Pharmacokinetics and Routes of Administration: Considerations for Dosing and Titrating

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Pharmacokinetics and Routes of Administration: Considerations for Dosing and Titrating

1. Describe cannabinoid pharmacokinetics and the impact of route of administration
2. Compare benefits and potential risks of different routes of administration

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Cannabinoid Pharmacokinetics

- **Distribution:** Highly **lipophilic** and widely distributed in body tissues. Highly plasma protein bound. Accumulates in adipose tissue and slowly released
- **Metabolism:**
  - Long terminal half-life **metabolized in the liver by** cytochrome P450 enzymes
  - Extensive first-pass metabolism, main active metabolite 11-hydroxy Δ9-THC which parallels action of drug
- **Excretion:** Excreted via biliary tract into feces, along with urinary excretion of acid metabolites

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Routes of Administration

Cannabis intended for medical use is most often taken via:

- **Inhalation –** smoking or vaporizing dried/fresh plant material
- **Oral ingestion - Cannabis extracts in oils or** capsule form

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Inhalation (Smoke or Vapour)

Smoking

- Combustion of plant material via cigarette (joint), pipe, water pipe (bong)
- Inhaled, absorption via pulmonary alveoli
- Smoke contains tar, toxins, irritants of airways etc.
- There is no evidence of reduced adverse effects between joints, pipes and bongs
- Counsel patients to avoid smoking

Vaporization

- Heating plant material in vaporization device (some devices use oils or concentrates)
- 2 devices (Volcano Medic™, the Mighty™) approved by Health Canada
- Vapour, not smoke, is inhaled
- Fewer reported respiratory symptoms compared to smoked cannabis, but not yet proven via clinical trials
- Recent reports of respiratory illness secondary to vapourizing

Rapid onset of action ~5-10 minutes, shorter duration of effect ~2-4 hours

https://www.canada.ca/en/public-health/services/diseases/vaping-pulmonary-illness.html

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Ingestion (oils)

- Cannabinoids converted to active form (decarboxylated) and diffused in carrier oil
- Provided in bottle, or in soft-gel capsules (more convenient, accurate dosing than inhalation)
- Swallowed orally; absorption via gastrointestinal tract, can be affected by gastric pH, stomach contents
- Variety of THC/CBD ratios; but max. allowed THC concentration of 30 mg/mL
- Dose consistency can be challenging if patients prepare own edibles, beverages using oils
- Oils can be added to edible products or beverages such tinctures, lozenges, baked goods, candies, etc.

Slower onset of action ~.5-3 hours, longer duration of effect ~4-6 hours, or longer

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Summary

Pharmacokinetics and Routes of Administration		
	Inhalation (smoked or vaporized)	**Oral Ingestion** (oil, capsule, others)
Bioavailability	15-50%	6-20%
Onset of physiologic effect	5-10 minutes	30-60 minutes (up to 3 hours)
Peak physiologic effect	10-20 minutes	2-4 hours (but can be 6 or more)
Duration of physiologic effect	2-4 hours (up to 24 hours)	Adults: 4-6 hours (up to 24 hours) Children: 6-12 hours (up to 36 hours)

Inhaled bioavailability varies based on number, depth, duration, frequency of inhalations; amount of time substance held in lungs; temperature of vaporizer (if vaporized)

Oral bioavailability is reduced due to extensive first-pass metabolism; administration with food may alter bioavailability (can increase absorption)

RxTx Ottawa (ON): Canadian Pharmacists Association; c2018. CPS online: Cannabis;

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Other Routes

Buccal, sublingual administration of oil:

- Avoids first pass metabolism, more rapid absorption than oral ingestion
- Avoids potential adverse effects associated with inhalation
- No robust data on pharmacokinetics by this route

Also

- Topicals for localized symptoms
- Suppositories for specific populations
- New devices under development cartridges and metered dose delivery units, inhalers

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General Dosing Considerations

- Average reported daily dose = 1-3 g cannabis plant material/day
  - Minimal effective starting dose of THC reported anecdotally to be 2.5 mg
- Do not need to experience euphoria for symptom management!
- Generally start with low THC, higher CBD concentration
- Minimize risk of adverse effects by allowing for sufficient time between a repeated dose
- Start low, go slow!
  - One inhalation – wait at least 10 minutes to assess effect
  - One aliquot – wait at least 60 minutes to assess effect

Inhaled doses of THC as low as 2.5 to 3 mg of THC have been associated with therapeutic benefit and minimal psychoactivity.
Effective dose of CBD is unknown

Information for Health Care Professionals; Cannabis (marihuana, marijuana) and the cannabinoids, Health Canada October 2018

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- MacCallum CA, Practical considerations in medical cannabis administration and dosing. Eur J Internal Med 2018; 49:12-19
- RxTx [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2018. CPS online: Cannabis; [cited 2019 July 2019]. Available from: www.myrxtx.ca
- Information for Health Care Professionals; Cannabis (marihuana, marijuana) and the cannabinoids, Health Canada October 2018 https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabis-cannabinoids.html

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Please proceed to the next module:

Safety: Contraindications, Adverse Events, Interactions, Cannabis Use Disorder

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