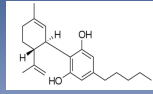


SCIENCE OF CANNABIDIOL MEDICATIONS

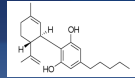


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CANNABIDIOL MEDICATIONS



Overview of the Presentation

- Discuss Antiseizure Effects and Doses
- Drug-Drug Interactions
- Evidence for Anxiolytic Effects
- Pharmacokinetic Food Effect



2

CANNABIDIOL AS AN ANTISEIZURE DRUG (ASD)

- Epidiolex (CBD) approved for rare childhood epilepsies- Dravets (DS) and Lennox Gastaut (LGS) syndromes
- **DS:** rare genetic condition frequent fever-related seizures (prior to 1st birthday), later other seizure types develop. High drug-resistance and mortality rate.
- **LGS:** Also rare ages 3-5, muscle contraction seizures, drop seizures and intellectual disabilities

Dose was 10-20 (Typically 20) mg/kg (~600mg+) CBD in addition to existing ASD regimen



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CANNABIDIOL AS AN ASD



- **DS:** 43% of CBD patients and 27% of placebo had >50% reduction in convulsive-seizure frequency
- **LGS:** 42% reduction in drop seizures in 20mg/kg group, 37% in 10mg/kg. 17% in placebo
- Adverse events included somnolence, decreased appetite, and diarrhea and abnormal liver-function (ALT/AST)

Trial of Cannabidiol for Drug-Resistant Seizures in the Dravet Syndrome. Devinsky et al N Engl J Med. 2017 May 25;376(21):2011-2020.

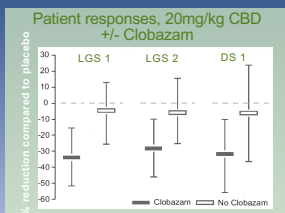
Effect of Cannabidiol on Drop Seizures in the Lennox-Gastaut Syndrome. Devinsky et al N Engl J Med. 2018 May 17;378(20):1888-1897.

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CANNABIDIOL DRUG INTERACTIONS

Some of the CBD effect may have been a drug interaction with one of the other ASDs (Clobazam)

Adverse Effects were also Interactive



- Sedation in 44% of CBD +Clobazam patients
- Sedation in 13% of CBD patients without Clobazam.
- CBD is not very sedative except as a drug interaction
- CBD Interaction with other ASDs were not significant

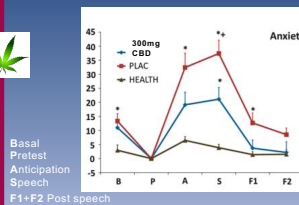
Reduced efficacy and risk of seizure aggravation when cannabidiol is used without clobazam (Rogowski MA, Epilepsy Behav. 2019. doi: 10.1016/j.yebeh.2019.106506)

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CANNABIDIOL AS AN ANXIOLYTIC

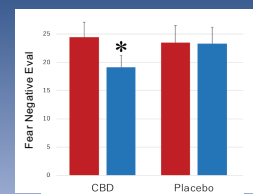
CBD Decreases Anxiety in Social Anxiety Patients

Simulated Public Speaking Test n=12



Beneguerche M-M, Quinlan R-H, Chagas M-H, de Oliveira D-C, De Martino B-S, Kugonowski F, Giamberini J, Rosser R, Schneider N, Nardi A-E, et al. (2019). Cannabidiol reduces the anxiety induced by simulated public speaking in treatment-naïve social phobia patients. *Neuropsychopharmacology*, 36, 1019-1026.

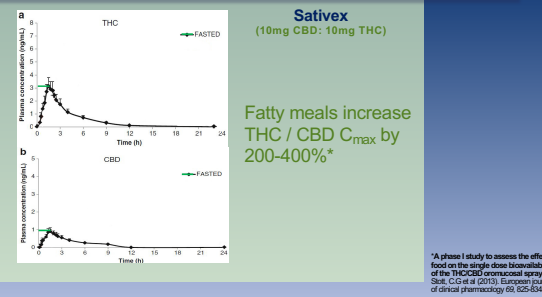
Social Anxiety n=37, 4wks 300mg CBD



Anxiolytic Effects of Repeated Cannabidiol Treatment in Teenagers With Social Anxiety Disorders. Masiata N. Front Psychol. 2019 Nov 6;10:2466. doi: 10.3389/fpsyg.2019.02466.

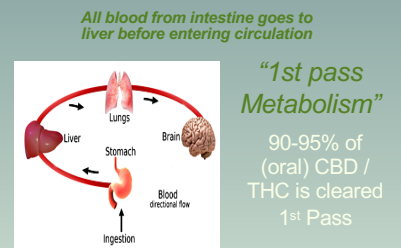
6

FATTY FOOD EFFECT ON CBD ABSORPTION



7

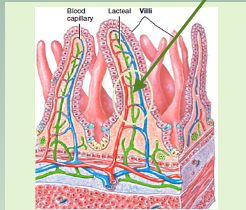
How does Fat increase Absorption?



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BUT!

Intestinal villi have a blood supply AND a lymphatic, "lacteal"

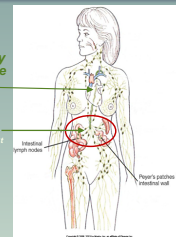


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Lymphatic bypass

Lymphatic lacteals empty into the circulation via the thoracic duct

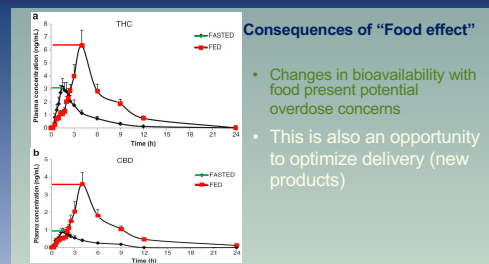
So when THC/CBD is dissolved in fat, hepatic first-pass elimination is reduced



Liposomal delivery systems for intestinal lymphatic drug transport Altmann JH, Park JH (2016) Biomater Res. (2016)

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FATTY FOOD EFFECT ON CBD ABSORPTION



*A phase I study to assess the effect of food on the single dose bioavailability of the THC/CBD oromucosal spray. Stoltz C et al (2013). European journal of clinical pharmacology 69, 525-534.

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Cannabidiol Summary

- Only "recognized indication" for CBD is Epilepsy. Dose is ~600-1500 mg/day
- Evidence for anxiety reduction is increasing (300-500 mg/day)
- Somnolence found with Epidiolex likely due to drug interaction
- CBD probably not sedative. No sedation in 900mg CBD anxiety study or in NIDA single dose study (1500 mg)
- Lots of discussion how much CBD interacts with other drugs. Not much demonstrated except clobazam.
- There is a large food effect with CBD, your actual dose may depend on how you take it.

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