANGLIA: ALTERED REACTION TIME AND MOVEMENT
- HYPOTHALAMUS: INCREASED APPETITE
- NUCLEUS ACCUMBENS: EUPHORIA (↑ DOPAMINE)
- AMYGDALA: PANIC AND PARANOIA
- CEREBELLUM: ATAXIA
- BRAINSTEM: ANTI-EMESIS
- SPINAL CORD: ANALGESIA
- OTHER: DRY MOUTH, CONJUNCTIVITIS, TACHYCARDIA, HYPOTENSION, AND BRADYPNEA

## CB2

- IMMUNE AND INFLAMMATORY FUNCTIONS




Canseco-Alba A, Rodríguez-Manzo G. Cannabis: Drug of Abuse and Therapeutic Agent, Two Sides of the Same Coin. *Rev Invest Clin*. 2023; 75(3): 105-1028.

Sheikh NK, Dua A. Cannabinoids. StatPearls. 2025: Jan-Feb.

7

# CANNABINOIDS – ADMINISTRATION

## MEDICAL

- DRONABINOL
  - 2.5MG, 5MG, AND 10MG CAPSULE
  - 5MG/ML SUSPENSION
- NABILONE
  - 1MG CAPSULE
- CANNABIDIOL
  - 100 MG/ML SUSPENSION

## RECREATIONAL

- SMOKE
- VAPE
- INFUSED TEAS OR OILS
- EDIBLES
- SUBLINGUAL
- VAGINAL OR RECTAL
- OCULAR
- TRANSDERMAL
- AEROSOL

Sheikh NK, Dua A. Cannabinoids. StatPearls. 2025: Jan-Feb.

8

## CANNABINOIDS – USES

- EARLIEST USE
  - 3,000 BC (RECREATIONAL), 400 AD (MEDICAL)
- CHRONIC PAIN
- OPIOID DEPENDENCE
- EPILEPSY
- APPETITE STIMULATION (HIV/AIDS, CANCER, ETC.)
- TOURETTE SYNDROME
- MULTIPLE SCLEROSIS
- CHEMOTHERAPY-RELATED NAUSEA/VOMITING
- INFLAMMATORY CONDITIONS (AD, PSO, HS)

- • 3 FORMS IN MEDICINE
  - PHYTOCANNABINOIDS - DERIVED NATURALLY FROM FLORA
  - ENDOCANNABINOIDS - PRODUCED ENDOGENOUSLY
  - SYNTHETIC CANNABINOIDS – CREATED ARTIFICIALLY
- 3 TYPES APPROVED BY THE FDA
  - DRONABINOL
  - NABILONE
  - CANNABIDIOL

Sheikh NK, Dua A. Cannabinoids. StatPearls. 2025: Jan-Feb.

9

## WHAT DOES THIS MEAN FOR HS PATIENTS?

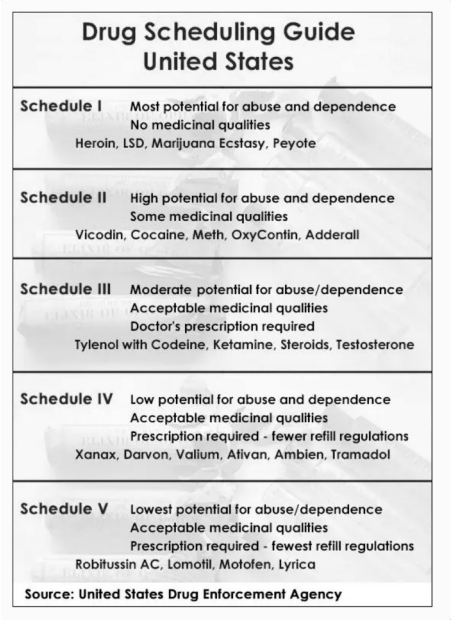
DEARTH OF RESEARCH!!!

10

# LEGALIZATION

- 48 STATES AND DC HAVE LEGALIZED MEDICAL USE
- 24 STATES FOR RECREATIONAL USE

- MARIJUANA IS A SCHEDULE 1 FEDERAL DRUG IN THE USA
  - HIGH ABUSE POTENTIAL
  - NO ACCEPTED MEDICAL USE
  - LACK OF ACCEPTED SAFETY
  - HEROIN, LSD, MDMA (ECSTASY), PEYOTE



**Drug Scheduling Guide**
**United States**

| | | |
|---|---|---|
| **Schedule I** | Most potential for abuse and dependence<br>No medicinal qualities | Heroin, LSD, Marijuana Ecstasy, Peyote |
| **Schedule II** | High potential for abuse and dependence<br>Some medicinal qualities | Vicodin, Cocaine, Meth, OxyContin, Adderall |
| **Schedule III** | Moderate potential for abuse/dependence<br>Acceptable medicinal qualities<br>Doctor's prescription required | Tylenol with Codeine, Ketamine, Steroids, Testosterone |
| **Schedule IV** | Low potential for abuse and dependence<br>Acceptable medicinal qualities<br>Prescription required - fewer refill regulations | Xanax, Darvon, Valium, Ativan, Ambien, Tramadol |
| **Schedule V** | Lowest potential for abuse/dependence<br>Acceptable medicinal qualities<br>Prescription required - fewest refill regulations | Robitussin AC, Lomotil, Motofen, Lyrica |

**Source: United States Drug Enforcement Agency**

11

# PATHOPHYSIOLOGY IN HS

- ABUNDANT EXPRESSION OF CANNABINOID RECEPTORS ON SEBOCYTES, KERATINOCYTES, HAIR FOLLICLES, MELANOCYTES, AND IMMUNE CELLS

- ANIMAL MODELS
  - ENDOCANNABINOIDS TARGET TRPV1 AND TRPA1 CHANNELS (SENSORY PERCEPTION, PARTICULARLY IN PAIN AND INFLAMMATION)
    - INCREASED PRODUCTION AND SECRETION OF PRO-INFLAMMATORY IMMUNOMODULATORS
      - IL-1A, IL-1B, IL-8, PROSTAGLANDIN E2
    - INCREASED RELEASE OF PROINFLAMMATORY AND VASODILATORY RELATED PEPTIDES
  - PHYTOCANNABINOIDS STIMULATE INCREASE IN SEBUM PRODUCTION

Saad A., Cahn B, Haber R. Unveiling the green connection: Cannabis as a potential trigger for hidradenitis suppurativa. *Arch Dermatol Res*. 2024; 316: 141.

12

# USAGE IN HS

- 2024:
  - HS: 34% (RANKS #3, AFTER ATOPIC DERMATITIS AND CONTACT DERMATITIS)
    - SMOKING (36.8%), EDIBLES (11.1%), COMBINATION OF BOTH (52.1%)
  - PSORIASIS: 11.6%
  - GENERAL POPULATION: 11.0%

- CANNABIS USAGE PRECEDES ONSET OF ANY HS SYMPTOMS IN 70%
  - NOTABLY FOR RECREATION VS PAIN MANAGEMENT OR MENTAL HEALTH

Saad A., Cahn B, Haber R. Unveiling the green connection: Cannabis as a potential trigger for hidradenitis suppurativa. *Arch Dermatol Res*. 2024; 316: 141.

13

# SYMPTOM BENEFITS

- REDUCED PAIN
  - 12% OF PROFESSIONALLY MANAGED HS PATIENTS ARE PRESCRIBED CANNABINOIDS AS A PHARMACOLOGIC ANALGESIC FOR CHRONIC HS PAIN
    - EVEN THE HIGHEST RATED PAIN MANAGEMENT MODALITIES ARE ONLY CONSIDERED MODERATELY EFFECTIVE BY HS PATIENTS
      - MARKEDLY BETTER COMPARED TO CONVENTIONAL ANALGESICS LIKE IBUPROFEN AND ACETAMINOPHEN ($P < .0001$)
      - SLIGHTLY GREATER COMPARED TO OPIOIDS
- ITCH
  - TRPV1 RECEPTOR, WHICH PLAYS A ROLE IN ITCH, CAN BE "CLOSED" BY CANNABINOIDS, BLOCKING ITCH SIGNALS
  - REDUCE INFLAMMATION

- SLEEP
  - DECREASE SLEEP LATENCY (THE TIME IT TAKES TO FALL ASLEEP) AND INCREASED SLOW-WAVE SLEEP (DEEP RESTORATIVE SLEEP)
  - REDUCED REM SLEEP

Metko D, Mehta S, Piguet V. Cannabis usage among patients with hidradenitis suppurativa: A scoping review. *J Cutan Med Surg*. 2024; 28(3): 307-308.

14

# SYSTEMIC BENEFITS

- IMMUNOSUPPRESSION
  - APOPTOSIS OF IMMUNE CELLS
  - DECREASED PROLIFERATION OF IMMUNE CELLS BY ↑ TREGS
  - REDUCED CYTOKINE PRODUCTION
  - EXPEDITED WOUND HEALING
- CARDIOVASCULAR
  - TACHYCARDIA
  - VASODILATION
  - HYPOTENSION
- RESPIRATORY
  - CARBON MONOXIDE
  - BRONCHIAL IRRITANTS
  - MUTAGENS (INITIATE TUMORS)
  - CARCINOGENS (PROMOTE TUMOR GROWTH)
    - BENZANTHRACENES AND BENZPYRENES

Ashton CH. Pharmacology and effects of cannabis: A brief review. Brit J Psych. 2001;178: 101-106.

15

# PSYCHOLOGICAL BENEFITS

- EFFECTS ON MOOD
  - EUPHORIA AND PLEASURE
- EFFECTS ON PERCEPTION
  - VISUAL, SPATIAL, AND TEMPORAL DISTORTION
  - HEIGHTENED EMOTIONS
- EFFECTS ON COGNITION AND PSYCHOMOTOR PERFORMANCE
  - SLOW REACTION TIME
  - MOTOR INCOORDINATION
  - SHORT-TERM MEMORY IMPAIRMENT

Ashton CH. Pharmacology and effects of cannabis: A brief review. Brit J Psych. 2001;178: 101-106.

16

# CANNABINOIDS – SHORT-TERM ADVERSE EFFECTS

## MILD

- EUPHORIA
- ANXIOLYSIS
- TACHYCARDIA
- VISUOTEMPORAL DISTORTION
- SENSORY AMPLIFICATION
- POSTURAL HYPOTENSION
- CONJUNCTIVITIS,
- HUNGER
- DRY THROAT, MOUTH, AND EYES

## SEVERE

- PANIC ATTACKS
- MYOCLONUS
- PSYCHOSIS
- HYPEREMESIS
- INHALATION BURNS,
- ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)
- BRONCHOSPASM

Sheikh NK, Dua A. Cannabinoids. StatPearls. 2025: Jan-Feb.

17

# CANNABINOIDS – LONG-TERM ADVERSE EFFECTS

- ADDICTION
- ALTERED BRAIN DEVELOPMENT
- COGNITIVE IMPAIRMENT
- CHRONIC BRONCHITIS
- ARDS
- LUNG CANCER
- INCREASED RISK FOR MYOCARDIAL INFARCTION, STROKE, AND THROMBOEMBOLIC EVENTS
- EXACERBATION OF MOOD DISORDERS (ANXIETY, DEPRESSION) AND PSYCHOTIC DISORDERS (SCHIZOPHRENIA)
- EXACERBATION OF NEURODEGENERATIVE DISEASES (MULTIPLE SCLEROSIS, ALZHEIMER DISEASE, PARKINSON DISEASE)
- WITHDRAWAL EFFECTS
  - ANXIETY, DEPRESSION, DECREASED APPETITE, HEADACHES, INSOMNIA, IRRITABILITY, MUSCLE TENSION, NAUSEA, NIGHTMARES AND UNPLEASANT VIVID DREAMS

Sheikh NK, Dua A. Cannabinoids. StatPearls. 2025: Jan-Feb.

18


19