

Key Webinar Points - FDA Drug Topics: Cannabis Products and the Potential Impact on Patients

Background:

- > 500 compounds in *Cannabis sativa* L. plant
 - Δ 9- tetrahydrocannabinol (Δ 9-THC) is intoxicating
 - cannabidiol (CBD) alone is not intoxicating
- State-regulated products vary widely (medical & adult-use)
- Hemp products largely unregulated & widely available (e.g., gas stations, online)
- Products can be manufactured from plant parts or from chemicals
- Labeling may be misleading (e.g., hidden ingredients)

Clinical:

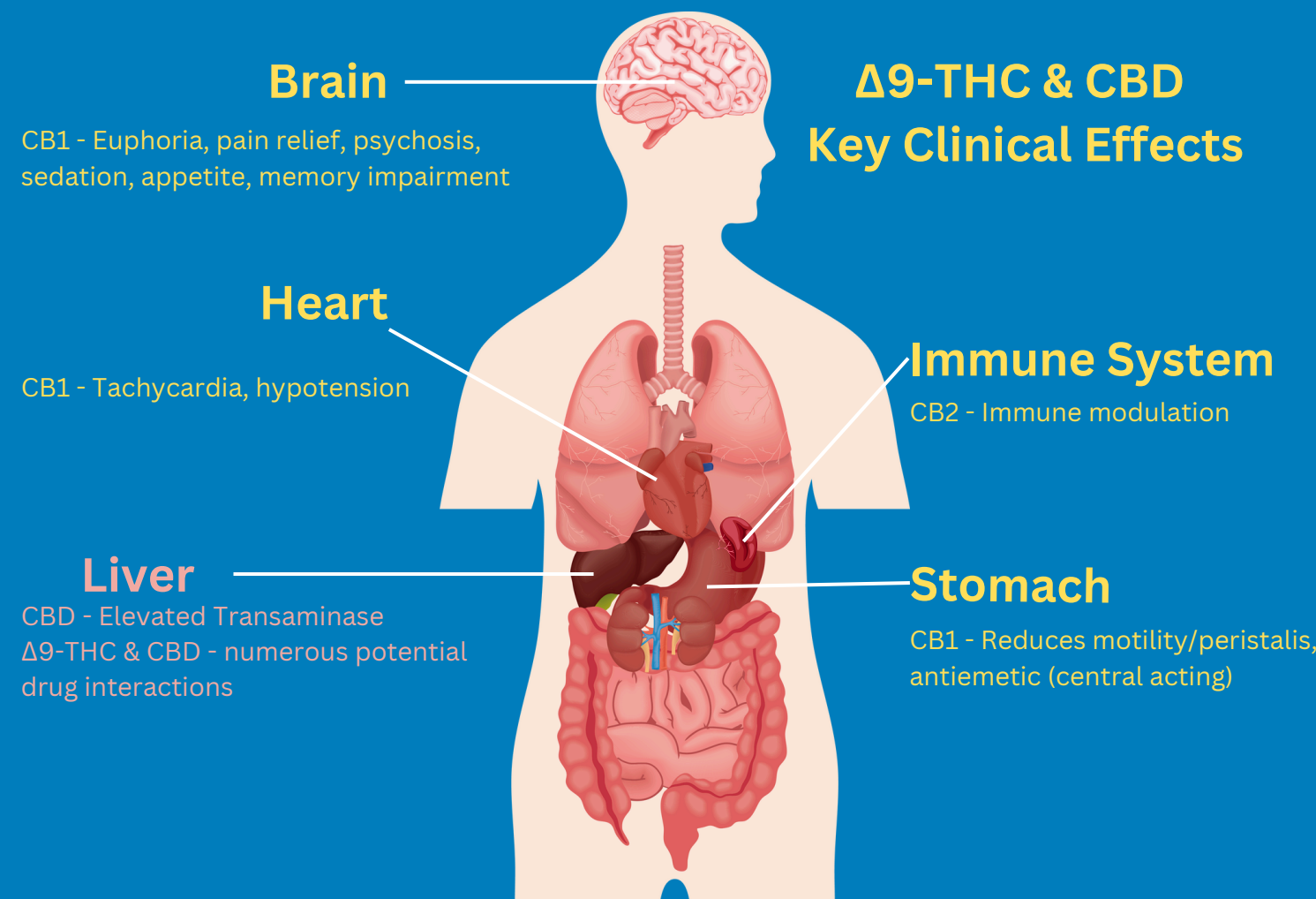
- Patients use cannabis or cannabis-derived products to self-medicate for pain, PTSD, sleep disorders, IBS, etc.
- Outside FDA approved drugs - general lack of high-quality evidence to support the above medical conditions
- Educate patients about risks including DDI, adverse events, abuse potential, & withdrawal syndromes (if chronic use)

Approach to Patient Conversation:

- Start:** Screen high risk patients (e.g., pain, psychiatric) using open-ended questions
- Inquire:** Reasons for use of cannabis products
 - “What benefits do you find from taking (product)?”
 - Duration/amount - “How often have you used (product) in past month/year?”
- Identify:**
 - Source of product “Where do you buy (product) and do you have the label?”
- Discuss:**
 - Potential or active concerns (e.g., AEs, substance use disorder, side effects, DDI)
 - Highlight available approved treatments

Δ 9-THC Pharmacodynamics & Pharmacokinetics:

- Orally peaks around 1-3 hr; Duration ~7hr
 - User may believe desired effects did not occur & may re-dose
- Inhalation peaks ~3-10 min; Impairment greatest in first hr; Duration ~2-4 hr
 - Much faster onset than oral with higher maximum plasma levels leading to more deleterious effects.



Key Pharmacodynamic Interactions

Precipitant	Mechanism	Substrate	Clinical Impacts
CBD	Combined liver inflammatory effects	Valproate	Discontinuation or reduction of CBD
CBD	Decreased renal clearance	Lithium	Consider lower lithium dose, frequent monitoring while dosing
Δ 9-THC	Additive CNS effects	Alcohol, benzos, opioids	Avoid concomitant use, educate patient, monitor for CNS adverse effects
Δ 9-THC	Additive cardiac effects	Stimulants	Avoid concomitant use, educate patients, monitor for cardiac effects (e.g., tachycardia, hypertension)

Key Pharmacokinetic Interactions

Precipitant	Mechanism	Substrate	Clinical Impacts
CBD/ Δ 9-THC	CYP3A4	↑ Sildenafil	Case reports of MI when combined with cannabis
CBD/ Δ 9-THC	CYP2C9-inhibit/protein binding	↑ Warfarin	Case reports of increased INR
CBD	CYP2C19 inhibit	↑ Diazepam, clobazam	Consider lower doses of the substrate
Smoked Cannabis	CYP1A2 induction	↓ Olanzapine, clozapine	Educate, watch for change in efficacy, check drug levels
Fluconazole	CYP2C19 inhibit	↑ CBD	Educate about possible adverse effects and/or stop CBD
Amiodarone	CYP2C9 inhibit	↑ THC	Educate about possible adverse effects/stop THC
Ketoconazole Macrolides	CYP3A4 inhibit	↑ CBD and THC	Educate about possible adverse effect and/or stop CBD

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Examples of Position Statements from Professional Organizations:

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2. AAN, 2020 Advocacy: AAN Position: Use of Medical Cannabis for Neurologic Disorders, American Academy of Neurology (AAN), <https://www.aan.com/advocacy/medical-cannabis-position-statement/>.
3. AES, 2022 Position Statements: AES Position Statement on Cannabis as a Treatment for Patients with Epileptic Seizures, American Epilepsy Society (AES), <https://www.aesnet.org/about/about-aes/position-statements/aes-position-statement-on-cannabis-as-a-treatment-for-patients-with-epileptic-seizures>.
4. APA, 2018 Resource Documents: 2018: Opposition to Cannabis as Medicine, Approved by the Joint Reference Committee, October 2018, American Psychiatric Association (APA), <https://www.psychiatry.org/Psychiatrists/Search-Directories-Databases/Resource-Documents/2018/Opposition-to-Cannabis-as-Medicine>.
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7. NAADAC, 2022 Position Statements and Issue Briefs: NAADAC Position Statement on the Medical and Recreational Use of Cannabis, 2023, <https://www.naadac.org/position-statement-on-the-medical-and-recreational-use-of-cannabis>.