

## 1 A CBD Primer

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## 2 What is CBD Exactly

- ▶ CBD = Cannabidiol
  - ▶ One of hundreds of bioactive phytochemicals of the cannabis sativa plant
- ▶ *Cannabis sativa*
  - ▶ Industrial hemp bred for very low THC content
  - ▶ Marijuana bred for high THC content
- ▶ CBD is the major non-psychoactive component of *Cannabis sativa*
  - ▶ NIH
- ▶ CBD was declassified as a drug in 2018 Farm Bill
- ▶ DEA no longer schedules CBD
- ▶

## 3 Medical Marijuana Movement

- ▶ THC is still schedule 1
  - ▶ “no currently acceptable medical use”
  - ▶ High abuse potential
  - ▶ Felony to possess
- ▶ 33 States have legalized Medical Marijuana
- ▶ 10 States have legalized Recreational marijuana
- ▶ CO tax revenue 2018 was \$266,529,637.00

## 4 Medical Marijuana Uses

- 1 ▶ Pain control in fibromyalgia, cancer, rheumatoid arthritis, chronic pain
  - ▶ Epilepsy treatment
  - ▶ MS
  - ▶ Alzheimer’s
  - ▶ HIV/AIDs
  - ▶ Glaucoma
  - ▶ ALS
  - ▶ Parkinson’s
  - ▶ PTSD
- 2 ▶ Safe – few deaths
  - ▶ Self-titratable
  - ▶ Relatively inexpensive
  - ▶ Could reduce use of opioids

## 5

## 6 Two sides to THC Story

- 1 ▶ Well designed and randomized trials are lacking
  - ▶ No rigorous FDA approval process
  - ▶ Standardization of components is lacking

- ▶ Adverse health effects (smoking)
- ▶ Unmasking of mental health disorders
- ▶ No packaging standards
- ▶ Inadvertent use by minors or pets is a risk
- 2 ▶ Evidence to support use in many conditions
  - ▶ Beneficial cannabinoids exist in plant as well
  - ▶ Relatively safe with few deaths
  - ▶ Public support
  - ▶ eCB system exists in human body

## 7 Regulation of Marijuana

- 1 ▶ Physicians cannot prescribe this, they may only RECOMMEND or CERTIFY
  - ▶ Insurance won't cover this
    - ▶ Federal, private, WC
  - ▶ Research is not funded except privately
  - ▶ Illegal to drive on marijuana, even with a 'certification', thus research even harder to do
  - ▶ No banking allowed for marijuana
    - ▶ Taxes are still taken
- 2 ▶ Evolved into a cash-based business
  - ▶ CBD has been an incidental component of THC
    - ▶ Plant-based therapy for eCB system
    - ▶ Largely ignored by modern medicine and MD/DOs due to connections to THC
    - ▶ Illegal to use or prescribe until now
    - ▶ Now it is safe to discuss the science and to use this awesome botanical (CBD, not THC)

## 8 Current FDA approved and studied THC drugs

- 1 ▶ Sativex
  - ▶ Dronabinol
  - ▶ Marinol
  - ▶ Cesamet
  - ▶ Cannador
  - ▶ Acomplia
  - ▶ Ajulemic acid
  - ▶
- 2 ▶ Cannabinor
  - ▶ Selective binding of CB2
  - ▶ Synthetic
  - ▶ Pharms Corporation

## 9 CBD

NON-PSYCHOACTIVE COMPONENT OF THE CANNABIS SATIVA PLANT

## 10 CBD is not an alkaloid

**It is an oxygen containing aromatic hydrocarbon without nitrogen**  
**Most psychoactive drugs are alkaloids**  
**morphine, cocaine, etc**

## 11 **The difference between CBD and THC**

### 12 **THC v CBD**

- ▶ THC likely works medically because most formulations also include CBD.
- ▶ CBD is the actual health component needed by humans
- ▶ THC is psychoactive and gets people high
- ▶ CBD is not and one simply feels better and healthier

### 13 **The Endocannabinoid System what makes it all possible**

- 1 ▶ Human cannabinoid receptors
  - ▶ Endogenous ligands
  - ▶ Metabolizing enzymes
  - ▶ "relax, eat, sleep, forget and protect"
  - ▶ Interacts and parallels major endogenous pain control systems
    - ▶ Endorphin/enkephalin
    - ▶ Vanilloid/transient receptor potential
- 2 ▶ 1988 – first cannabinoid receptor identified (CB1)
- ▶ 1993 – CB2
- ▶

### 14 **Nature has provided most pain medications already**

- 1 ▶ Papaver somniferum
  - ▶ Capsicum annuum
  - ▶ Capsicum frutescens
  - ▶ Cannabis sativa
  - ▶ Salix

### 15 **CBD: activates mainly the CB2 receptors of eCB**

- ▶ Anti-inflammatory
- ▶ Anti-spasmodic
- ▶ Analgesic
- ▶ Enhances circulation
- ▶ Promotes cellular regeneration
- ▶ Immunomodulator
- ▶ Anti-cancer

### 16 **Pain control with eCS system and CBD**

- ▶ Cannabinoids presynaptically inhibit glutamate release
- ▶ Glutamate is integral to neuropathic pain
- ▶ Via NMDA system, the glutamatergic system causes secondary and tertiary hyperalgesia associated with migraines and fibromyalgia

### 17

- 1 ▶ Cannabinoids block capsaicin-induced hyperalgesia
- ▶ Cannabinoids also reduce hyperalgesia by inhibiting calcitonin gene-related peptide
- ▶ CBD has more antioxidant activity than vitamin C or tocopherol.

- ▶ CBD inhibits TNF-alpha
  - ▶ MS, RA
- ▶ Beta-sitosterol is in cannabis and reduces skin edema and inflammation by 41% and 65%

#### 18 **CBD v NSAIDs**

- 1 ▶ NSAIDs have significant side effects
  - ▶ Gastric: Cox-1
  - ▶ Cardiac: Cox-2
- ▶ CBD has no effect on COX system
- ▶ CBD reduces PGE-2 and other inflammatory components
- 2 ▶ Animal study showed CBD potent anti-inflammatory
  - ▶ Reduced edema
  - ▶ Reduced PGE-2
  - ▶ Reduced Cox activity
  - ▶ Reduced production of nitric oxide and other free radicals
- ▶ Dose-dependent response
- ▶ Chemical injected into a paw

#### 19 **CBD and the brain**

- 1 ▶ Neuroprotective
  - ▶ Anti-oxidant
  - ▶ NFLPA recommends THC and CBD for TBI
  - ▶ Improves symptoms of insomnia as well
- 2 ▶ Nabilone studied for PTSD:
  - ▶ Better than placebo for improving nightmares, global clinical rate and general well-being
- ▶ CBD studied for social anxiety (public speaking)
  - ▶ Improved anxiety
  - ▶ This action has been shown to occur in the limbic and paralimbic areas of brain by SPECT

#### 20 **CBD Neuroprotection**

- ▶ Copes with oxidative stress
- ▶ Helps mitochondrial dysfunction
- ▶ Inflammatory changes
- ▶ Excitotoxicity
- ▶ Reduces iron accumulation
- ▶ Reduces protein aggregation
- ▶ Reduces infarct size in stroke models
- ▶ Up-regulates Cu-Zn superoxide dismutase; enzyme in endogenous defenses against oxidative stress

#### 21 **CEDS: clinical eCB deficiency syndromes**

- ▶ Migraine
- ▶ Fibromyalgia
- ▶ Irritable Bowel Syndrome
- ▶ Possibles
  - ▶ Depression
  - ▶ Parkinsons

- ▶ Anorexia
- ▶ Motion sickness
- ▶ Failure to thrive
- ▶ Huntingtons
- ▶ MS
- ▶ Schizophrenia

## 22 **CB1, CB2 and eCB system** **ENDOCANNABINOID**

- ▶ ECB SYSTEM DISCOVERED IN HUMANS
- ▶ SYSTEM IS MILLIONS OF YEARS OLD
  - ▶ EVOLUTIONARY
  - ▶ FOUND IN MAMMALS, FISH, BIRDS, MOLLUSCS, LEECHES
- ▶ IMPORTANT FOR NORMAL FUNCTINO OF THE BODY
- ▶ PHYTOCANNABINOIDS BIND TO SAME RECEPTORS AS ENDOCANNABINOIDS

## 23 **eCB system and CBD**

- 1 ▶ There are more endocannabinoid receptors in the body than all other receptors combined
  - ▶ 55% of all receptors
  - ▶ Only 13% of medical schools even mention eCB system
- ▶ eCB system keeps all other systems functioning properly
- 2 ▶ 20,000 published studies on eCB system
  - ▶ CBD and others are better as supplements than as drugs
    - ▶ They support other systems
    - ▶ They support homeostasis
    - ▶ They support normal function
    - ▶ They should not be used to treat a specific disease

## 24 **CB1, CB2 receptors**

- ▶ Inhibits conversion of ATP to cyclic AMP
- ▶ Interactions with ion channels
- ▶ G-protein-coupled receptors (GPCR)
- ▶ 1000-2000 such receptors known
- ▶ CB1 most abundant of GPCRs in brain

## 25 **CB2 receptor**

- ▶ Occur principally in immune cells
  - ▶ Leukocytes
  - ▶ Spleen
  - ▶ Tonsils
- ▶ Modulate the release of cytokines
  - ▶ Responsible for inflammation and immune regulation

## 26 **Endocannabinoids are amplified by phytocannabinoids**

- 1 ▶ Anandamide
  - ▶ 2-AG
    - ▶ FAAH breaks these down

- ▶ CBD inhibits FAAH
  - ▶ Fatty acid amide hydrolase
- ▶ More endogenous endocannabinoids are left to act on the cells and to reduce inflammation and control pain
- ▶ THC acts directly on CB1 and CB2 receptors
- ▶ CBD increases natural, body-made endocannabinoids that hit CB2

2 Regulates systems: Maintains homeostasis

- ▶ Limbic
- ▶ Metabolic
- ▶ Nociceptive
- ▶ Immune
- ▶ Gastric
- ▶ Circulatory

27  **Summary of CBD**

- ▶ Non-psychoactive component of hemp plant
  - ▶ Decriminalized federally
  - ▶ Not on DEA list
- ▶ Highly effective for improving the eCB system
- ▶ Very good pain control and anti-inflammatory activity
- ▶ No known side-effects
- ▶ Neuroprotective and anti-oxidant