



ARTHRITIS TALKS

ARTHRITIS PAIN AND MEDICAL CANNABIS

NOVEMBER 6, 2024



Presenters



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Q&A

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What is cannabis?



Treatment and Dosage



Q & A

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Q: Why do some people think medical cannabis may be suitable for treating arthritis?

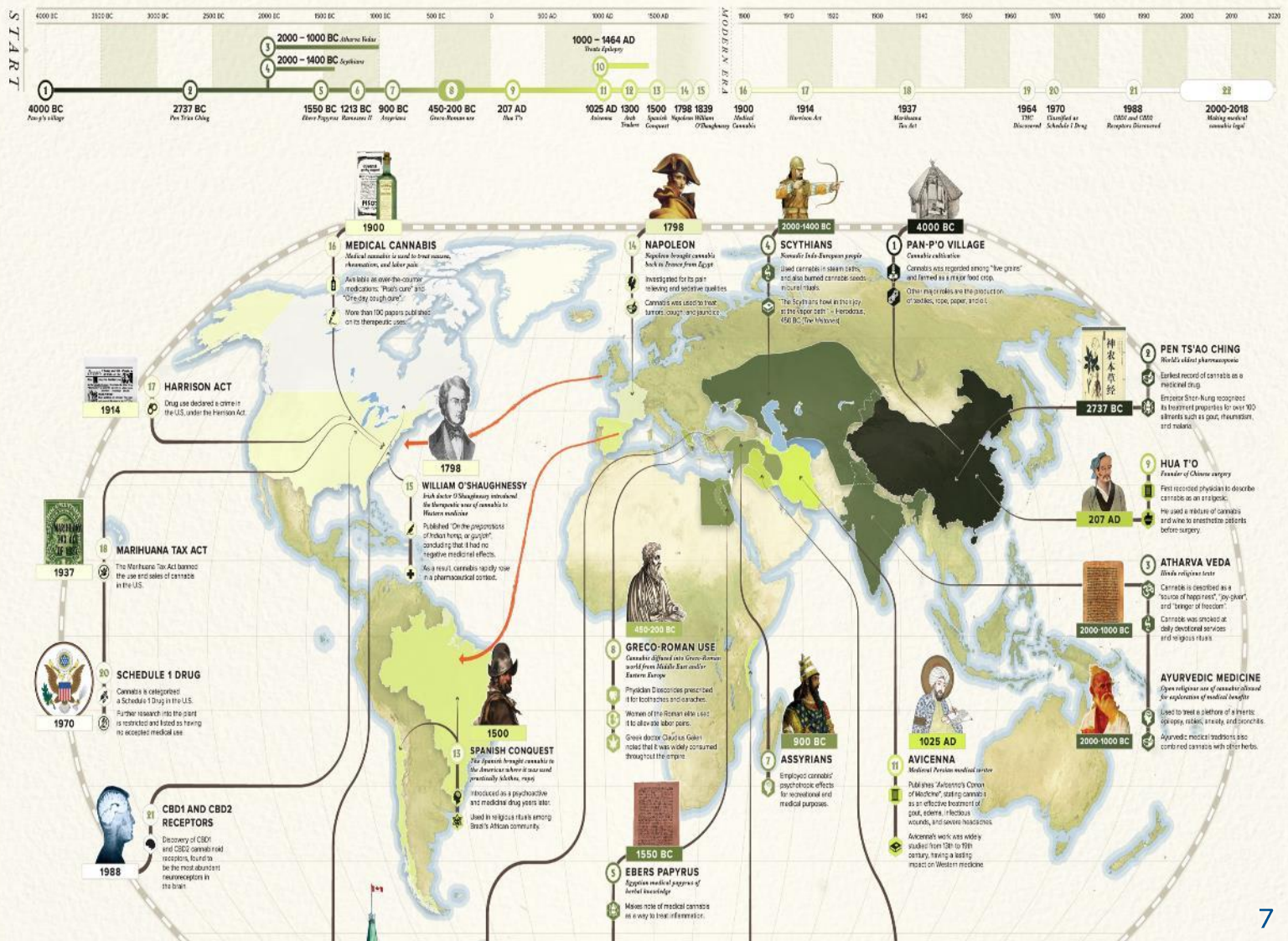
What is Cannabis?

- Oldest known cultivated plant used for medicine, recreational, industrial and spiritual purposes
- “Pharmacy in a Plant”
 - >100 cannabinoids
 - 537 known molecules (terpenes, flavonoids)

a 6,000 YEAR HISTORY of CANNABIS

THE CANNABIS SPACE IS HIGHLY POLARIZED TODAY.

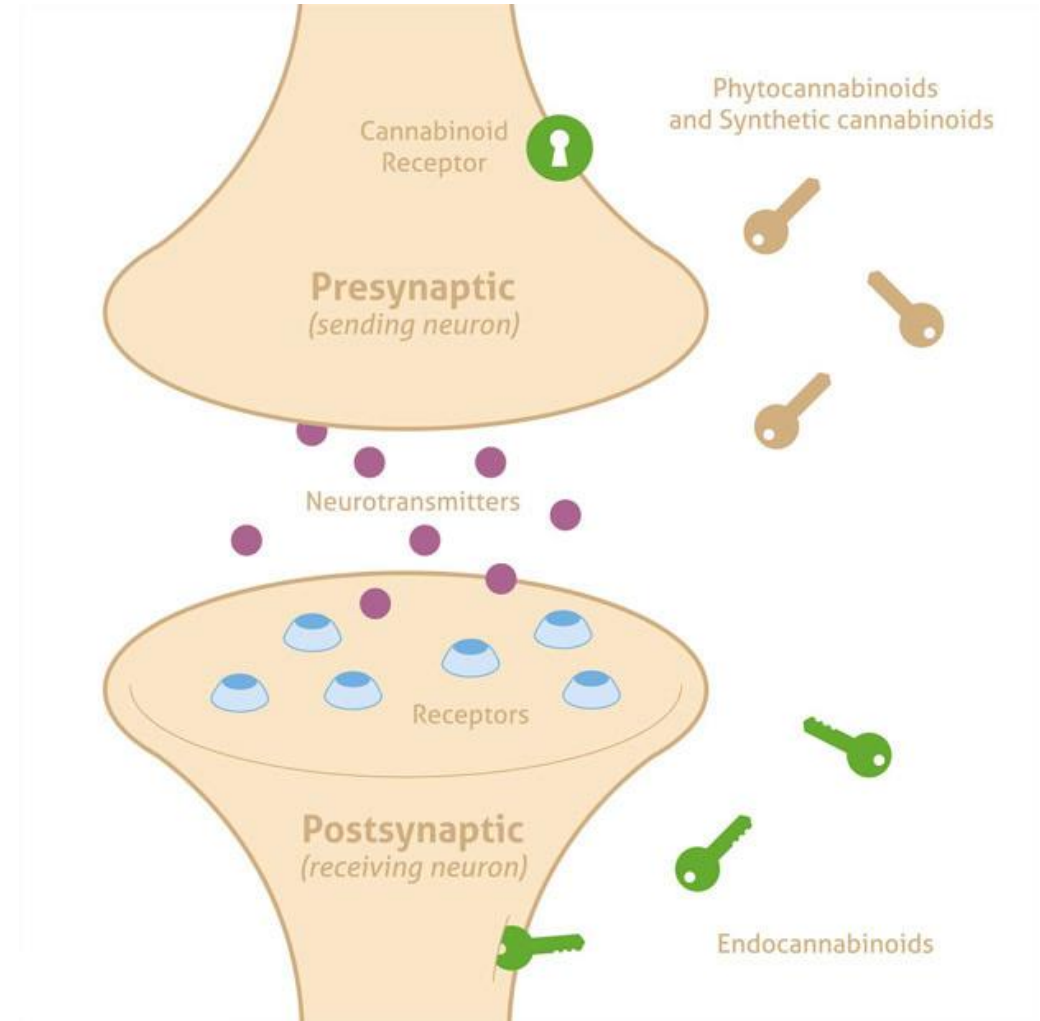
However, it's less known that the plant has over 6,000 years of documented history – and its therapeutic applications appear to have been realized by most cultures. With medical cannabis making a comeback around the world, it's worth tracing the plant's humble beginnings and how it played a vital role throughout the centuries.



ENDOCANNABINOID SYSTEM

REGULATES MANY FUNCTIONS SUCH AS: central nervous system, peripheral nervous system, stress, anxiety, digestive, immune and motor functions.

- Seizures
- PTSD
- CINV
- Arthritis
- Cachexia
- Inflammation
- Gastrointestinal Disorders
- Fibromyalgia
- Cancer Symptoms
- Multiple Sclerosis
- Chronic Pain
- Spasticity
- Anxiety



Endocannabinoid System
it's in you to live

Cannabidiol as a treatment for arthritis and joint pain: an exploratory cross-sectional study

Frane N, Stapleton E, Iturriaga C, Ganz M, Rasquinha V, Duarte R. Cannabidiol as a treatment for arthritis and joint pain: an exploratory cross-sectional study. *J Cannabis Res.* 2022;4(1):47. Published 2022 Aug 24. doi:10.1186/s42238-022-00154-9

N= 428 respondents to online survey

**83% improvement in pain (Best results in OA)
44% reduced pain scores by 2.58**

66% improvement in physical function

66% improvement in sleep quality

**60.5% reduced/stopped other medications
17.8% stopped NSAIDs/Tylenol®
18.9% stopped Opioids**

- **Talk with your MD/NP/HCP**
- **Have you failed other therapies?**
- **Are you restricted from other therapies?**



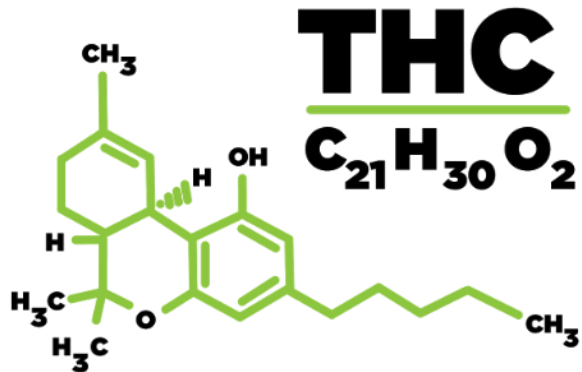
**ARTHRITIS
TALKS**



Q: What is the difference between CBD and THC?

Delta-9-Tetrahydrocannabinol (THC)

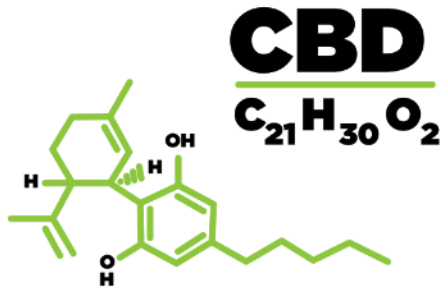
- Most abundant phytocannabinoid
- Infamous for causing psychoactive effects at moderate-high doses (aka "stoned").
- Side effects: Dry mouth, dry eye, cognitive impairment, dizziness, sedation, increase in heart rate, fatigue
- Uses:
 - Pain
 - Spasticity
 - Appetite Stimulation
 - PTSD
 - Insomnia
 - Anti-nauseant



****YOU DO NOT NEED TO GET "HIGH"
TO ELICIT THCs BENEFICIAL EFFECTS****

Cannabidiol (CBD)

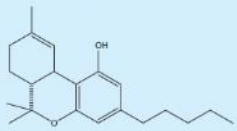
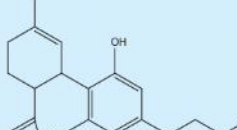
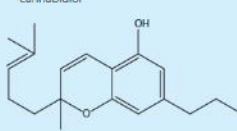
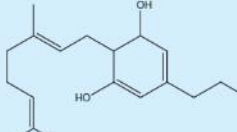
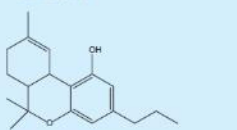
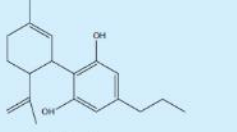
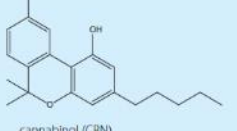
- 2nd most abundant phytocannabinoid found in cannabis
- Side effects: Dry mouth, dry eye, dizziness, reduce blood pressure, fatigue, somnolence,
- Uses:
 - Pain
 - Seizure Disorder
 - Anti-inflammatory
 - Insomnia
 - Anti-nauseant
 - Neuroprotective effectsb



No evidence for dependency or abuse potential with CBD use – WHO Expert Committee on Drug Dependence

WHO. Cannabidiol (CBD): World Health Organization Expert Committee on Drug Dependence Thirty-ninth Meeting. 2017. Available from: https://www.who.int/medicines/access/controlled-substances/5.2_CBD.pdf. Accessed November 1, 2019.

Table 1
Phytocannabinoid activity table

Phytocannabinoid structure	Selected pharmacology (reference)	Synergistic terpenoids
 delta-9-tetrahydrocannabinol (THC)	Analgesic via CB ₁ and CB ₂ (Rahn and Hohmann, 2009) AI/antioxidant (Hampson <i>et al.</i> , 1998) Bronchodilatory (Williams <i>et al.</i> , 1976) ↓ Sx. Alzheimer disease (Volicer <i>et al.</i> , 1997; Eubanks <i>et al.</i> , 2006) Benefit on duodenal ulcers (Douthwaite, 1947) Muscle relaxant (Kavla <i>et al.</i> , 2010) Antipruritic, cholestatic jaundice (Neff <i>et al.</i> , 2002)	Various Limonene <i>et al.</i> Pinene Limonene, pinene, linalool Caryophyllene, limonene Linalool? Caryophyllene?
 cannabidiol	AI/antioxidant (Hampson <i>et al.</i> , 1998) Anti-anxiety via 5-HT _{1A} (Russo <i>et al.</i> , 2005) Anticonvulsant (Jones <i>et al.</i> , 2010) Cytotoxic versus breast cancer (Ligresti <i>et al.</i> , 2006) ↑ adenosine A _{2A} signalling (Carrier <i>et al.</i> , 2006) Effective versus MRSA (Appendino <i>et al.</i> , 2008) Decreases sebum/sebocytes (Biro <i>et al.</i> , 2009) Treatment of addiction (see text)	Limonene <i>et al.</i> Linalool, limonene Linalool Limonene Linalool Pinene Pinene, limonene, linalool Caryophyllene
 cannabichromene	Anti-inflammatory/analgesic (Davis and Hatoum, 1983) Antifungal (EISOhiy <i>et al.</i>, 1982) AEA uptake inhibitor (De Petrocellis <i>et al.</i> , 2011) Antidepressant in rodent model (Deyo and Musty, 2003)	Various Caryophyllene oxide - Limonene
 cannabigerol	TRPM8 antagonist prostate cancer (De Petrocellis <i>et al.</i> , 2011) GABA uptake inhibitor (Banerjee <i>et al.</i> , 1975) Anti-fungal (EISOhiy <i>et al.</i>, 1982) Antidepressant rodent model (Musty and Deyo, 2006); and via 5-HT _{1A} antagonism (Cascio <i>et al.</i> , 2010) Analgesic, α-2 adrenergic blockade (Cascio <i>et al.</i> , 2010) ↓ keratinocytes in psoriasis (Wilkinson and Williamson, 2007) Effective versus MRSA (Appendino <i>et al.</i> , 2008)	Cannabis terpenoids Phytol, linalool Caryophyllene oxide Limonene Various adjunctive role? Pinene
 tetrahydrocannabivarin	AI/anti-hyperalgesic (Bolognini <i>et al.</i> , 2010) Treatment of metabolic syndrome (Cawthorne <i>et al.</i> , 2007) Anticonvulsant (Hill <i>et al.</i> , 2010) Inhibits diacylglycerol lipase (De Petrocellis <i>et al.</i> , 2011)	Caryophyllene <i>et al.</i> ... - Linalool -
 cannabidivarin	Anticonvulsant in hippocampus (Hill <i>et al.</i> , 2010)	Linalool
 cannabinal (CBN)	Sedative (Musty <i>et al.</i> , 1976) Effective versus MRSA (Appendino <i>et al.</i>, 2008) TRPV2 agonist for burns (Qin <i>et al.</i> , 2008) ↓ keratinocytes in psoriasis (Wilkinson and Williamson, 2007) ↓ breast cancer resistance protein (Holland <i>et al.</i> , 2008)	Nerolidol, myrcene Pinene Linalool adjunctive role? Limonene

5-HT, 5-hydroxytryptamine (serotonin); AEA, arachidonylethanolamide (anandamide); AI, anti-inflammatory; CB₁/CB₂, cannabinoid receptor 1 or 2; GABA, gamma aminobutyric acid; TRPV, transient receptor potential vanilloid receptor; MRSA, methicillin-resistant *Staphylococcus aureus*; Sx, symptoms.

The Other Cannabinoids

- CBN – Sedative
- CBG – Analgesic, anxiety/depression?
- CBC – Anti-inflammatory, analgesic
- THCV – Anti-convulsant, Appetite suppressant

Anti-inflammatory effects of CBD in combination with THC appear to be more significant than CBD alone

de Carvalho JF et al. (2023)



Q: How can you safely access cannabis?

Current Status of Cannabis In Canada

Legal Framework





Recreational Model

- Retail Store Fronts
- OCS is a Crown Corporation & central distributor for ON stores
- ⚠ Regulations stipulate the ban on therapeutic discussions



Medical Model

- Medical Cannabis has been legal since 2001 in Canada
- Licensed Producers (Manufacturers)
- Mail Order (Online only) – NO STOREFRONTS
- 1-800 # call centers with non-medical professionals assisting patients with product selection, questions and even dosing!
- >900 LPs exist as per Health Canada
- CANNOT leave Canada with Cannabis. Period.
- ¹Data on medical client registrations. (2022). Retrieved 20 April 2022, from <https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/research-data/medical-purpose.html>

Patient Journey:

1. Obtain medical document
2. Register with an LP
3. Wait 2-7 days for approval
4. Patient receives an email
5. Patient orders online
6. Product(s) ship directly to patient

Difference between medical and recreational = INTENTION



Patient Information

First Name(s): _____

Last Name: _____

Birth Date: _____

Gender: Male Female N/A

Health Card #: _____

Exp: _____ (Veterans please enter K#)

Phone #: _____ **Email:** _____

Drug Allergies: NKDA Yes (please specify): _____

Affix Patient Label or Stamp here

Diagnosis: _____

Daily Quantity: 1g 2g 3g 4g 5g **Other:** _____
of dried gram per day

Duration in Days: 60 90 120 150 180 365 **Other:** _____
365 days maximum

Special Considerations: _____
Dosage form, limitations, dose, etc.

Health Care Practitioner Information

First Name(s): _____ **Last Name:** _____

Profession: _____ **License #:** _____ **Province Authorized to Practice in:** _____

Address: _____ **City:** _____ **Postcode:** _____ **Province:** _____

Phone #: _____ **Fax:** _____ **Email:** _____

Consultation Method: In-Person Telemedicine **Name of Office or Clinic:** _____

By signing this document, the health care practitioner is attesting that the

Physician Signature : _____

Medical Document

aka prescription

- Any MD/NP may authorize a medical document
- CANNABIS IS NOT COVERED BY OHIP – THERE IS NO DIN NUMBER
- Other provinces have differences in how they regulate medical cannabis (different legal age to buy it and different models for who can sell it)
- Private Insurance MAY cover it – usually for: Cancer-therapy, MS, Seizure Disorder, RHEUMATOID ARTHRITIS, palliative care
 - Green Shield
 - Canada Life
 - Sunlife
 - *Find these forms at www.hybridpharm.com

- ¹<https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/information-medical-practitioners/cannabis-medical-purposes-regulations-daily-amount-fact-sheet-dosage.html>



Speak with your doctor, rheumatologist, specialist about cannabis

- Medical Cannabis Clinics

- Hybrid Pharm (www.hybridpharm.com)
- Greenleaf (<https://greenleafmc.ca/>)
- Canadian Cannabis Clinics (*Owned by Aurora)
- Apollo and Bodystream Cannabis Clinics (*Owned by Spectrum/Tweed)

All LEGAL cannabis products adhere to Good Production Practices set by Health Canada Regulations within the Cannabis Act.



Q: What are the safest ways to use medical cannabis and how do you know what the appropriate dosage is?

You Don't Have to Smoke It!

Cannabis Formats

**Safest route =
Non-inhaled formats**



DOSING

CBD Oil/Capsule:



CBD Oils varying in concentration

20mg/g
50mg/g
100mg/g
200mg/g

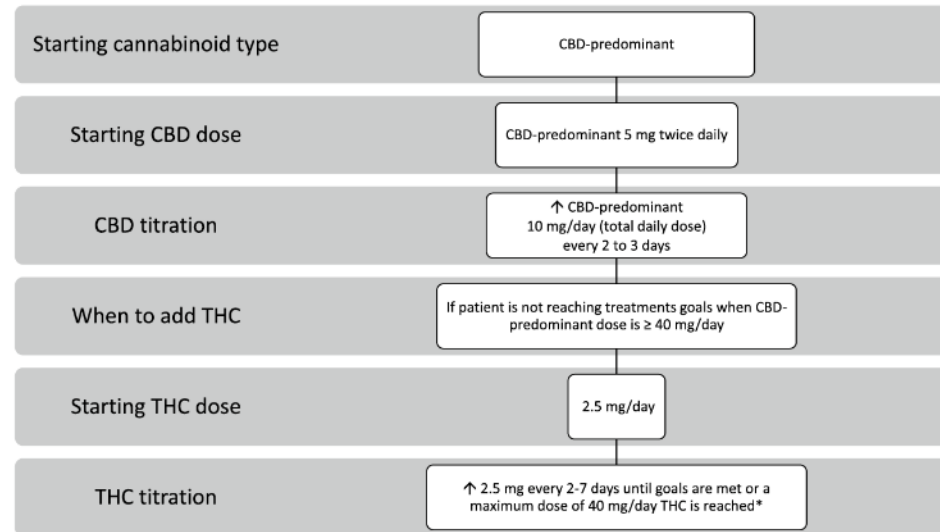
1ml = 20/50/100/200mg

Chronic Pain (arthritis, fibromyalgia, etc): – 25mg-100mg twice daily

Anxiety: 25-50mg once/twice daily

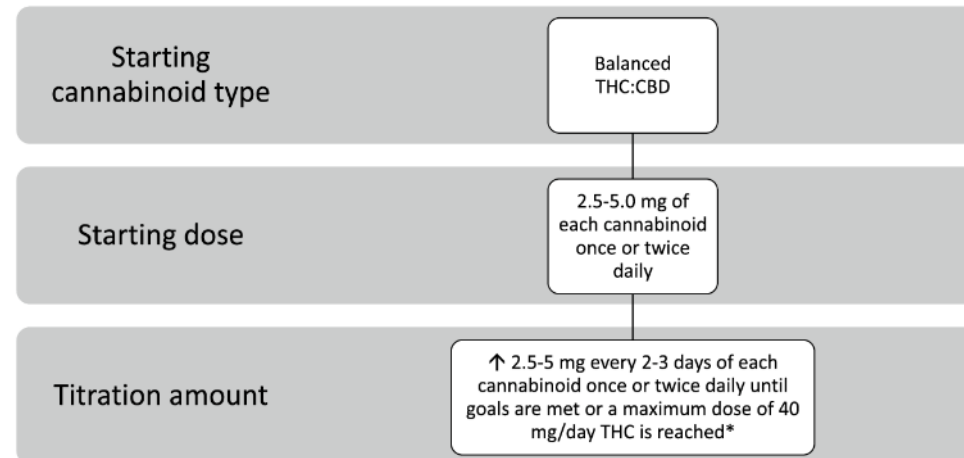
Sleep: 25-100mg 1-2 hours prior to bed.

DOSING



*Refer for expert consultation if considering > 40 mg/day THC

Fig. 2 Routine protocol for medical cannabis dosing and administration



*Refer for expert consultation if considering > 40 mg/day THC

Fig. 4 Rapid protocol for medical cannabis dosing and administration

Bhaskar, A., Bell, A., Boivin, M., Briques, W., Brown, M., & Clarke, H. et al. (2021). Consensus recommendations on dosing and administration of medical cannabis to treat chronic pain: results of a modified Delphi process. *Journal Of Cannabis Research*, 3(1). doi: 10.1186/s42238-021-00073-1



Q: What are the side effects of medical cannabis?

Notable Side Effects

Table 4
Adverse events associated with cannabis-based medicines.

Side effect	Most common	Common	Rare
Drowsiness/fatigue	✓		
Dizziness	✓		
Dry mouth	✓		
Cough, phlegm, bronchitis (Smoking only)	✓		
Anxiety	✓		
Nausea	✓		
Cognitive effects	✓		
Euphoria		✓	
Blurred vision		✓	
Headache		✓	
Orthostatic hypotension			✓
Toxic psychosis/paranoia			✓
Depression			✓
Ataxia/dyscoordination			✓
Tachycardia (after titration)			✓
Cannabis hyperemesis			✓
Diarrhea			✓

THC

- Anxiety
- Rapid heart rate
- Dry mouth/eyes
- “Munchies”

CBD

- Mild – little to no side effects
- Drowsiness
- Dry mouth
- GI (diarrhea, nausea, upset stomach)



Q: How do I know if it is working?



Q: What drug interactions should I be aware of?

Table 2

Potential Cannabinoid Drug Interactions*

Enzyme	Interaction and effect	Drugs
CYP 3A4	Inducers: may decrease THC and/or CBD Inhibitors: may increase THC and/or CBD Substrates: CBD is potential inhibitor of CYP3A4 and could increase 3A4 substrates. Caution with medications with smaller therapeutic index (e.g. tacrolimus). Unlikely to have effect on THC	Carbamazepine, phenobarbital, phenytoin, rifampin, St. John's wort Azole antifungals, clarithromycin, diltiazem, erythromycin, grapefruit, HIV protease inhibitors, macrolides, mifepristone, verapamil Alprazolam, atorvastatin, carbamazepine, clobazam, cyclosporine, diltiazem, HIV protease inhibitors, buprenorphine, tacrolimus, cyclosporine, phenytoin, sildenafil, simvastatin, sirolimus, verapamil, zopiclone
CYP 2C9	Inducers: may decrease THC concentration. Unlikely to have effect on CBD Inhibitors: may increase THC concentration. Unlikely to have effect on CBD Substrates: THC and/or CBD may increase drug levels, should monitor for toxicity	Amiodarone, fluconazole, fluoxetine, metronidazole, valproic acid, sulfamethoxazole Carbamazepine, rifampin Warfarin, rosuvastatin, phenytoin
CYP 2C19	Inducers: may decrease CBD and THC Inhibitors: may increase CBD and THC Substrates: CBD may increase the level of medications metabolized by 2C19 such as norclobazam (active metabolite in clobazam). CBD may also prevent clopidogrel from being activated. Unlikely to have effect on THC	Carbamazepine, rifampin, St. John's wort cimetidine, omeprazole, esomeprazole, ticlopidine, fluconazole, fluoxetine, isoniazid aripiprazole, citalopram, clopidogrel, diazepam, escitalopram, moclobemide, norclobazam, omeprazole, pantoprazole, sertraline
CYP 1A1 and 1A2	Substrates: Smoking cannabis can stimulate these isoenzymes and increase the metabolism of these medications.	Amitriptyline, caffeine, clozapine, duloxetine, estrogens, fluvoxamine, imipramine, melatonin, mirtazapine, olanzapine, theophylline
p-glycoprotein	Substrates: CBD may inhibit p-glycoprotein drug transport. Should monitor for toxicity. No effect from use of THC	Dabigatran, digoxin, loperamide

* Formal drug interaction studies with cannabinoids have not been conducted. Other drug interactions are possible as more individuals use cannabinoids with other medications. © Caroline MacCallum, MD, 2021; used with permission. Information gathered from [3,4,14,16,26,34,44,53,74].

Drug Interactions

“Clinically, significant drug interactions have proven rare, and there is no drug that cannot be used with cannabis, if necessary.”

MacCallum CA, Russo EB. Practical considerations in medical cannabis administration and dosing. Eur J Intern Med. 2018;49:12-19. doi:10.1016/j.ejim.2018.01.004

Common Drugs to Note

Amitriptyline

- Cannabis may cause more dry mouth, sedation, lethargy

Anti-Convulsants:

- Clobazam → CBD increases toxic effects by 500%
- Valproic Acid → increase in liver enzymes

Cymbalta (duloxetine)

- If smoked, levels of Cymbalta will decrease
- CBD may increase side effects of Cymbalta (drowsiness)

Blood Thinners

- Plavix (clopidogrel) - CBD may reduce Plavix effectiveness
- Coumadin (Warfarin) – CBD may increase bleeding
- Dabigatran – CBD may increase bleeding

Anti-Rheumatics

- Xeljanz - CBD may increase Xeljanz effects

Drug interactions are theoretical. Drug interactions are more commonly pharmacodynamic in effect.



Q: Does medical cannabis research evidence align with what you see in practice?

Table 3

Levels of evidence for cannabis-based medicines in various conditions.

Cannabis and nabiximols supporting evidence	
Level of evidence	Benefits
Conclusive or substantial evidence of efficacy	<ul style="list-style-type: none"> • Adult chronic pain treatment • Multiple sclerosis spasticity symptoms • Chemotherapy-induced nausea and vomiting • Treatment of intractable seizures in Dravet and Lennox-Gastaut syndromes (CBD)
Moderate evidence of efficacy	<ul style="list-style-type: none"> • Improving outcomes in individuals with sleep disturbances associated with chronic pain, multiple sclerosis, fibromyalgia, obstructive sleep apnea syndrome • Decreasing intraocular pressure in glaucoma
Limited evidence of efficacy	<ul style="list-style-type: none"> • Symptoms of dementia • Symptoms of Parkinson disease • Positive and negative symptoms of schizophrenia • Symptoms of posttraumatic stress disorder • Appetite and decreasing weight loss associated with HIV/AIDS • Multiple sclerosis spasticity (clinician-measured) • Traumatic brain injury/intracranial haemorrhage associated disability, mortality, and other outcomes • Symptoms of anxiety in social anxiety disorders (CBD) • Symptoms of Tourette syndrome
Limited evidence of inefficacy	<ul style="list-style-type: none"> • Depressive symptoms in chronic pain or multiple sclerosis patients
Insufficient evidence of efficacy or inefficacy	<ul style="list-style-type: none"> • Addiction abstinence • Symptoms of irritable bowel syndrome • Cancers, including glioma • Cancer-associated anorexia, cachexia syndrome and anorexia nervosa • Symptoms of amyotrophic lateral sclerosis • Chorea and some neuropsychiatric symptoms associated with Huntington disease • Dystonia

Levels of Evidence of Efficacy:

1) Conclusive Evidence:

- Chronic Pain
- MS spasticity
- Dravet and Lennox-Gastaut
- CINV

2) Moderate Evidence:

- Insomnia 2⁰ chronic pain, MS, fibromyalgia, obstructive sleep apnea

3) Limited Evidence:

- Dementia, Parkinson's disease
- PTSD
- TBI
- GAD, SAD
- Appetite Stimulation
- Tourette's Syndrome



Q: What excites you about current research into medical cannabis and arthritis?

Table 2 – A summary of studies investigate effects of CBD on arthritis

References	Study sample (patient population, sample size, gender and age)	Treatment schedule	Study design	Conclusion
Malfait et al. (2000)	mices induced by model of murine CIA	p.o. applied – CBD doses were 10 mg/kg, 25 mg/kg, and 50 mg/kg (n=6 per group). Control group dose olive oil (n=6). Intraperitoneal administration – CBD – 20 mg/kg (n=12), 10 mg/kg (n=17), 5 mg/kg (n=15), and 2.5 mg/kg (n=9) and placebo (n=23)	disease-induced animal model	CBD was equally effective when administered i.p. or orally. The dose with an optimal effect at 5 mg/kg per day i.p. or 25 mg/kg per day orally. Clinical improvement was associated with the protection of the joints against severe damage.
Hammell et al. (2016)	54 rats were used in the experiments described here of which 21 were used as controls and 23 were subjected to adjuvant-induced arthritis	CBD gels (0.6, 3.1, 6.2 or 62.3 mg/day) were applied for 4 consecutive days after arthritis induction	parallel (control vs. disease-induced animal model)	Transdermal CBD gel with this dose significantly reduced joint swelling, limb posture scores as a rating of spontaneous pain, immune cell infiltration and thickening of the synovial membrane.
Jelinek et al. (2022)	14 rats with RA (induced by CIA)	7.5 mg of CBD per oral for 24 days	randomized, single-dose, laboratory-blinded	They observed the improvement of clinical parameters of RA after administration of CBD.
Gamble et al. (2018)	16 dogs diagnosed with osteoarthritis	CBD/placebo, 2 mg/kg every 12 h for 4 weeks. After 2-weeks of washouts period cross-over	randomized, placebo-controlled, owner and veterinarian double-blind, cross-over	Dogs were more comfortable and active when were treated by CBD.
Heineman et al. (2022)	18 participants with joint arthritis	treat by CBD twice a day 2 weeks (6.2 mg/ml CBD with shea butter) or placebo, followed by a 1-week washout period and then crossover	phase 2, double-blinded, randomized controlled	Topical CBD treatment showed a substantial reduction in associated disability and pain with specific joint arthritis.

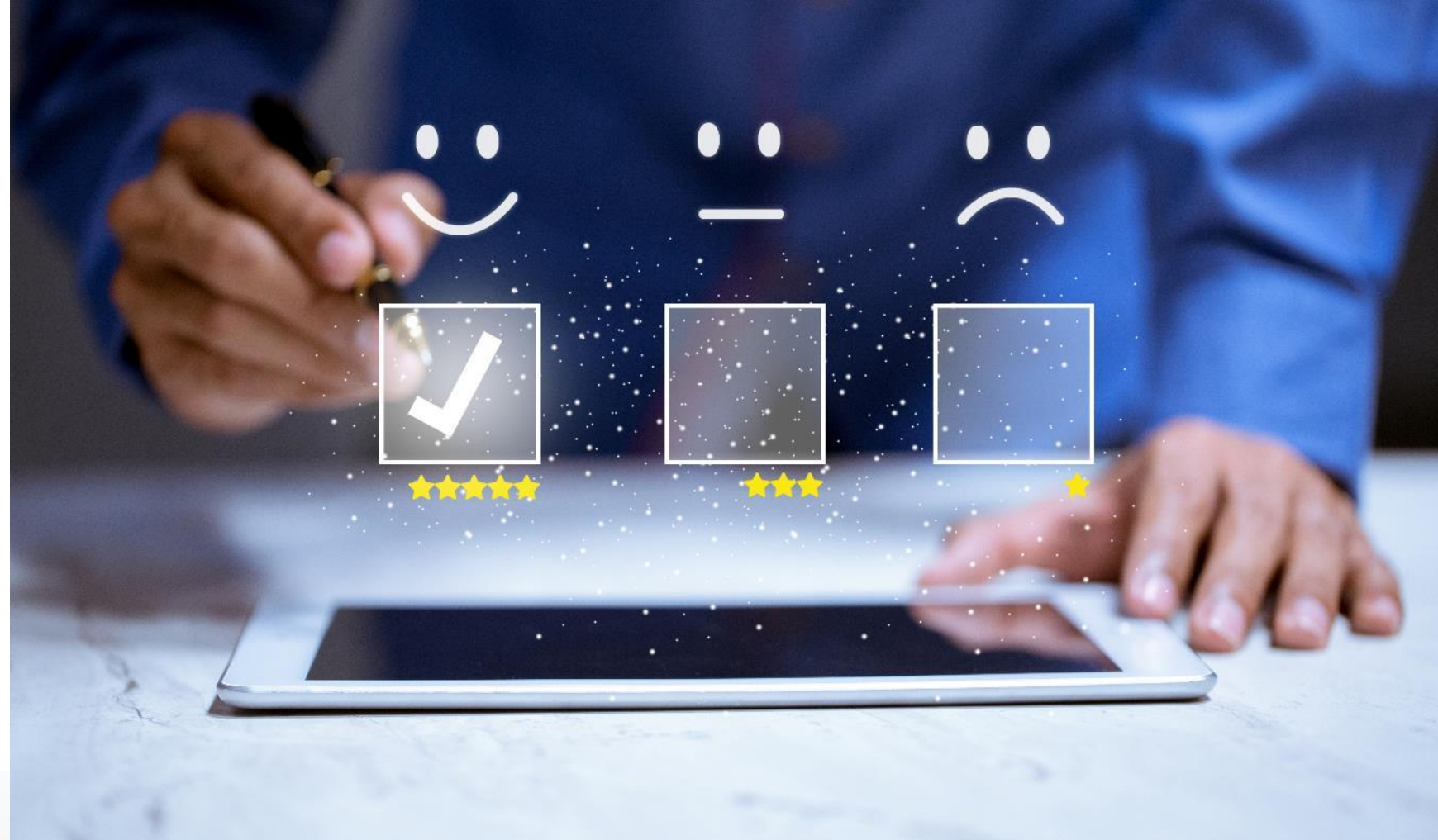
CBD – cannabidiol; RA – rheumatoid arthritis; CIA – collagen-induced arthritis



Q: Any final thoughts or recommendations?



Q: Questions



Q: Tell us what you think...



- ▼ Join Dr. Robert Sealey and Rina Charalampis at a virtual information booth immediately following the live webinar.
- ▼ Dr. Sealey will be available to answer your questions about medical cannabis and share how he has used it with some of his patients.
- ▼ Link to the virtual information booth is in your reminder email and will be posted in the live webinar.



arthritis.ca/booth

