

Cannabinoids and chronic pain

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Disclosures

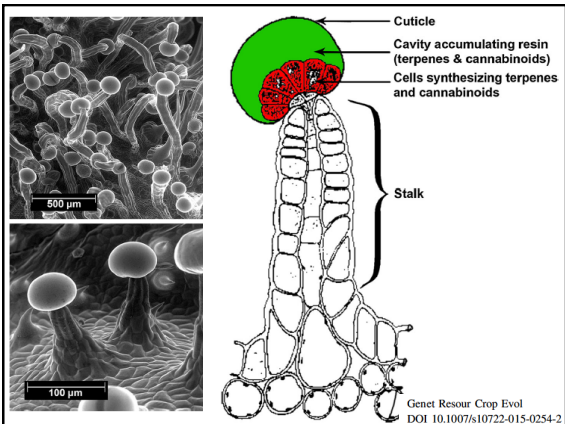
- Executive Director of Canadian Consortium for the Investigation of Cannabinoids (CCIC)
- Grant from CanniMed for RCT of vapourised cannabis for OA of the knee

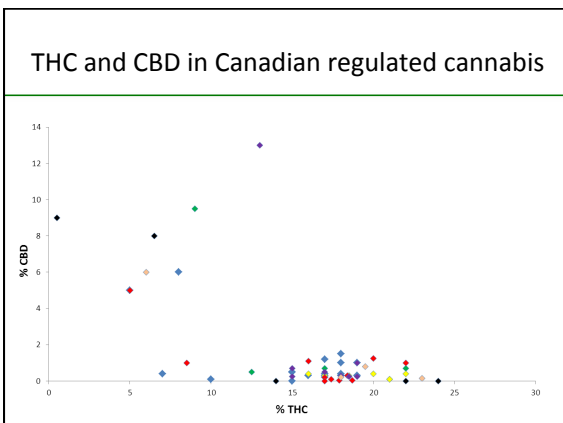
Objectives

- Communicate in a patient centred way with patients requesting a prescription for medical cannabis
- Recognise cannabis use disorder and when medical cannabis might be a reasonable option fo patients
- Use existing tools that assist with medical cannabis decision making

Ralph

- Is he a candidate for medical cannabis?
 - Insomnia
 - Anxiety
 - Pain
 - Refractory
- Two scenarios:
 - He tried it and ‘it helped’
 - He is curious having heard about it in the media and friends say he should try it





- ### Other cannabis constituents
- Myrcene
 - Analgesic effect
 - Blocked by naloxone or yohimbine
 - Anti-inflammatory effect
 - Through PGE2 inhibition
 - Linalol
 - Possible reduction of stress
 - Limonene
 - Adenosine agonist
 - Caryophyllene
 - CB2 agonist
 - Anti-inflammatory
 - Beta-caryophyllene is an FDA approved dietary supplement
 - Humulene
 - Anti-inflammatory
 - Effects similar to dexamethasone
 - Inhibits TNF α and IL1B

Cannabis 'oils'

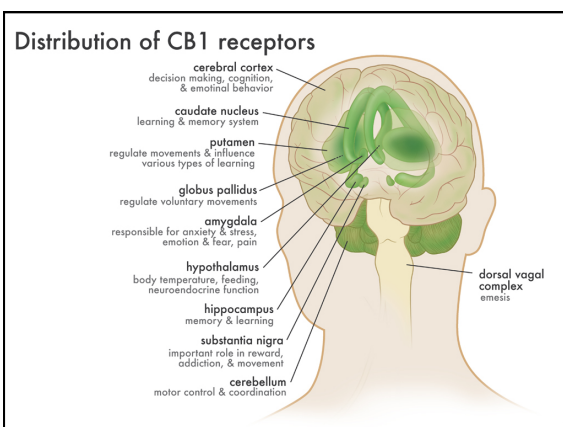
Concentration
 The maximum concentration of THC in the cannabis oil cannot exceed 30 mg/ml (taking into account the potential for THCA to convert into THC upon heating for example). If cannabis oil is provided or sold in a capsule or a similar dosage form, the maximum amount of THC cannot exceed 10 mg of THC (taking into account the potential for THCA to convert into THC upon heating etc.).

Restrictions on vehicle
 The definition of "oil" is "an oil, in liquid form, that contains cannabis or dried marijuana". "Cannabis oil" is considered a finished product resulting from a process such as dilution of a cannabis extract/concentrate (e.g. cannabis resin) into an oil carrier. The finished product must be an oil that is liquid, non-polar, hydrophobic, lipophilic, and viscous at room temperature. Cannabis oil can only be produced using marijuana plants or dried marijuana, meaning no synthetic preparations are allowed. Tinctures are outside the scope of the Section 56 class exemptions for licensed producers.

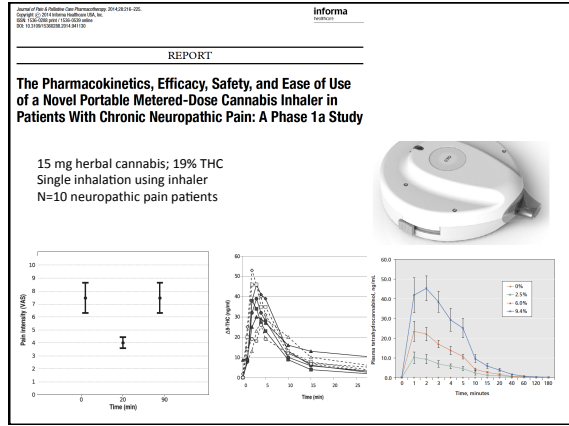
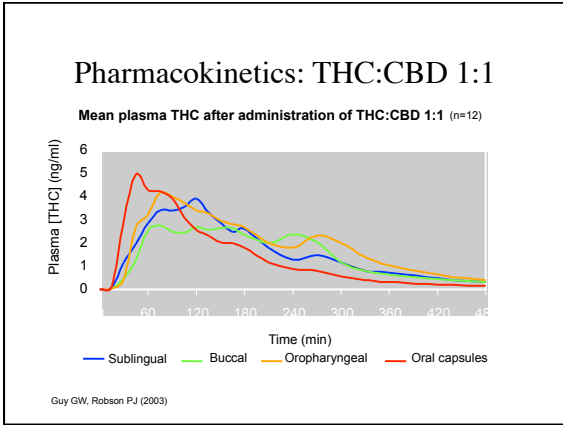
Health Canada does not have a recommended carrier agent or vehicle. However the finished product must be an oil and must meet the most recent version of the ICH Q3C guidelines for Class 3 residual solvents and any other applicable Canadian guidelines that ensure the finished product is appropriate for the intended route of administration and is suited for human use.

Vapourization 101

- Solvents
 - Naphtha
 - Butane
 - Ethanol
 - CO₂
- Device constituents
 - Heat source
 - Thermoplastics
 - Screens
- Control
 - Temperature
 - Dose



- ### Prescription cannabinoids
- Dronabinol (Δ -9 tetrahydrocannabinol – THC) (2.5 - 10mg)**
 - Oral capsule
 - Approved for **chemotherapy-induced nausea and vomiting and anorexia associated with HIV/AIDS**
 - Nabilone (0.25 - 1.0mg)**
 - Oral capsule
 - Approved for **chemotherapy-induced nausea and vomiting**
 - Nabiximols (2.7mg THC + 2.5mg CBD)**
 - Oromucosal spray
 - Approved in Canada for **multiple sclerosis-associated neuropathic pain, spasticity and advanced cancer pain**
 - Herbal cannabis (varying THC levels)**
 - State programs (USA)
 - Federal programs (Canada, Holland, Israel)
 - **No formal 'approval'**



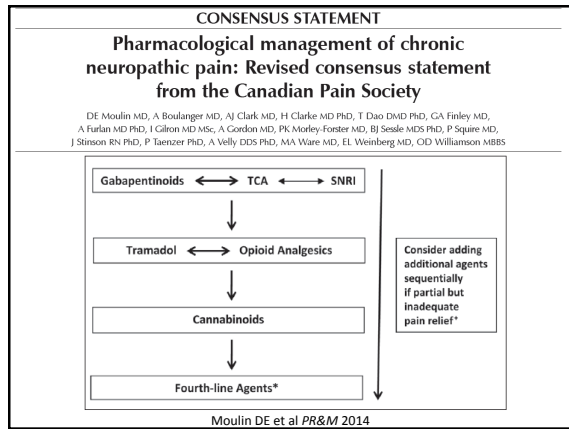
Cannabinoids for Medical Use

A Systematic Review and Meta-analysis

Penny F. Whiting, PhD; Robert F. Wolff, MD; Sohan Deshpande, MSc; Marcello Di Nisio, PhD; Steven Duffy, PgD; Adrian V. Hernandez, MD, PhD; J. Christiaan Keurentjes, MD, PhD; Shona Lang, PhD; Kate Misso, MSc; Steve Ryder, MSc; Simone Schmidtkofer, MSc; Marie Westwood, PhD; Jos Kleijnen, MD, PhD

There was moderate-quality evidence to support the use of cannabinoids for the treatment of chronic pain and spasticity. There was low-quality evidence suggesting that cannabinoids were associated with improvements in nausea and vomiting due to chemotherapy, weight gain in HIV, sleep disorders, and Tourette syndrome. Cannabinoids were associated with an increased risk of short-term AEs.

JAMA. 2015;313(24):2456-2473. doi:10.1001/jama.2015.6358



THE NEW ENGLAND JOURNAL OF MEDICINE

Table 1. Adverse Effects of Short-Term Use and Long-Term or Heavy Use of Marijuana.

Effects of short-term use

- Impaired short-term memory, making it difficult to learn and to retain information
- Impaired motor coordination, interfering with driving skills and increasing the risk of injuries
- Altered judgment, increasing the risk of sexual behaviors that facilitate the transmission of sexually transmitted diseases
- In high doses, paranoia and psychosis

Effects of long-term or heavy use

- Addiction (in about 9% of users overall, 17% of those who begin use in adolescence, and 25 to 50% of those who are daily users)*
- Altered brain development*
 - Poor educational outcome, with increased likelihood of dropping out of school*
 - Cognitive impairment, with lower IQ among those who were frequent users during adolescence*
- Diminished life satisfaction and achievement (determined on the basis of subjective and objective measures as compared with such ratings in the general population)*
- Symptoms of chronic bronchitis
- Increased risk of chronic psychosis disorders (including schizophrenia) in persons with a predisposition to such disorders

* The effect is strongly associated with initial marijuana use early in adolescence.

Cannabis use disorder (DSM-V)

Table 3. Clinical features of cannabis use disorder in patients with chronic pain

- Insists on a medical document for dried cannabis rather than trying other treatments known to be effective for his or her condition
- Uses cannabis daily or almost daily, spending considerable non-productive time on this activity
- Has poor school, work, and social functioning
- Is currently addicted to or misusing other substances (other than tobacco)
- Has risk factors for cannabis use disorder: is young, has current mood or anxiety disorder or a history of addiction or misuse
 - Reports having difficulty stopping or reducing use
 - Reports cannabis withdrawal symptoms after a day or more of abstinence: intense anxiety, fatigue
- Has friends or family members concerned about his or her cannabis use

FCPP Preliminary Guidance document 2014

Sample Medical Document for the Marijuana for Medical Purposes Regulations

This document may be completed by the applicant's authorized health care practitioner as defined in the Schedule to the Medical Purposes Regulations. An authorized health care practitioner includes physicians in all provinces and territories, and some practitioners in provinces and territories where prescribing dried marijuana for medical purposes is permitted under their scope of practice. If another document is used, it must contain all of the information below.

.....
 Patient's Given Name and Surname

Daily quantity of dried marijuana to be used by the patient: _____ g/day


The period of use is _____ day(s) _____ week(s) _____ month(s).

.....
 Full business address of the location at which the patient consulted the health care practitioner (if different than above):

Phone Number: _____
 Fax Number (if applicable): _____
 Email Address (if applicable): _____
 Provincial/Licensed to Practice in: _____
 Health Care Practitioner's Licence number: _____


By signing this document, the health care practitioner is attesting that the information contained in this document is correct and complete.

Health Care Practitioner's Signature: _____
 Date Signed (DD/MM/YYYY): _____

 THE CANADIAN MEDICAL PROTECTIVE ASSOCIATION

- “Physicians must be familiar with the existing program for patients currently accessing medical marijuana and must also familiarize themselves with the new regulations.
- Physicians are expected to know and comply with the regulations and policies of their College.”

http://www.cmpa-acpm.ca/cmpapd04/docs/resource_files/web_sheets/2013/com_w13_005-e.cfm

 THE CANADIAN MEDICAL PROTECTIVE ASSOCIATION

- Physicians should only sign medical documents when they have the **necessary clinical knowledge** to engage in a **meaningful consent discussions** with patients.
- Physicians requested to provide a medical document should discuss with the patient the **lack of information available to date**.
- All consent-related discussions should be documented in the patient's medical record. The discussion should include:
 - information provided about **what is known, and not known**, regarding the risks and benefits of using marijuana for medical purposes.
- ...the CMPA **no longer advises physicians to ask patients to sign a release** when assisting with a request under the new regulations.

http://www.cmpa-acpm.ca/cmpapd04/docs/resource_files/web_sheets/2013/com_w13_005-e.cfm

A “cannabis curriculum”

Topic	Learning objectives
History of medical cannabis	Describe the historical perspective of medical cannabis use and the effects of cannabis policy on research and drug development. Comparison with opioid drug development may be useful.
Botany of Cannabis sativa	Describe the plant based production of cannabinoids and other aromatic ingredients; describe genetic and phenotypic interspecies differences
Biology of the endocannabinoid system	Describe the identity, location and functional characteristics of cannabinoid receptors and endogenous ligands; endocannabinoid synthesis and metabolism; mechanism of action and role of endocannabinoids in normal physiology
Pharmacology of cannabinoids	Describe the clinical pharmacology (absorption, distribution, metabolism and elimination) of cannabinoid molecules; potential drug-drug interactions
Safety of medical cannabis use	Discuss known adverse effects of acute and chronic cannabis use; consideration of differences between safety of medical and recreational cannabis use; methods of studying cannabis safety; absolute and relative contraindications
Cannabis misuse and abuse	Recognize and discuss cannabis use disorder characteristics and treatment
Legal considerations in medical cannabis	Discuss medical cannabis policy: international, national and local concerns; identify pragmatic factors in medical cannabis authorization (where legally possible)
Communicating with patients about medical marijuana	Discuss the stigma of medical cannabis; establishing therapeutic relationship and goals of treatment; use of treatment agreements and compliance

Ware & Ziemianski *Clin Pharm Ther* 2015

Table 1 - Precautions	Table 2 - Sample treatment agreement
<p>Requirements Applicable</p> <p>Consent of Patient</p> <p>Must not apply to fee Must not be given Must not be given by the pharmacist/distributor or Must not be given to the patient's medical record</p> <p>State patient's medical history with significant chronic conditions, and list of all medications and other substances taken in the last 24 hours</p> <p>Keep all medical disc information by the CMA</p> <p>May not authorize the patient to participate in the research if the patient is not competent and does not understand the nature and consequences of the research</p> <p>Ask the patient to sign a consent form and to provide a copy of the consent form to the pharmacist/distributor and to the patient's medical record</p> <p>Complete this consent form in the presence of the pharmacist/distributor and the patient</p> <p>Signature of the pharmacist/distributor Date</p> <p>Signature of the patient Date</p> <p>Signature of the pharmacist/distributor Date</p> <p>Signature of the patient Date</p>	<p>1. 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http://www.cmpa-acpm.ca/Orient-Cannabis_Prelim_Guidance/

Precautions and contraindications

- **Contraindications:**
 - psychosis
 - unstable heart disease
 - pregnancy
- **Precautions**
 - Age <25y
 - History of legal issues/criminal charges
 - Screen for cannabis use disorder
 - Validate that desire for cannabis is ‘medical’

Ralph...

- Central sensitization? Muscle spasm? Insomnia? Anxiety?
- Treatment agreement
- Treatment plan
 - Reduce other meds
 - Functional goals
 - Validate with family
- Counseling
 - Use low dose, low THC
 - Non-smoked delivery
 - Caution with driving while titrating and after exposure
- Document and follow up

Resources

- Cannabis: the use of medical marijuana and cannabinoids
 - Foundation for medical practice evaluation
 - www.fmpe.org
- Health Canada monograph
 - www.hc-sc.gc.ca/dhp-mps/marihuana/med/infoprof-eng.php
- CCIC Cannabinoid checklist
 - <https://surveys.mcgill.ca/limesurvey/index.php?sid=53929>

Questions to ask a licensed producer

Some questions you may wish to ask a licensed producer include:

- Do you have a wait list to register?
- What paperwork is required from my physician? From me?
- What types of strains do you provide and how are their effects different?
- What is the chemical composition of your strains (THC, CBD) levels?
- If a certain strain does not work well for me, can I change the strain I purchase?
- What forms of medical cannabis do you offer? (e.g., dried, oils, etc.) How should I use them to ensure accurate dosing?
- How much does your product cost per gram?
- Is there a maximum quantity that I can order at one time?
- How frequently can I place an order?
- How is your product delivered? Does it need to be delivered to my home or are there other options?
- How do you ensure safety, quality and consistency of your product?
- Do you have enough product to ensure there is no gap in my requirements?
- What are the regulations that you are required to follow?
- Do you have a patient support program to help me in case I have other questions?
- How do you protect my privacy with respect to the personal information you keep on file and the disposition of your shipping procedures and methods?
- Do you have any programs to help me if I have a limited income or if I am on disability?
- What training do your support staff have? Are they pharmacists/nurses, etc.?
- How do I report any adverse effects?

The need for research

Safety and improved care for people living with arthritis are The Arthritis Society's top priorities. Given the regulations governing medical cannabis and its use in treating arthritis symptoms, the Society is actively supporting additional research, the goal of which is to provide patients and physicians with greater access to credible and complete information upon which to base treatment decisions.

Some of the questions about medical cannabis and arthritis that research will help us answer include:

- How does medical cannabis work?
- How effective is medical cannabis for managing pain and fatigue caused by arthritis? How does medical cannabis affect inflammation?
- If effective, what is the best delivery method?
- What factors affect dosage, delivery route and efficacy? Do they vary depending on the patient, disease type or amount of pain being experienced?
- Does medical cannabis have any adverse interactions with other medications or conditions?
- Is it possible to separate the cannabinoid molecules that contribute to pain relief from those that have unwanted side effects?
- Which patients will benefit the most from medical cannabis?
- What are the risks associated with using medical cannabis?

Canadian Consortium for the Investigation of Cannabinoids
www.ccic.net

Promoting education and research on the role of cannabinoids in health and disease.

CCIC Cannabinoid Congress
 Toronto April 7 & 8 2016