Cannabinoids in Long-term Care

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About the Presenters

Dr. Jess Goodman MD

Has been practicing as a Physician in General Practice for 38 years with experience in family medicine, long-term care and rehabilitative medicine. He became concerned that his patients did not have access to comprehensive and credible assessments for medical cannabis and is currently working on a best practice model to support this. Dr. Goodman is currently developing a therapeutic patch for the transdermal application of cannabis for residents in long-term care.

Alanna Coleman NP-PHC MN

Is a Primary Health Care Nurse Practitioner with experience in geriatric medicine and medical cannabis with extensive knowledge in prescribing cannabis in long-term care. She has completed the Medical Cannabis Certificate Program from the Canadian Council on Continuing Education in Pharmacy and is currently taking the Science of Cannabis Certificate Program at McMaster University.

Disclosure of Financial Support

This program has not received financial or in- kind support from any organizations

Agenda

Part 1. Foundation of Knowledge

a) Endocannabinoid System
b) Cannabinoids
c) Overview of cannabis
d) Current evidence for medicinal use
e) Contraindications

Part 2. Application of Knowledge

a) Comprehensive assessment for medical cannabis in LTC
b) Initiation of medical cannabis therapy
c) Accessing medical cannabis in LTC
d) Small group work

Part 1. Foundation of Knowledge

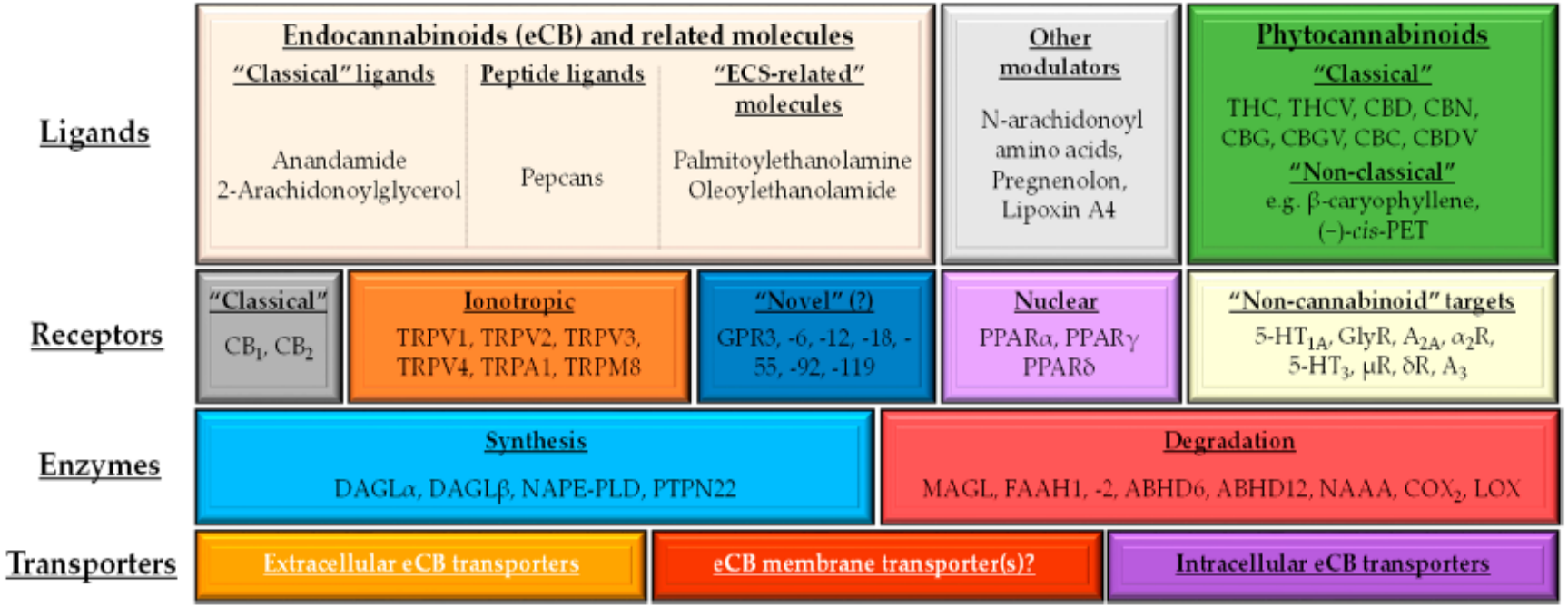
Endocannabinoid System (ECS)

- Lipid signaling system found in all vertebrates with regulatory systems throughout the human body.
- Implicated in several physiological processes including the maintenance of homeostasis, nervous system development, cardiovascular function, metabolism, stress regulation, sleep/wake cycles etc.
- Strong evidence suggests that dysregulation of the ECS contributes to pain, inflammation, neurodegenerative disease and psychiatric disorders.
  - Changes in the ECS with the aging process seen in animal studies suggests an important role for support of the ECS with tissue function.
- Mainly consists of CB1 and CB2 receptors
  - CB1 receptors are located primarily in the nervous system and gastrointestinal system
    - Human brains have more CB1 receptors then opioid receptors with very few CB1 receptors in the brain stem → No risk for overdose
  - CB2 receptors are located throughout the rest of the body, but are more prevalent in elements of the immune system → tonsils, bone marrow, spleen, leukocytes etc.

(Health Canada, 2018; Government of the District of Columbia ,n.d.)

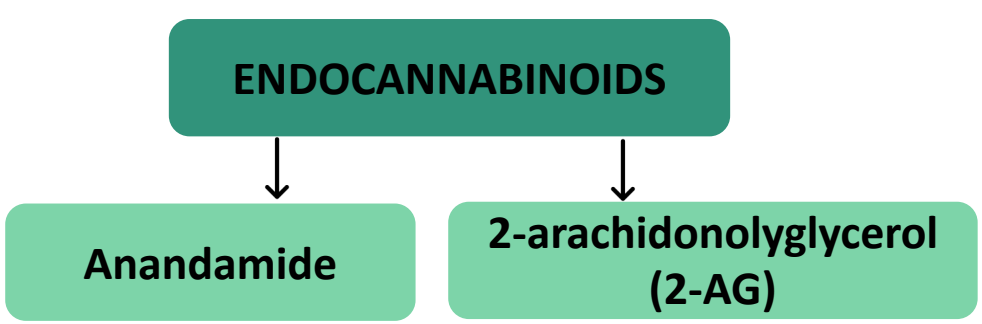
Schematic Overview of the ECS

Note the other ligands and receptors of the ECS

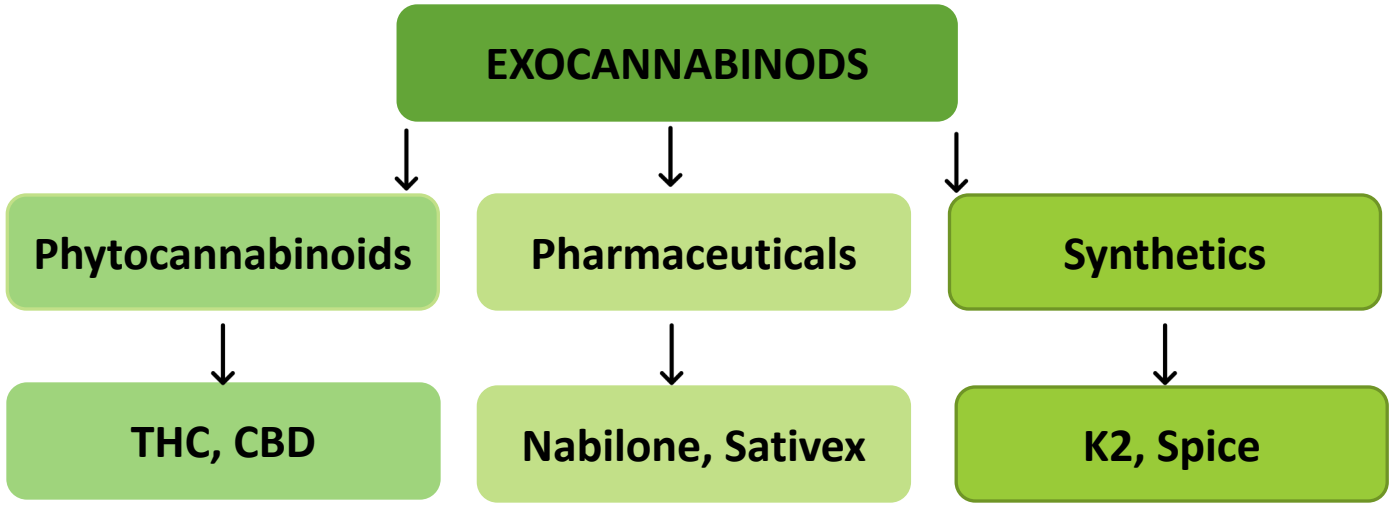


(Toth et al., 2019)

Cannabinoids



Primary endogenous ligands (activators) of the ECS
Synthesized on demand to control tight signaling/tone



High stimulation of CB1 receptors
Unpredictable / life threatening side effects.

(Health Canada, 2018; National Institute on Drug Abuse, 2018)

Pharmaceuticals

Nabilone (Cesamet)

- Synthetic form of THC
- Available in 0.25mg to 1mg capsule
  - Average dose may be 0.25mg to 2mg, once to twice daily
- Has no CBD to moderate its effects
  - Side effects such as drowsiness, dry mouth, palpitations and dizziness can effect its tolerability
- Approved for nausea and vomiting associated with chemotherapy

Nabiximols (Sativex)

- Standard whole plant extract from Cannabis sativa
  - THC and CBD are principle active components with few minor cannabinoids and terpenes
- Available in 27mg THC and 25mg CBD per mL in a buccal spray → 2.7mg THC and 2.5mg CBD per spray
- Limitations are its high cost, high THC content and poor taste → $700 per pack or $2.60 per spray
- Approved for pain secondary to cancer and muscle spasticity associated with MS

(Crawley et al., 2019)

Cannabis

- Cannabis is a complex plant-based substance
  - Over 500 compounds have been identified within the cannabis plant
  - Compounds include phytocannabinoids (100+), terpenes, flavonoids, vitamins (A, B complex), fatty acids etc.
  - Some of these compounds are thought to have potential medicinal properties
- Terpenes are common aromatic compounds found in many plants
  - Terpenes found in cannabis include myrcene, limonene, pinene, linalool etc.
  - May modify or enhance the physiological effects of major cannabinoids → “entourage effect”
- The most commonly utilized and best understood cannabinoids are THC (tetrahydrocannabinol) and CBD (cannabidiol)

(Health Canada, 2018; Government of the District of Columbia ,n.d.)

Phytocannabinoids

MAJOR

THC
delta-9-tetrahydrocannabinol

- ✓ Partial agonist at CB1/CB2 receptors
- ✓ Most psychoactive
- ✓ Anti-emetic, analgesic, anti-spasmodic & appetite stimulating

CBD
Cannabidiol

- ✓ No significant affinity for CB1/CB2 receptors →
- ✓ Reduces side effects of THC to improve therapeutic activity
- ✓ Anti-inflammatory, anti-emetic, anti-psychotic, anti-epileptic, anti-anxiety & anti-oxidant

MINOR

CBN
Cannabinol

- ✓ Some activity at CB1 receptor
- ✓ Possible immunosuppressive properties

CBG
Cannabigerol

- ✓ Partial CB1/CB2 receptor agonist
- ✓ Possible anti-inflammatory/analgesic properties

(Health Canada, 2018; Government of the District of Columbia ,n.d.)

Current State of Evidence

- Large meta-analysis with research obtained from relevant data bases (Medline, Cochrane, PsychInfo etc.)
- Over 10,700 abstracts were considered for establishing the evidence of the health effects of cannabis and cannabinoids from the National Academy of Sciences, Engineering and Medicine.

Conclusive or Substance Evidence of Efficacy	Moderate Evidence of Efficacy	Limited Evidence of Efficacy
✓ Chemotherapy induced nausea and vomiting ✓ Improving patient reported MS spasticity ✓ Treatment of chronic pain in adults	✓ Improving short-term sleep outcomes in individuals with sleep disturbance associated with OSA, fibromyalgia, chronic pain & MS.	✓ Increase appetite/decreasing weight loss with HIV/AIDS ✓ Improving anxiety/PTSD symptoms ✓ Improving symptoms of Tourette's ✓ Improving clinician measured MS spasticity symptoms ✓ Improving intraocular pressure ✓ Improving symptoms associated with dementia* ✓ Reducing depressive symptoms in MS

(National Academies of Sciences, Engineering, and Medicine, 2017)

Current Evidence in Older Adults

- Use of Nabilone in LTC settings can improve agitation and aggression in patients with moderate to severe Alzheimer's disease.
  - 45% experienced sedation

Lanctôt, K et al. (2018). Nabilone significantly improves agitation/aggression in patients with moderate-to-severe AD: Preliminary results of a placebo-controlled, double-blind, cross-over trial. Presented at: Alzheimer's Association International Conference. July 22-26; Chicago.

- Use of THC predominant cannabis oil in the elderly used mostly for the indication of chronic pain resulted in a 93.7% reduction in pain, reduction of opioids/benzodiazepines, decreased falls and improvement in quality of life (as measured by QOL surveys).
  - Most common side effects were dizziness and dry mouth

Abuhasira, R et al. (2018). Epidemiological characteristics, safety and efficacy of medical cannabis in the elderly. *European Journal of Internal Medicine, 49*, 44-50.

- Use of 1:2 (THC:CBD) oral cannabis resulted in a significant reduction in agitation associated with dementia in residents with Alzheimer's disease, vascular and mixed dementia
  - 40% reduction in negative behavior, 50% reduction in muscular rigidity, 50% decreased or stopped psychotropic medications, and a reduction in opioid use/medication for constipation
  - Staff appreciated the reduction in rigidity/negative behaviours→ Transfers/overall care became easier.

Broers B, et al. (2019). Prescription of a THC/CBD-based medication to patients with dementia: A pilot study in Geneva. *Med Cannabis Cannabinoids*. 1-4.

Indications for Further Research

Presently

- ✓Research related to the use of cannabis in LTC is limited
- ✓Most data available on the pharmacokinetics and pharmacodynamics of cannabis are from studies on health volunteers or current cannabis users
- ✓Most clinical studies of cannabis have been conducted with dried cannabis containing more THC then CBD
- ✓Significant biases exist within published material

- Urgent need for studies using whole spectrum CBD dominant cannabis oil in LTC for pain and behaviours psychological symptoms of dementia (BPSD)
- CBD dominant strains are safer to start with
- Most side effects are secondary to THC
  - ✓Risk of falls, increased agitation and anxiety
- Our experience with CBD dominant strains (chemovars):
  - ✓Shown symptom improvement
  - ✓Well tolerated

(Health Canada, 2018; Luca et al., 2018)

Contraindications to Use

Cannabis is contraindicated

- Individuals with a history of a hypersensitivity to any cannabinoids or smoked cannabis (if smoking)
  - Reports of hypersensitivity/allergic reactions ranging from allergic rhinitis to angioedema
  - Cannabis allergy has also been associated other allergies such as nuts, latex etc.
- Individuals with severe cardiovascular disease or cerebrovascular disease
  - Risk for hypertension, hypotension, syncope, tachycardia or stroke
- Individuals with severe liver or renal disease
  - Daily cannabis use has been shown to be a predictor of steatosis severity with chronic Hep C
  - 20% of cannabis is excreted in urine → Individuals with ESRD/CKD may have symptoms relief from cannabis, but further research is needed to explore the effects of cannabis on kidney disease
- Individuals with a history of psychiatric disorders such as psychosis and schizophrenia
  - Strains containing primarily THC with little CBD.
- Smoked cannabis is not recommended in individuals with a history of respiratory disease such as COPD or asthma

Cannabis should be used with caution

- Individuals with a history of substance abuse → Risk for cannabis use disorder is 9% in general

(Health Canada, 2018; Joshusa, & Wyatt, 2017; MacCallum & Russo, 2018; Vandrey et al., 2008)

Recreational Use versus Medical Use

Recreational

- Most individuals who use recreational cannabis use high amounts of THC with little CBD
  - Seeking euphoria
- Cannabis with high THC is associated with a greater severity of addiction relative to cannabis with low THC content
- Purchased illegally from a dispensary
- Purchased legally in Ontario on-line through the Ontario Cannabis Store or in personal at a licenced retail store
  - Produced from a regulated licensed producer
- Individuals may be purchasing recreational cannabis for medicinal purposes

Medicinal

- Individuals who use medical cannabis are often looking for relief of symptoms without euphoria and other negative effects
  - Individuals who use cannabis for medical purposes also use cannabis for recreational purposes

Lucas et al., 2018; Maida & Daeninck, 2016)

Part 2. Application of Knowledge

Potential Therapeutic Use of Medical Cannabis in LTC

AGITATION AND AGGRESSION ASSOCIATED WITH DEMENTIA

CHRONIC PAIN

ANXIETY

INSOMNIA

ANOREXIA

REDUCTION OF POLYPHARMACY

Comprehensive Medical Cannabis Assessment

- Review of medical history through EMR and chart
  - ✓Multidisciplinary documentation from BSO, nursing, dietitian, physiotherapy as appropriate
  - ✓Obtain collateral information from family as appropriate
  - ✓Administration of cannabis considerations→ Dysphagia, PEG tube, capability for self administration etc.
- Review of past medical history
  - ✓Determine potential contraindications → Review of goals of care (risk for symptom relief vs. potential for event)
  - ✓Requirement for monitoring
- Review of current medications
  - ✓Drug-drug interactions → Similar side effect profile/CYP P40
- Physical assessment
- Use of relevant screening tools → Baseline/follow-up
  - ✓GDS, GAD7, ABID, PAINAD, Epworth, CUDIT-R, MoCA etc.
  - ✓Some of this information may be made available through a self reported questionnaire (PQRST)
  - ✓Use the tools that you have and use them consistently

Side Effects of Cannabis

Most Common	Common	Rare
Drowsiness/Fatigue	Euphoria	Orthostatic hypotension
Dizziness	Blurred vision	Ataxia/dyscoordination
Dry mouth	Headache	Tachycardia (after titration)
Cough, phlegm, bronchitis (smoking)		Cannabis hyperemesis
Anxiety		Diarrhea
Nausea		
Cognitive effects		

Increased Dose = Increased Potential for Side Effect

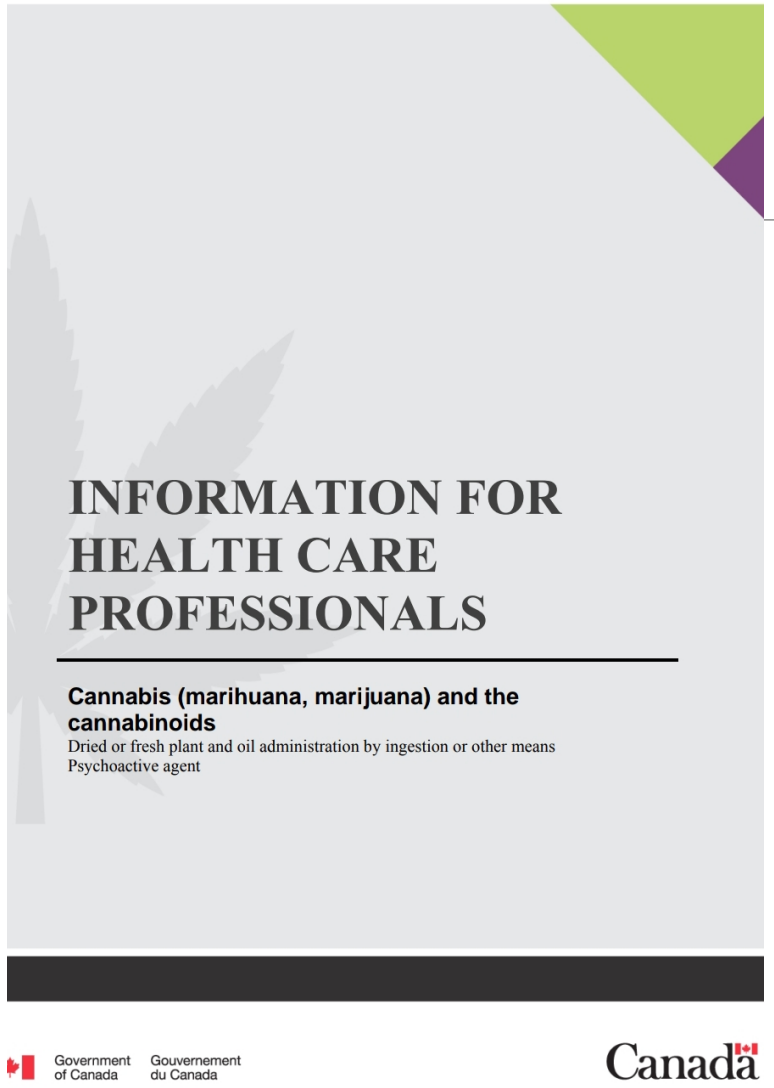
Combine CBD with THC to reduce the negative side effects of THC
→ Psychotropic/cardiovascular (tachycardia)

(Lucas et al., 2018; MacCallum & Russo, 2018)

Risk for Side Effects Based on the Aging Process

- Older adults are more sensitive to drugs that act on the central nervous system
  - Decreased brain volume/neurons, alterations in neurotransmitter sensitivity etc.
- Cannabinoids are lipophilic
  - May tend to accumulate more readily in older adults due to increased adipose tissue/decrease lean muscle mass
  - Potential for increased volume of distribution
- Cannabinoids are metabolized in the liver
  - Decreased Hepatic hepatic flow and slower metabolism may result in prolonged half life
- Decreased renal clearance may result in reduce elimination

(Health Canada, 2018; Luca et al., 2018)



Drug-Drug Interactions

- THC and CBD are metabolized by a variety of cytochrome P450 enzymes
- Drug levels can be increased or decreased by THC and CBD
- Substances can alter the bioavailability of THC and CBD
- Many drug-drug interactions are theoretical
  - ✓Prescribers should continue to be mindful of the potential for interactions
- For more information refer to Information for Health Care Professionals: Cannabis (marihuana, marijuana) and the cannabinoids.

Substances that Affect Cannabis Bioavailability Include:

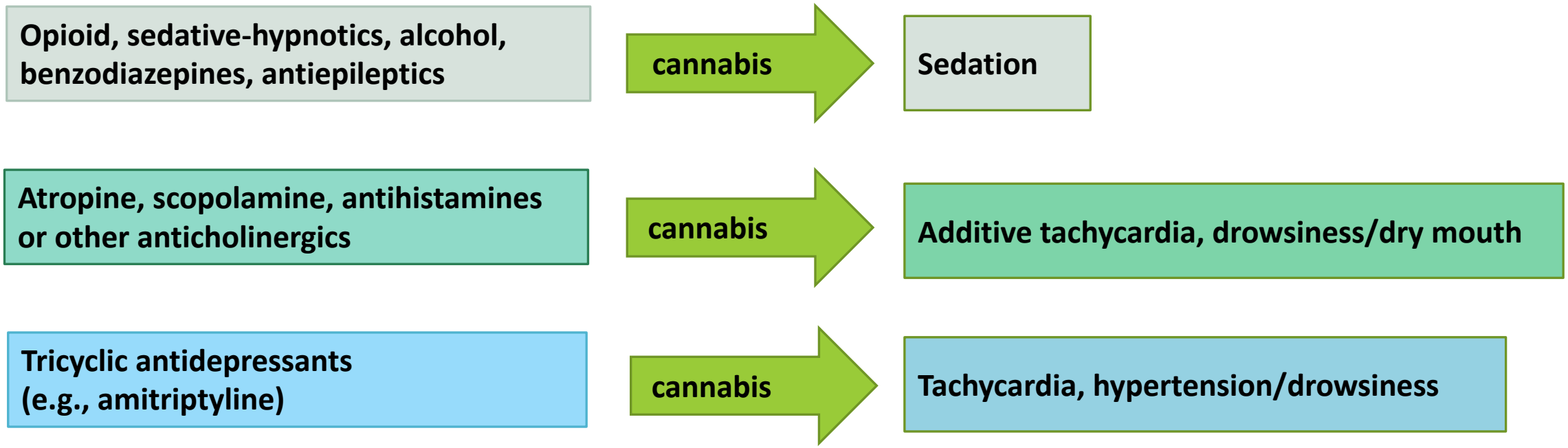
Substances that Increase the Bioavailability of THC	Substances that Increase the Bioavailability of CBD	Substances that Decrease the Bioavailability of THC and CBD
Fluoxetine, Fluvoxamine	Bupropion	Rifampicin
Cimetidine, Omeprazole	Paroxetine	Carbamazepine, Phenobarbital, Dilantin
Erythromycin, Azithromycin	Quinidine	Primidone
Itraconazole, Fluconazole, Ketoconazole		Rifabutin
Diltiazem, Verapamil		St. Johns Wort
Ritonavir, Indinavir		
Amiodarone		
Grapefruit juice		

Cannabis Effects on the Bioavailability of Substances Include:

Substances that are Increased by THC	Substances that are Decreased by THC	Substances that are Increased by CBD
Alcohol	Clozapine	Codeine, Oxycodone
Warfarin	Duloxetine	Atorvastatin, Simvastatin
	Naproxen	Haloperidol
	Olanzapine	Warfarin
	Cyclobenzaprine	Clobazam
	Haloperidol	SSRI's, Tricyclic antidepressants
	Chlorpromazine	Beta Blockers, Calcium Channel Blockers
		Macrolides

High Risk Side Effects

Remain cognisant of drugs that share similar side effect profiles to cannabis



Methods of Administration

	Smoking	Vaporization	Oral	Topical
Onset (m)	5 – 10	5 – 10	60 - 180	Variable
Duration (h)	2 – 4	2 – 4	6 – 8 (up to 12)	Variable
Pros	Rapid onset for acute relief	Rapid onset for acute relief, less waste of cannabis from side smoke, reduction in carcinogen exposure	Longer duration of action for chronic conditions, discrete, odorless	Less systemic effect, localised comfort
Cons	Exposure to carcinogens, waste of cannabis from side smoke	Cost of vaporize is expensive initially	Titrating can be more challenging, administration can be messy (if oil)	Need a pharmacy to compound or nursing to compound with cream base, direct application of oil is greasy
Practicality in LTC	Exposure of other residents to secondhand smoke, use outdoors, nursing administration	Exposure of other residents to second hand smoke, use out doors, nursing administration	Preferred method, less administration from nursing	Same as pros

(MacCallum & Russo, 2018)

Strain Selection

20:1 of CBD to THC

(Exp.20mg CBD/1mg THC per mL)

- Agitation and aggression associated with dementia
  - ✓Reduces the risk of psychoactivity from THC
- Anxiety
  - ✓CBD enhances mood through stimulation of 5-HT1A
- Chronic pain
  - ✓Neuropathic/Arthritic pain

1:1 of CBD to THC

(Exp.10mg THC/ 10mg CBD per mL)

- Insomnia
  - ✓THC decreases sleep latency onset/Increases sleep duration
- Anorexia
  - ✓ THC increases appetite

Do not prescribe based on indica or sativa
Start low and go slow

Prescribing Medical Cannabis

- Start low and go slow to find the lowest effective dose
- Start with CBD predominate strains
  - Add THC slowly if poor symptoms response with CBD
- Initiate with 2.5 to 5.0mg of CBD oil
  - ✓ For ease of titratability
  - ✓ Oil can be mixed with applesauce, pudding, yogurt etc.
  - ✓ Can also be added to feeding tube preparations as appropriate
- Increase by 5.0mg CBD or less every 48 hrs or more if tolerated
- Titrate to a reduction in symptoms → If unwanted side effect, then take a step back
- Introduce soft gel cap(s) or capsule(s) if taking equivalent amount of cannabis, able to swallow safely and has reached a stable dose in their regimen
- For uncontrolled insomnia or anorexia add THC 1.0mg and titrate up by 1.0mg every 48 hrs or more
  - monitoring carefully for side effects
- Slowly reduce opiates, antipsychotics and/or benzodiazepines after symptoms controlled with cannabis → If return in symptoms, then increase cannabis

European Journal of Internal Medicine 49 (2018) 12–19

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Review Article

Practical considerations in medical cannabis administration and dosing

Caroline A. MacCallum[a,*], Ethan B. Russo[b]

[a] Faculty of Medicine, University of British Columbia, BC, Canada
[b] International Cannabis and Cannabinoids Institute, Prague, Czech Republic

- First published article to discuss administration and dosing
- Methods for administration including onset and duration of each
- Tactics for titration with recommendation for follow-up

Engaging Key Stakeholders

LTC RESIDENT

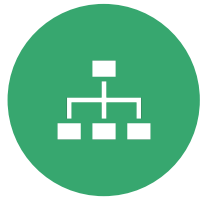
SDM/FAMILY

PHYSICIAN/NURSE PRACTITIONER

NURSING

PHARMACY

PSYCHOGERIATRIC TEAM



ADMINISTRATION

Steps to Access Medical Cannabis

Registration completed by resident or SDM

- ✓ LTC home may have a preferred licensed producer

Medical document completed by MD or NP

- ✓ Cannabis is ordered in grams whether dry cannabis or cannabis oil
- ✓ Can limit percentage of THC
- ✓ Can limit to oil only, otherwise resident or SDM can purchase dry cannabis

Cannabis mailed to LTC home through registered mail

- ✓ Nursing, SDM or resident to order cannabis

Cannabis mailed to pharmacy to dispense

- ✓ Pharmacy will assist with registration and order cannabis.
- ✓ Not all LTC home's have access to this

Financial assistance

- ✓ Compassion pricing
- ✓ Veteran Affairs Canada
- ✓ Private insurance
- ✓ Association memberships (Canadian Association of Retired Persons)
- ✓ Seniors discount

Product supply

- ✓ Some licensed producers have a product supply commit for residents in LTC

Let Us Know How We Did

Your feedback is important to use!

Log onto the OLTCC app under the “conference bag icon” to complete an evaluation about todays workshop

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