

Pragmatic use of cannabis products for chronic pain

Cannabinoid mechanisms, effects, and methods of ingestion

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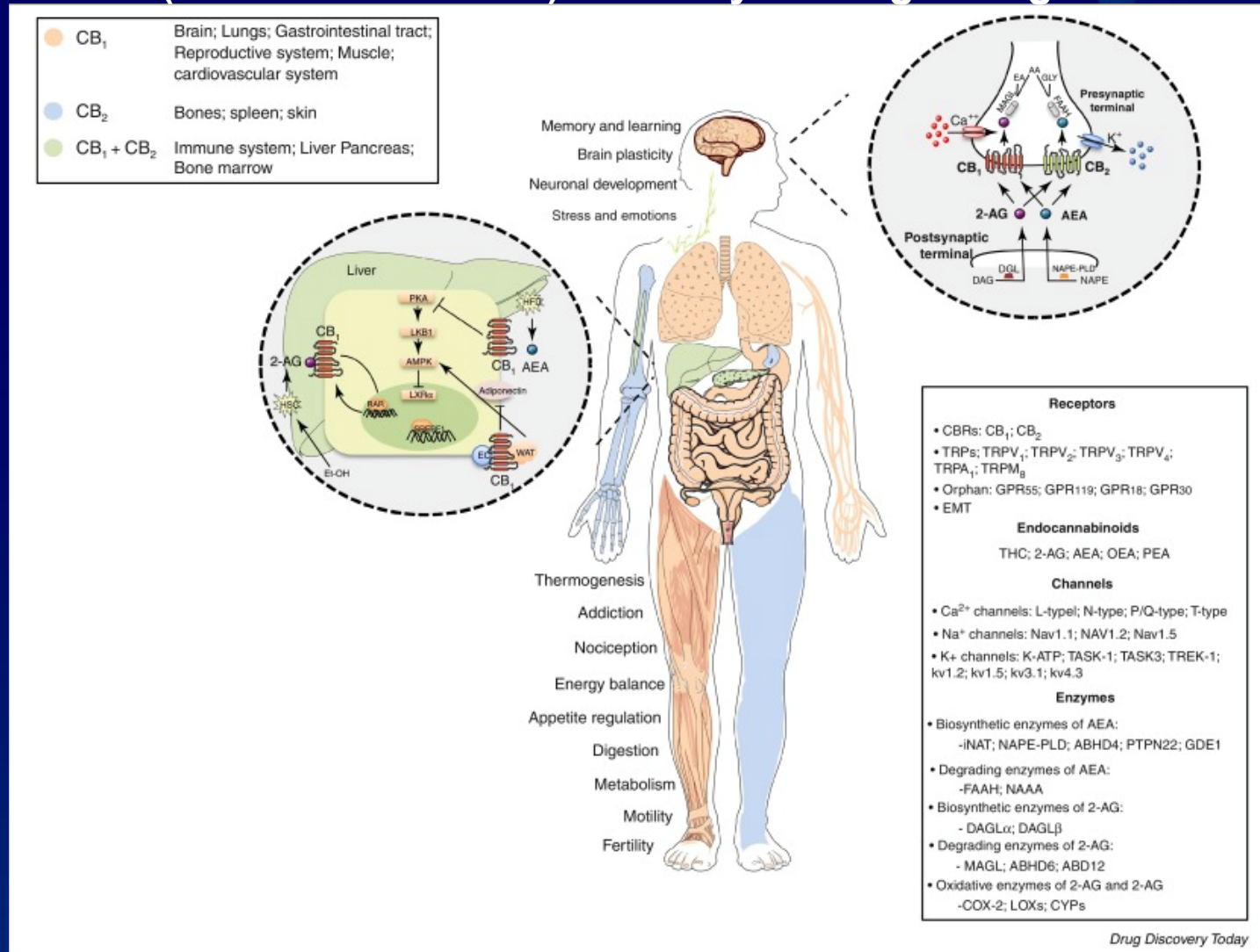
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Disclosures

<i>Sponsor Name</i>	<i>Honoraria/ Expenses</i>	<i>Consulting/ Advisory Board</i>	<i>Funded Research</i>	<i>Royalties/ Patent</i>	<i>Stock Options</i>	<i>Ownership/ Equity Position</i>	<i>Employee</i>	<i>Other (please specify)</i>
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Endocannabinoid system - I

A set of receptors and their naturally occurring ligands (endocannabinoids) and enzymes regulating control



Endocannabinoid system – II

Some known functions of the endocannabinoid system:

- Functions: “Relax, eat, sleep, forget, protect”
- Memory
- Neurogenesis
- Analgesia
- Immune function
- Stress
- Appetite

1. Rom S. Journal of Neuroimmune Pharmacology. 2013; 8(3): 608-620. 2. Hill et. al. PNAS 2010; 107(20) 9406–9411. 3. Crowe S et. al. Brain, Behavior, and Immunity, Volume 42, 2014, 1 - 5

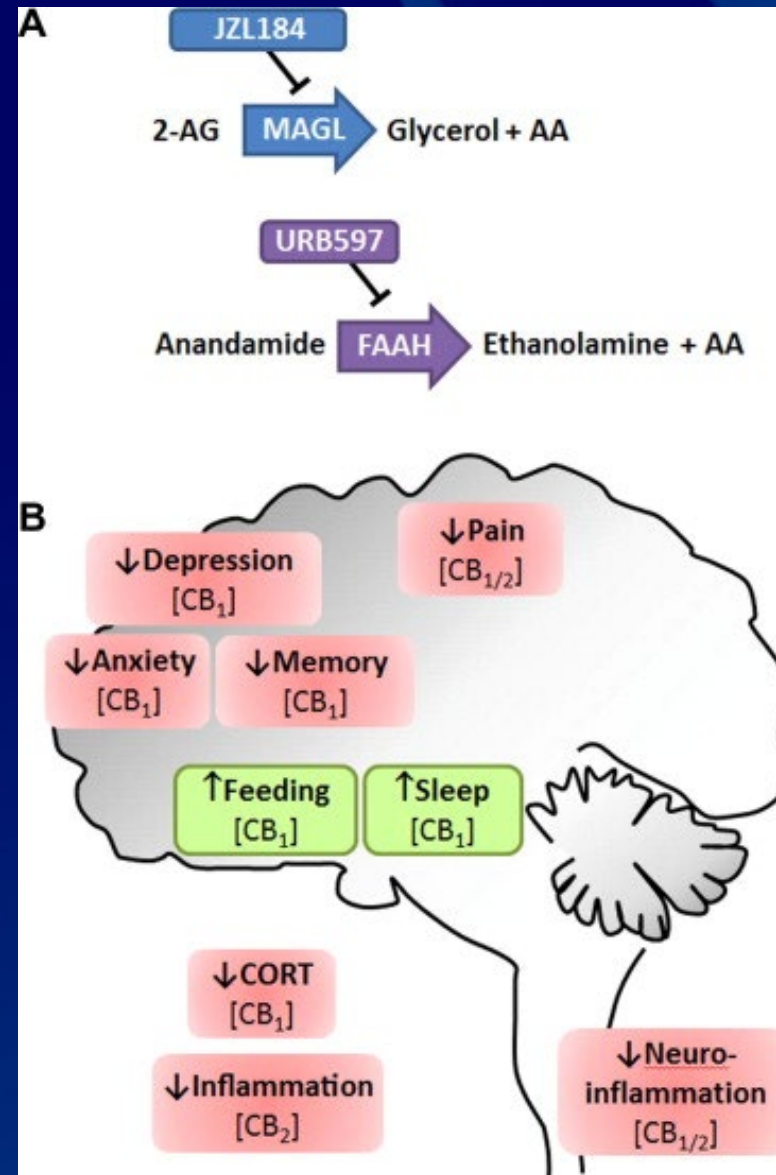


Figure from Crowe et al, 2014.

Two popular phytocannabinoids: THC and CBD

- **Δ-9-Tetrahydrocannabinol (THC)**
 - Analgesic, mood-altering, appetite stimulating¹
- **Cannabidiol (CBD)**
 - Non-intoxicating, potentially protective against psychoactive effects of THC²
 - Anti-convulsant³
 - Some anxiolytic evidence⁴
 - In non-human animal studies, anti-inflammatory⁵
- **Other cannabinoids: CBN, CBG, CBC, etc. –The “Entourage Effect”²**



<http://www.floridamarijuanainfo.org/marinol-the-prescription-thc-pill/>



1. National Academies of Sciences, engineering, and medicine. Health effects of cannabis and cannabinoids (2017). 2. Russo, Ethan B. *British journal of pharmacology* 163.7 (2011): 1344-1364 3. Devinsky, Orrin, et al. *New England Journal of Medicine* 376.21 (2017): 2011-2020. 4. Masataka, Nobuo. *Frontiers in Psychology* 10 (2019): 2466.5. Malfait, A. M., et al. *Proceedings of the National Academy of Sciences* 97.17 (2000): 9561-9566.

Risks of Cannabis (mostly from THC)

Long term:

- Respiratory effects (if smoked)¹
- Dependence and addiction^{1,2}
- Psychotic illnesses: higher rates of illness developed, especially under age of 25³

Short term:

- Common side effects: Dizziness, somnolence, euphoria, light-headedness, anxiety, and others¹
- Uncommon side effects: Vomiting, hallucinations, paranoia, seizures¹
- Uncertain quality – especially for illicit market
- Vehicle accidents¹



<http://arts.bio/en/products/budrot-mildew-rust-control>



Risks of CBD



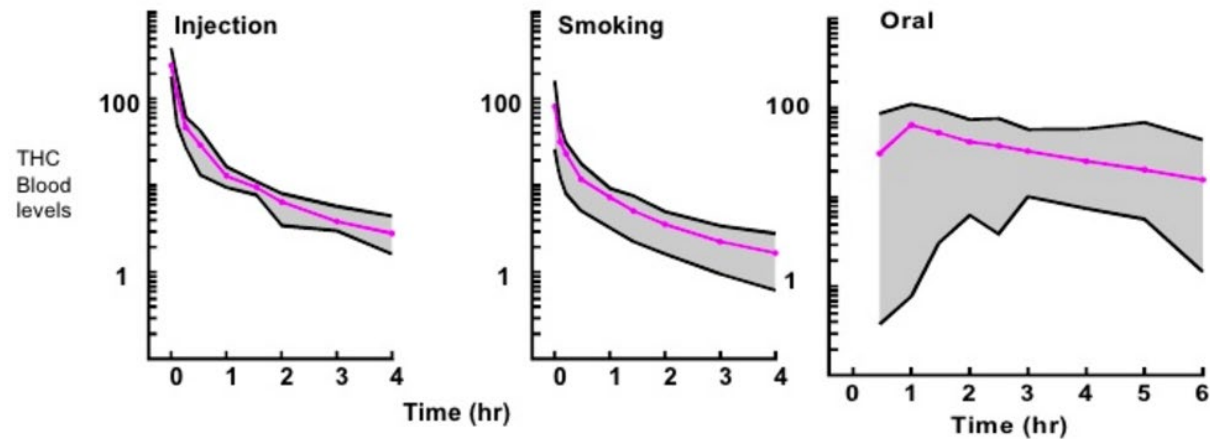
- Generally well tolerated: multiple studies demonstrate safety of ≥ 600 mg/day CBD in several different conditions¹
- Drug-drug interactions: Can inhibit or affect liver enzyme activity which can affect CBD plasma concentrations^{1,2}
- Epidiolex effects (high doses): Drowsiness, decreased appetite, diarrhea, fatigue, malaise, weakness/lethargy, rash, difficulty sleeping, infections²
- Quality control!
 - Pesticides, solvents, heavy metals can be left behind by sloppy manufacturing





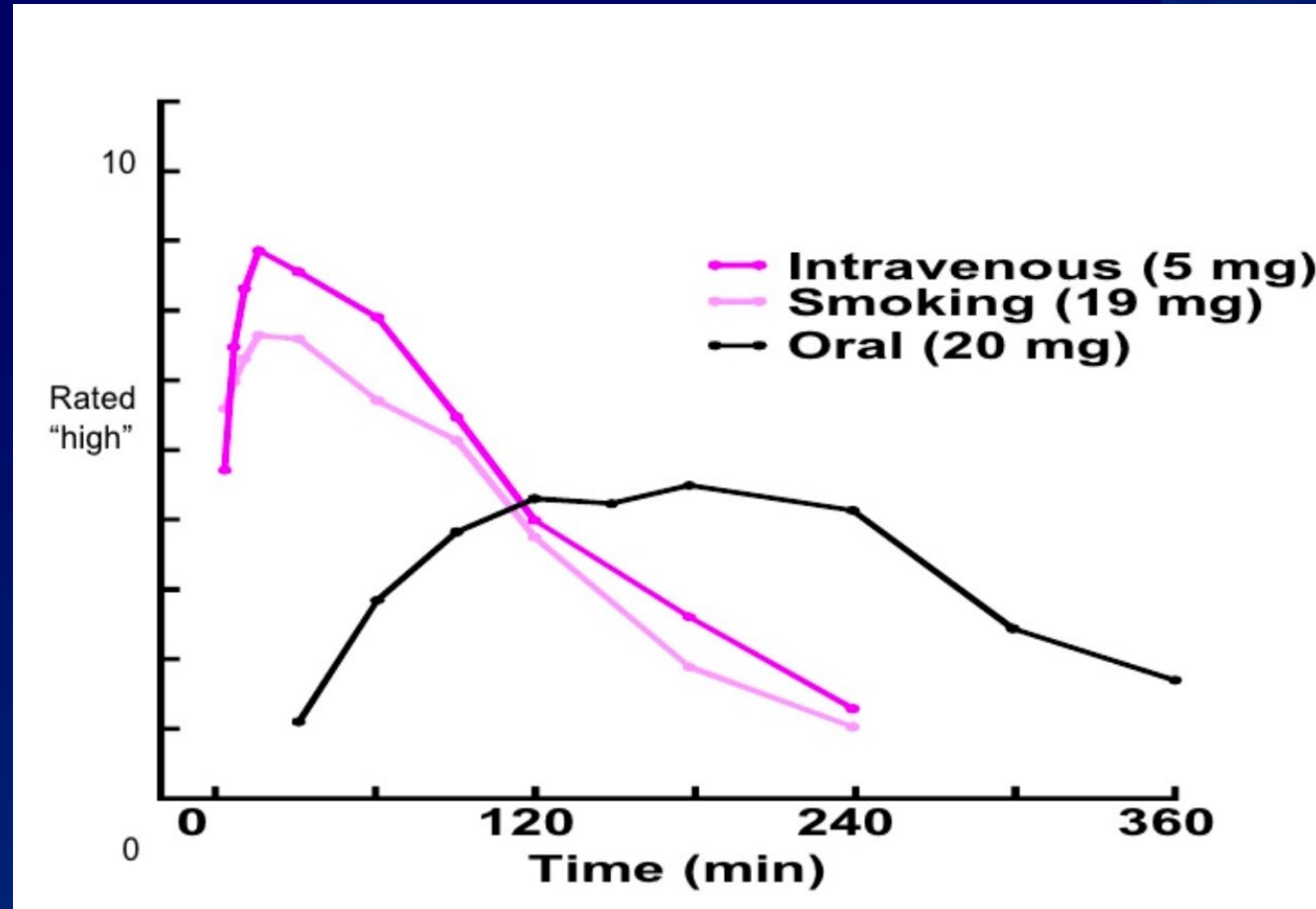
Pharmacokinetics

Pharmacokinetics



Route of administration influences THC pharmacokinetics, left = 5 mg i.v. injection, center = smoking 13.0 mg, or right = consuming cookie with 20 mg (Agurell et al. 1986).

Feelings of 'high' from different administration routes





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Table 2
Administration factors in cannabis delivery methods.

Issue	Smoking/vaporisation	Oral	Oromucosal	Topical
Onset (min)	5–10	60–180	15–45	Variable
Duration (h)	2–4	6–8	6–8	Variable
Pro	Rapid action, advantage for acute or episodic symptoms (nausea/pain)	Less odor, convenient and discrete, advantage for chronic disease/symptoms	Pharmaceutical form (nabiximols) available, with documented efficacy and safety.	Less systemic effect, good for localised symptoms
Con	Dexterity required, vaporisers may be expensive, and not all are portable	Titration challenges due to delayed onset	Expensive, spotty availability	Only local effects

MacCallum, Caroline A., and Ethan B. Russo. "Practical considerations in medical cannabis administration and dosing." *European journal of internal medicine* (2018).

Summary

- The endocannabinoid system is ancient, complex, and a promising target for therapies related to pain
- Phytocannabinoids show promise for treating pain related symptoms
- Cannabinoid content and route of administration are critical