CBD CLINICAL UPDATES: PAIN MANAGEMENT

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MOSS COMPOUNDING PHARMACY

JUNE 22, 2021

TOPICS TO COVER

- Review CBD Pharmacology
- Review Clinical Literature on CBD for pain
- Review Clinical experience with patient CBD use for pain

Cannabinoids

Endocannabinoids (brain derived)

- Anandamide (AEA)
- 2-Arachidonylglycerol (2-AG)

Phytocannabinoids (plant derived)

- Cannabidiol (CBD)
- Tetrahydrocannabinol (THC)
- Cannabichromene (CBC)
- Cannabigerol (CBG)
- Many others

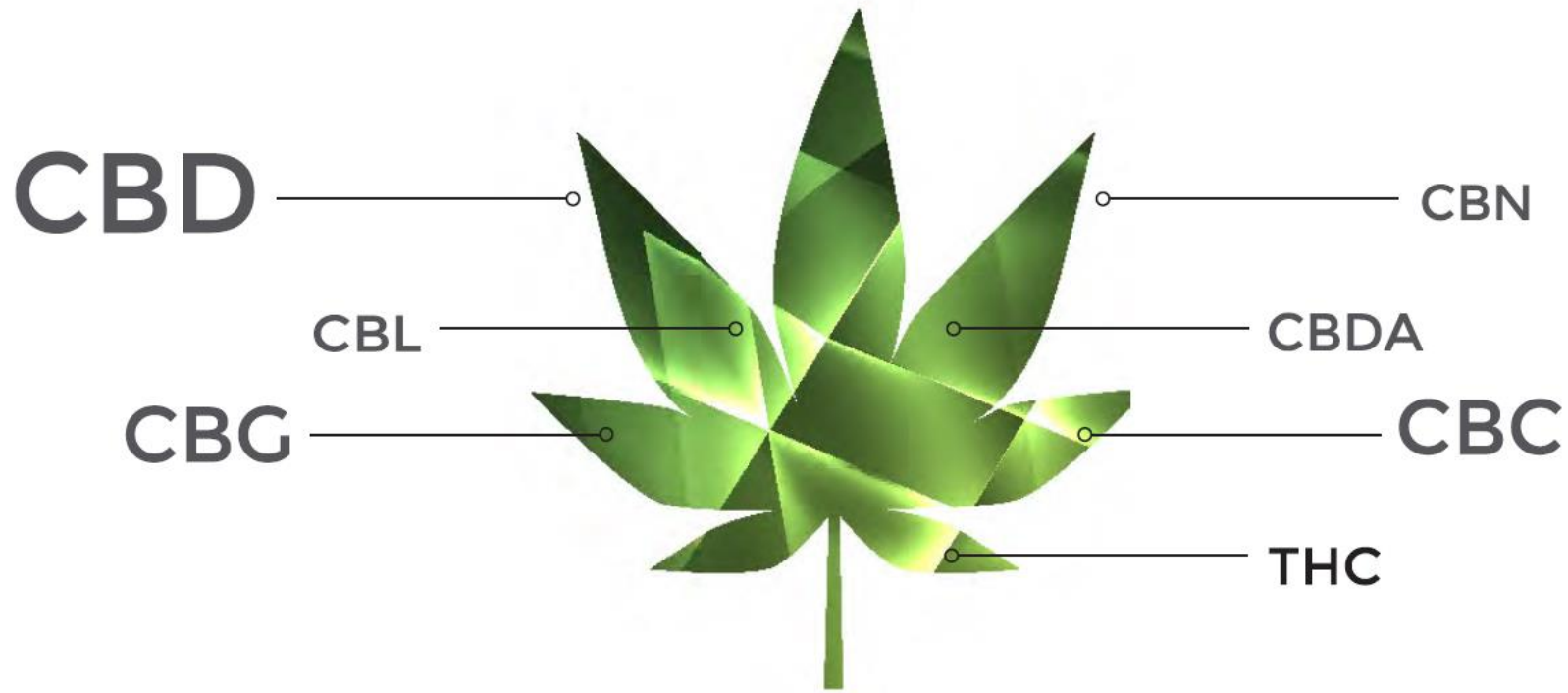
Synthetic cannabinoids (laboratory derived)

- Dronabinol
- Nabilone

Reference: Clinicians' Guide to Cannabidiol and Hemp oils. *Mayo Clinic Proceedings* 2019 94, 1840-1851DOI: (10.1016/j.mayocp.2019.01.003)

WHAT IS FULL SPECTRUM HEMP EXTRACT?

Full spectrum hemp extract incorporates an assortment of cannabinoids that occur naturally in industrial hemp. Isolate CBD oil has been available for a longer period of time, but studies are showing that full spectrum hemp extract benefits our health the most.



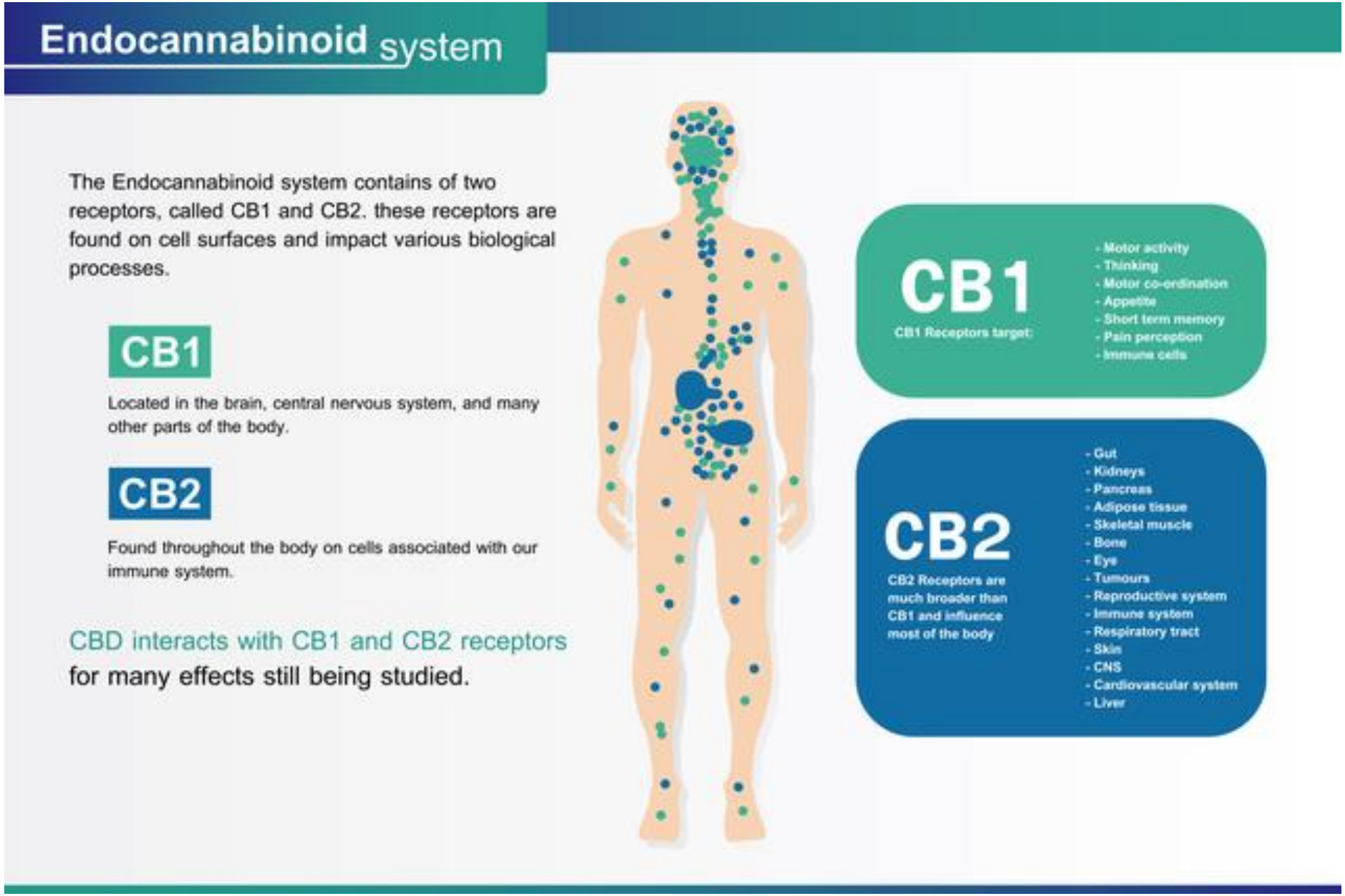


Image source: https://cbdoilreview.org/cbd-cannabidiol/cbd-oil-endocannabinoid-production-human-body/

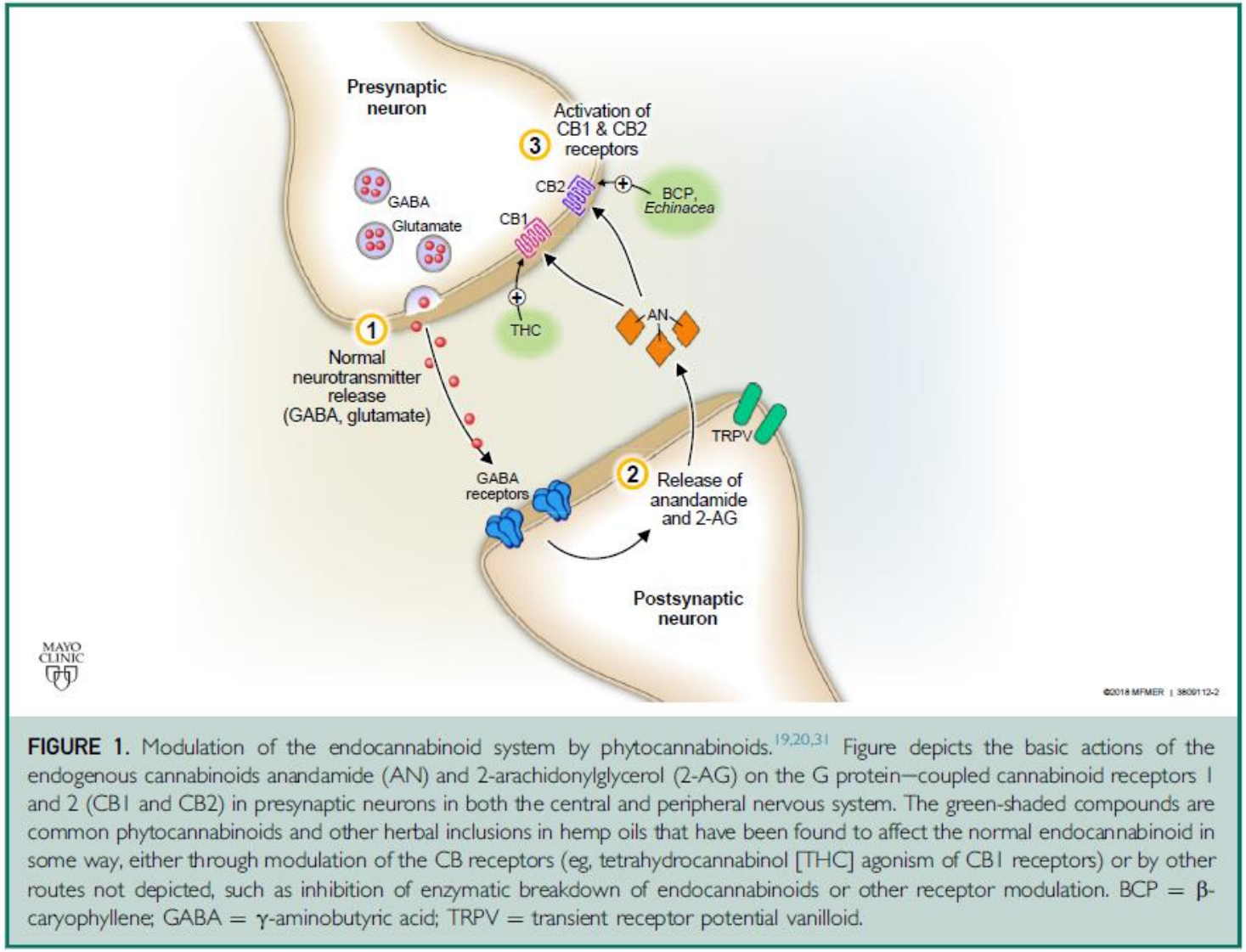


FIGURE 1. Modulation of the endocannabinoid system by phytocannabinoids.[19,20,31] Figure depicts the basic actions of the endogenous cannabinoids anandamide (AN) and 2-arachidonylglycerol (2-AG) on the G protein–coupled cannabinoid receptors 1 and 2 (CB1 and CB2) in presynaptic neurons in both the central and peripheral nervous system. The green-shaded compounds are common phytocannabinoids and other herbal inclusions in hemp oils that have been found to affect the normal endocannabinoid in some way, either through modulation of the CB receptors (eg, tetrahydrocannabinol [THC] agonism of CB1 receptors) or by other routes not depicted, such as inhibition of enzymatic breakdown of endocannabinoids or other receptor modulation. BCP = β-caryophyllene; GABA = γ-aminobutyric acid; TRPV = transient receptor potential vanilloid.

Upregulation of ECS

- Some direct effects
- Increase Anandamide levels by blocking degradation by FAAH

Multiple other MOA:

- Activation of 5-HT1A
- Activation of TRPV1-2 vanilloid receptors
- Blocks low-voltage Ca2+ channels
- Stimulated inhibitory Glycine receptor
- Increase antioxidants, particularly glutathione
- Possibly more…..

References: Harrison J, et al. Clinicians' Guide to Cannabidiol and Hemp oils. *Mayo Clinic Proceedings* 2019 94, 1840-1851DOI: (10.1016/j.mayocp.2019.01.003)
Mlost J, et al. Cannabidiol for Pain Treatment: Focus on Pharmacology and Mechanism of Action. *Int. J of Molecular Sciences*. 2020(21); 8870:1-21.

TABLE 2. Common Components and Added Ingredients in CBD and Hemp Oil Products

Ingredient	Chemical classification	Approximate concentration in hemp[39]	Other sources	Mechanism of action	Potential therapeutic actions
Cannabidiol	Phytocannabinoid	Up to 40%	None known	Anandamide uptake inhibitor, TRPV1 receptor activation, GPR55 receptor activation, 5-HT_{1A} activation[27,28,31]	Antiepileptic, antinociceptive, anti-inflammatory, anxiolytic, antidepressive, addiction management/treatment, inflammatory dermatologic conditions, neuroprotective, others[42-62]
Tetrahydrocannabinol	Phytocannabinoid	<0.3%	None known	Binds to CB1 receptors[31]	Antiemetic, antinociceptive, others[31]
β-Caryophyllene	Sesquiterpenoid	Less than 1%	Black pepper, clove, rosemary, hops	Binds to CB2 receptors[63]	Anxiolytic, anti-nociceptive[64-67]
Limonene	Terpenoid	Less than 1%	Citrus fruits, rosemary	Induction of glutathione	Antioxidant, antitumor activity[68]
Cannabichromene	Phytocannabinoid	Varies considerably with strain	None known	Anandamide uptake inhibitor[69]	Antinociceptive[70]
Cannabigerol	Phytocannabinoid	Varies considerably with strain	None known	Anandamide uptake inhibitor[70]	Anti-inflammatory, neuroprotective[71,72]
Echinacea	Alkylamides	None	*Zanthoxylum* (Sichuan pepper)	Binds to CB2 receptors[73-75]	Anti-inflammatory, antioxidant, antimicrobial[75-78]
Boswellia	Triterpenes	None	Also known as frankincense	Inhibition of prostaglandin E_2 synthase[79]	Anti-inflammatory[79]
Turmeric	Curcuminoids (eg, diferuloylmethane, demethoxycurcumin)	None	None known	May bind to CB1 receptors[80]	Unclear in preclinical, purported antinociceptive and anti-inflammatory properties[81]
Ashwaganda	Steroidal alkaloids and lactones	None	Also known as *Withania somnifera*	Possible mimicry of GABA[82]	Stress reduction, anxiolytic, immuno-modulatory[82]
Magnolia	Polyphenols	None	Also known as magnolia bark	Binds to CB2 receptors[83]	Antioxidant, anti-inflammatory[84]

GABA = γ-aminobutyric acid; GPR55 = G protein–coupled receptor 55; TRPV1 = transient receptor potential vanilloid 1.

Reference: Clinicians' Guide to Cannabidiol and Hemp oils. *Mayo Clinic Proceedings* 2019 94, 1840-1851DOI: (10.1016/j.mayocp.2019.01.003)

TABLE 1. Hemp Seed, CBD, and Cannabis Oils

Variable	Hemp seed oils[40]	Hemp/CBD oils[22]	Cannabis oils[22,41]
Part of plant extracted	Seeds	Flowers and leaves of hemp plant	Flowers and leaves of marijuana plant
Main components	Omega-6 and omega-3 fatty acids, γ-linolenic acid, nutritious antioxidants	Mostly CBD and BCP with other smaller-quantity phytocannabinoids and terpenoids	Mostly THC with some CBD and other phytocannabinoids and terpenoids
THC levels	None	<0.3% Dry weight	>0.3% Dry weight (often very high amounts such as 80%)
CBD levels	Little to none	More than average cannabis plants (12%-18% CBD, often higher due to postextraction enrichment)	Lower levels (10%-15%)
Uses	Nutritional supplement, other uses of hemp such as clothing and fibers	Medicinal uses of CBD and full-spectrum hemp oils	Medicinal uses of THC

BCP = β-caryophyllene; CBD = cannabidiol; THC = tetrahydrocannabinol.

Reference: Clinicians' Guide to Cannabidiol and Hemp oils. *Mayo Clinic Proceedings* 2019 94, 1840-1851DOI: (10.1016/j.mayocp.2019.01.003)

LITERATURE REVIEW

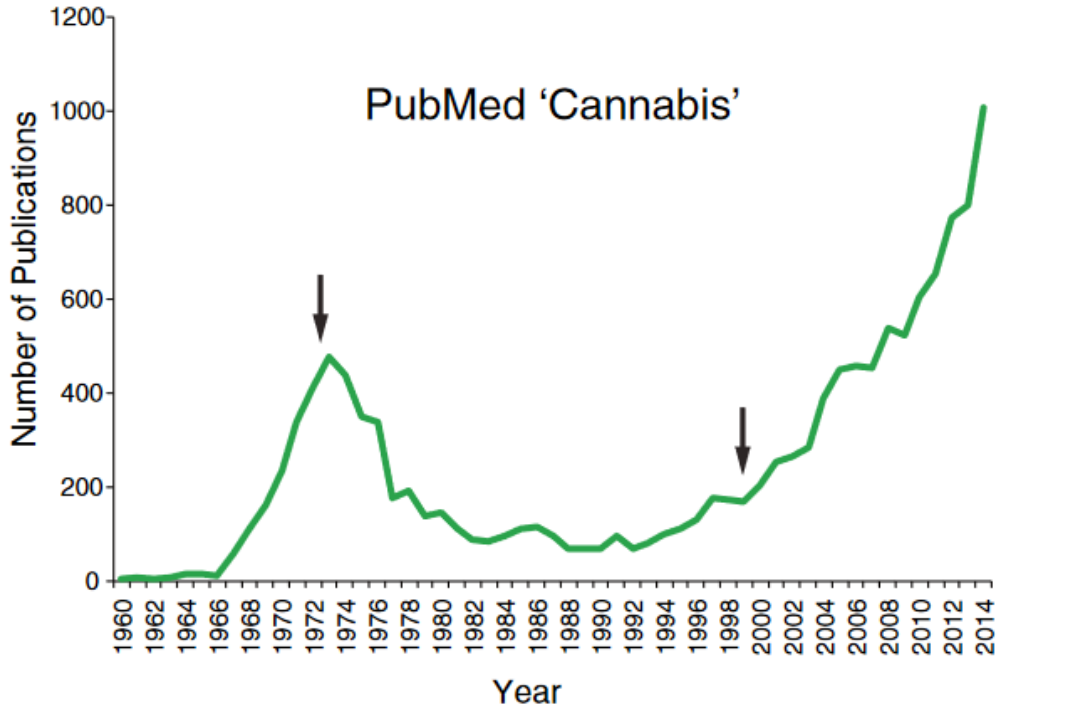
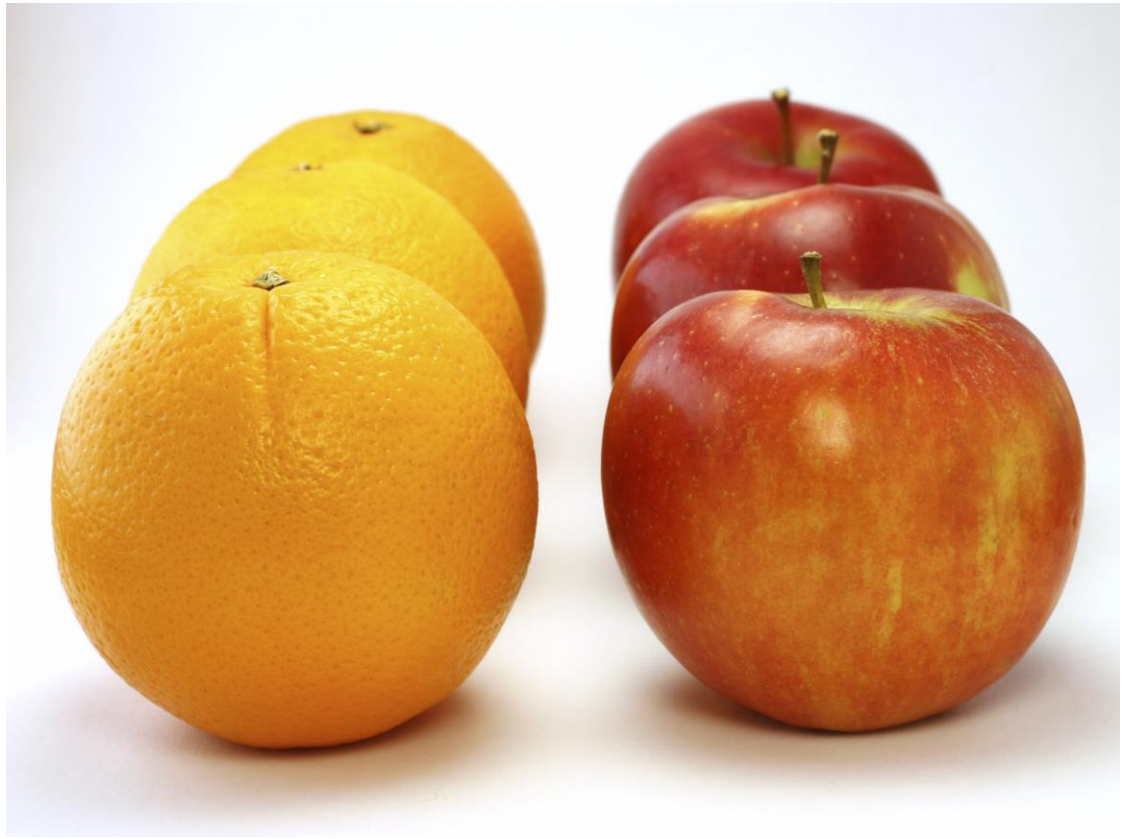


Fig. 1 The number of publications based on PubMed search for the term "cannabis". Patterns coincides with governmental policy and societal changes (some denoted by arrows), such as cannabis becoming a Schedule I drug in the USA in 1970, in the 1970s state laws and local regulations begin to ban possession or sale of cannabis, in 1996 California voters passed Proposition 215 that legalized medical cannabis, and in 2000 there were increased attempts for decriminalization and legalized marijuana use around the USA. No other cannabinoid-related PubMed search term showed the same temporal pattern

Reference: Hurd, et al. Early Phase in the Development of Cannabidiol as a Treatment for Addiction: Opioid Relapse Takes Initial Center Stage. *Neurotherapeutics*. 2015 (12): 807-815

CHALLENGES IN THE LITERATURE REVIEW

- Cannabis vs Cannabidiol vs Cannabidiols
- Delivery methods
- Dosing
- Quality of product



Research

Original Investigation

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 Schmidlkofer, MSc; Marie Westwood, PhD; Jos Kleijnen, MD, PhD

IMPORTANCE Cannabis and cannabinoid drugs are widely used to treat disease or alleviate symptoms, but their efficacy for specific indications is not clear.

OBJECTIVE To conduct a systematic review of the benefits and adverse events (AEs) of cannabinoids.

DATA SOURCES Twenty-eight databases from inception to April 2015.

STUDY SELECTION Randomized clinical trials of cannabinoids for the following indications: nausea and vomiting due to chemotherapy, appetite stimulation in HIV/AIDS, chronic pain, spasticity due to multiple sclerosis or paraplegia, depression, anxiety disorder, sleep disorder, psychosis, glaucoma, or Tourette syndrome.

DATA EXTRACTION AND SYNTHESIS Study quality was assessed using the Cochrane risk of bias tool. All review stages were conducted independently by 2 reviewers. Where possible, data were pooled using random-effects meta-analysis

Editorial page 2431

Related article page 2474

Supplemental content at jama.com

Reference: Whiting, P. et al. Cannabinoids for Medical Use: A Systemic Review and Meta-analysis. JAMA. 2015; 313 (24): 2456-2473

Research

Original Investigation

Cannabinoids for Medical Use

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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 Schmidlkofer, MSc; Marie Westwood, PhD; Jos Kleijnen, MD, PhD

- Reviewed 28 clinical trials
- Evaluated a wide variety of cannabinoids - THC, CBD, CBD/THC, cannabis (marijuana), synthetic
- Most of the research focused on THC drugs dronabinol, nabilone, and nabiximols
- CBD specific info:
  - Studies used isolate capsules or oral mucosal spray (only 4 trials total)
  - Study indications (Primary outcome GRADE rating):
    - Spasticity with MS (moderate)
    - Anxiety (low)
    - Psychosis (low)
- Overall author conclusion
  - Moderate quality evidence that cannabinoids may result in marked pain reduction

Reference: Whiting, P. et al. Cannabinoids for Medical Use: A Systemic Review and Meta-analysis. JAMA. 2015; 313 (24): 2456-2473

REVIEW

MAYO CLINIC

Clinicians' Guide to Cannabidiol and Hemp Oils

Harrison J. VanDolah, BA; Brent A. Bauer, MD; and Karen F. Mauck, MD

Abstract

Cannabidiol (CBD) oils are low tetrahydrocannabinol products derived from *Cannabis sativa* that have become very popular over the past few years. Patients report relief for a variety of conditions, particularly pain, without the intoxicating adverse effects of medical marijuana. In June 2018, the first CBD-based drug, Epidiolex, was approved by the US Food and Drug Administration for treatment of rare, severe epilepsy, further putting the spotlight on CBD and hemp oils. There is a growing body of preclinical and clinical evidence to support use of CBD oils for many conditions, suggesting its potential role as another option for treating challenging chronic pain or opioid addiction. Care must be taken when directing patients toward CBD products because there is little regulation, and studies have found inaccurate labeling of CBD and tetrahydrocannabinol quantities. This article provides an overview of the scientific work on cannabinoids, CBD, and hemp oil and the distinction between marijuana, hemp, and the different components of CBD and hemp oil products. We summarize the current legal status of CBD and hemp oils in the United States and provide a guide to identifying higher-quality products so that clinicians can advise their patients on the safest and most evidence-based formulations. This review is based on a PubMed search using the terms *CBD*, *cannabidiol*, *hemp oil*, and *medical marijuana*. Articles were screened for relevance, and those with the most up-to-date information were selected for inclusion.

 ■ Mayo Clin Proc. 2019;94(9):1840-1851

Mayo Clinic Proceedings 2019 94, 1840-1851 DOI: (10.1016/j.mayocp.2019.01.003)

ARTICLE HIGHLIGHTS

- Cannabidiol (CBD) is a nonintoxicating compound extracted from *Cannabis sativa* plants that has gained popularity for medical uses ranging from epilepsy to pain control and addiction treatment because of its differing mechanism of action from marijuana and its safety profile.
- Although important preclinical and pilot human studies have suggested a potential role for CBD in numerous clinical situations, thorough clinical studies have only been performed on intractable epilepsy syndromes for which Epidiolex, a CBD drug, was approved by the US Food and Drug Administration for use.
- The legal landscape of CBD remains complex because of differing state and federal laws giving access to medical hemp and marijuana products.
- The CBD and hemp oil product market remains a concerning one because of noted variability in CBD and tetrahydrocannabinol levels in products, as well as lack of regulation in production and distribution.
- Although CBD and hemp oils remain an unproven therapeutic option, physicians should remain open to the possible future role these products may play in the management of a variety of difficult to treat diseases, in particular pain and addiction treatment in the context of the opioid crisis.

Reference: Clinicians' Guide to Cannabidiol and Hemp oils. *Mayo Clinic Proceedings* 2019 94, 1840-1851DOI: (10.1016/j.mayocp.2019.01.003)

REVIEW

MAYO CLINIC

Check for updates

Clinicians' Guide to Cannabidiol and Hemp Oils

Harrison J. VanDolah, BA; Brent A. Bauer, MD; and Karen F. Mauck, MD

- "As for CBD and hemp oils' potential for use in the treatment of chronic pain, in the most recent review on the topic in 2018, Donvito et al[42] wrote that "an overwhelming body of convincing preclinical evidence indicates that cannabinoids produce antinociceptive effects in inflammatory and neuropathic rodent pain models."
- "Additionally, it has been reported that CBD may be able to treat addiction through reduced activation of the amygdala during negative emotional processing and has been found to reduce heroin-seeking behavior, likely through its modulation of dopamine and serotonin. [43,44,85,86]"
- "Cannabidiol therefore represents an attractive option in chronic pain treatment, particularly in the context of opioid abuse, not only because of its potential efficacy but also because of its limited misuse and diversion potential as well as safety profile.[86] More research will be needed because these were pilot human studies with small sample sizes, but they represent potential future areas of cannabinoid use in the clinical treatment of pain relief and opioid abuse."

Reference: Clinicians' Guide to Cannabidiol and Hemp oils. *Mayo Clinic Proceedings* 2019 94, 1840-1851DOI: (10.1016/j.mayocp.2019.01.003)

POSTGRADUATE MEDICINE
2020, VOL. 132, NO. 1, 56–61
https://doi.org/10.1080/00325481.2019.1685298

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CLINICAL FOCUS: PAIN MANAGEMENT
ORIGINAL RESEARCH

Evaluation of the effects of CBD hemp extract on opioid use and quality of life indicators in chronic pain patients: a prospective cohort study

Alex Capano[a,b], Richard Weaver[c] and Elisa Burkman[c]

[a]Ecofibre Ltd, Philadelphia, PA, USA; [b]Lambert Center for the Study of Medicinal Cannabis & Hemp Philadelphia, Philadelphia, PA, USA; [c]University of Louisville, Louisville, KY, USA

ABSTRACT

Context: Chronic pain is highly prevalent in most of the industrialized nations around the world. Despite the documented adverse effects, opioids are widely used for pain management. Cannabinoids, and specifically Cannabidiol, is proposed as an opioid alternative, having comparable efficacy with better safety profile.

Objectives: We aim to investigate the impact of full hemp extract cannabidiol (CBD) on opioid use and quality of life indicators among chronic pain patients.

Methods: An initial sample of 131 patients was recruited from a private pain management center's investigative population. Ninety-seven patients completed the 8-week study. The primary inclusion criteria included patients between 30 and 65 years old with chronic pain who have been on opioids for at least 1 year. Data were collected at three different time points: baseline, 4, and 8 weeks. Opioid and other medication use were evaluated via the medication and psychiatric treatment receipt. Improvement was evaluated using four indices: Pain Disability Index (PDI-4); Pittsburgh Sleep Quality Index (PSQI), Pain Intensity and Interference (PEG); and Patient Health Questionnaire (PHQ-4).

Results: Over half of chronic pain patients (53%) reduced or eliminated their opioids within 8 weeks after adding CBD-rich hemp extract to their regimens. Almost all CBD users (94%) reported quality of life improvements. The results indicated a significant relationship between CBD and PSQI ($p = 0.003$), and PEG ($p = 0.006$). There was a trend toward improvement but no significant relationship between CBD use and PHQ and PDI.

Conclusion: CBD could significantly reduce opioid use and improve chronic pain and sleep quality among patients who are currently using opioids for pain management.

Key Message: This is a prospective, single-arm cohort study for the potential role of cannabinoids as an alternative for opioids. The results indicate that using the CBD-rich extract enabled our patients to reduce or eliminate opioids with significant improvement in their quality of life indices.

ARTICLE HISTORY
Received 25 September 2019
Accepted 23 October 2019

KEYWORDS
Cannabinoid; chronic pain; opioids; cannabidiol; sleep; cannabis

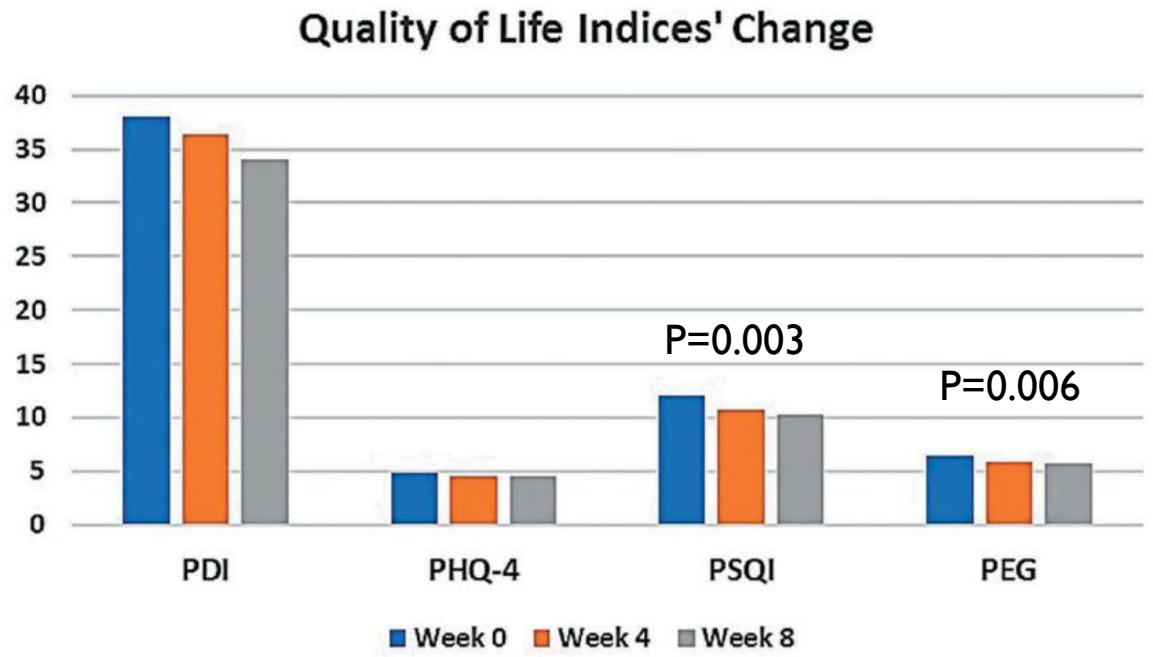

Figure 1. Quality of Life Indices' Change.

Reference: Capano, et al. Evaluation of the effects of CBD hemp extract on opioid use and quality of life indicators in chronic pain patients: a prospective cohort study. Postgraduate Medicine. 2020(132): 51-61

POSTGRADUATE MEDICINE
2020, VOL. 132, NO. 1, 56–61
https://doi.org/10.1080/00325481.2019.1685298

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CLINICAL FOCUS: PAIN MANAGEMENT
ORIGINAL RESEARCH

Evaluation of the effects of CBD hemp extract on opioid use and quality of life indicators in chronic pain patients: a prospective cohort study

Alex Capano[a,b], Richard Weaver[c] and Elisa Burkman[c]

- This study used used Ananda Professional Hemp Extract Oil capsules (same as we carry at our pharmacy)
- Study conducted in pain clinic in West Virginia
- 53% of chronic pain patients reduced or eliminated opioids in 8 weeks.

Cannabis and Cannabinoid Research
Volume 2.1, 2017
DOI: 10.1089/can.2017.0012

Cannabis and Cannabinoid Research

Mary Ann Liebert, Inc. publishers

ORIGINAL RESEARCH Open Access

Cannabis as a Substitute for Opioid-Based Pain Medication: Patient Self-Report

Amanda Reiman,[1,*] Mark Welty,[2] and Perry Solomon[3]

Abstract

Introduction: Prescription drug overdoses are the leading cause of accidental death in the United States. Alternatives to opioids for the treatment of pain are necessary to address this issue. Cannabis can be an effective treatment for pain, greatly reduces the chance of dependence, and eliminates the risk of fatal overdose compared to opioid-based medications. Medical cannabis patients report that cannabis is just as effective, if not more, than opioid-based medications for pain.

Materials and Methods: The current study examined the use of cannabis as a substitute for opioid-based pain medication by collecting survey data from 2897 medical cannabis patients.

Discussion: Thirty-four percent of the sample reported using opioid-based pain medication in the past 6 months. Respondents overwhelmingly reported that cannabis provided relief on par with their other medications, but without the unwanted side effects. Ninety-seven percent of the sample "strongly agreed/agreed" that they are able to decrease the amount of opiates they consume when they also use cannabis, and 81% "strongly agreed/agreed" that taking cannabis by itself was more effective at treating their condition than taking cannabis with opioids. Results were similar for those using cannabis with nonopioid-based pain medications.

Conclusion: Future research should track clinical outcomes where cannabis is offered as a viable substitute for pain treatment and examine the outcomes of using cannabis as a medication assisted treatment for opioid dependence.

Keywords: opiates; pain; harm reduction; substitution; opioids; cannabis

Reference: Reiman, A, et al. Cannabis as a Substitute for Opioid-based- Pain Medication: Patient Self-Report. Cannabis and Cannabinoid Research. 2017; 2(1).

Cannabis and Cannabinoid Research
Volume 2.1, 2017
DOI: 10.1089/can.2017.0012

Cannabis and Cannabinoid Research
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ORIGINAL RESEARCH Open Access

Cannabis as a Substitute for Opioid-Based Pain Medication: Patient Self-Report

Amanda Reiman,[1,*] Mark Welty,[2] and Perry Solomon[3]

- Study used cannabis (marijuana)
- Applications to CBD:
  - Marijuana = high THC/Low CBD content

Reference: Reiman, A, et al. Cannabis as a Substitute for Opioid-based- Pain Medication: Patient Self-Report. Cannabis and Cannabinoid Research. 2017; 2(1).

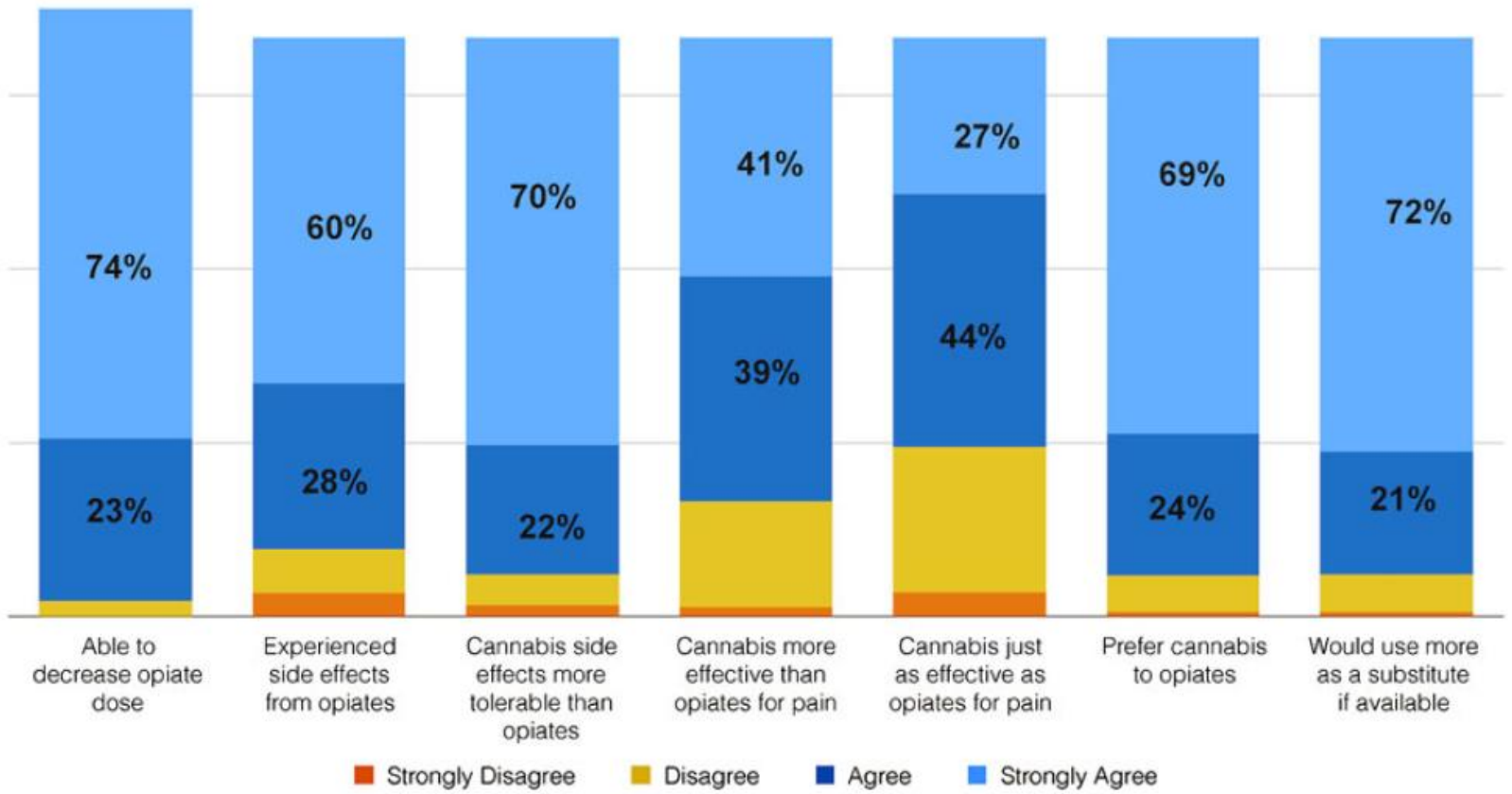


FIG. 2. Use of cannabis as a substitute/in conjunction with opioid-based pain medication ($n = 828$).

Reference: Reiman, A, et al. Cannabis as a Substitute for Opioid-based- Pain Medication: Patient Self-Report. Cannabis and Cannabinoid Research. 2017; 2(1).

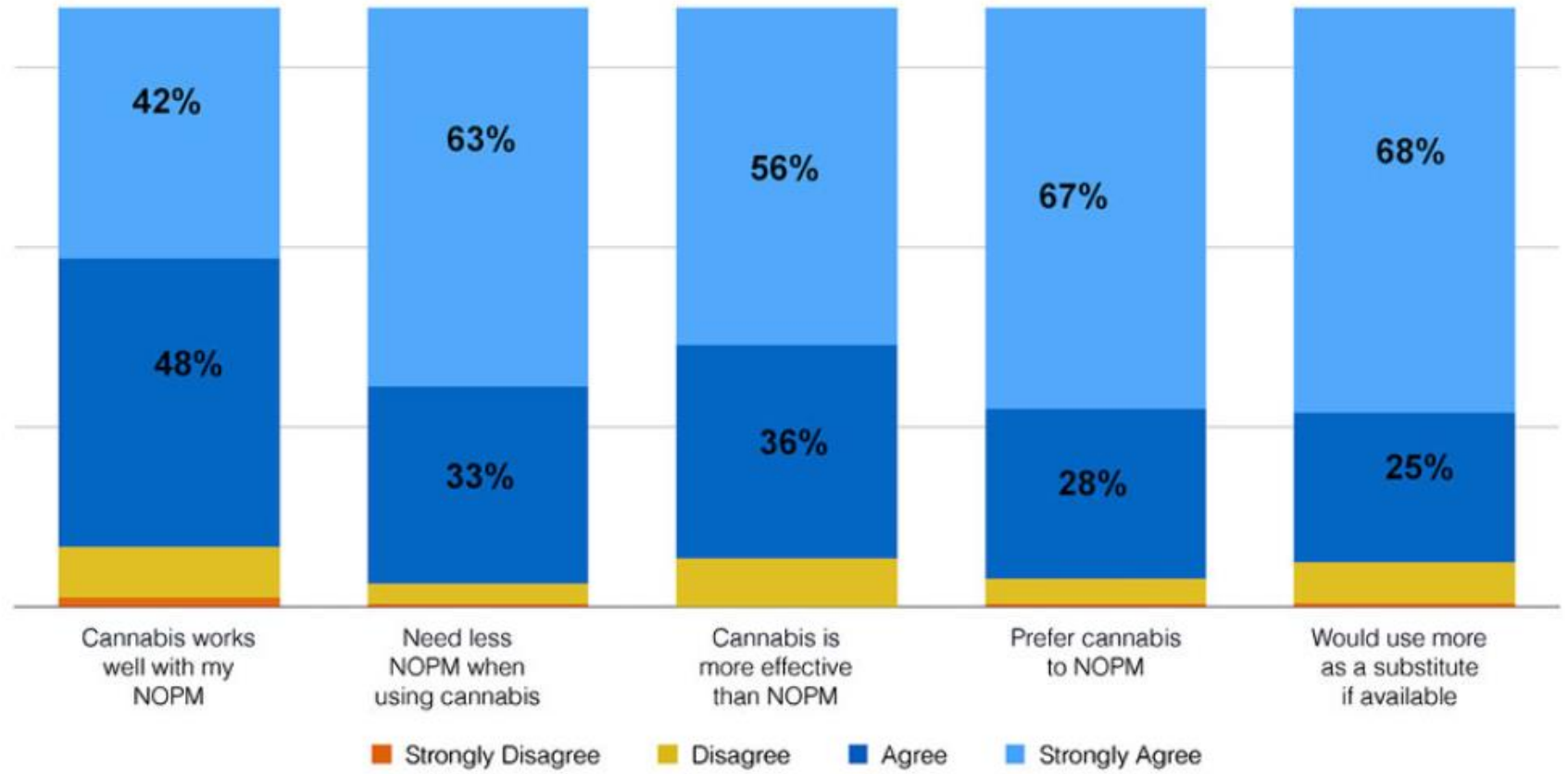


FIG. 3. Use of cannabis as a substitute/in conjunction with nonopioid based medication ($n = 1684$).

Reference: Reiman, A, et al. Cannabis as a Substitute for Opioid-based- Pain Medication: Patient Self-Report. Cannabis and Cannabinoid Research. 2017; 2(1).

Arthritis Care & Research
Vol. 68, No. 5, May 2016, pp 681–688
DOI 10.1002/acr.22727

ORIGINAL ARTICLE

Efficacy, Tolerability, and Safety of Cannabinoid Treatments in the Rheumatic Diseases: A Systematic Review of Randomized Controlled Trials

MARY-ANN FITZCHARLES,[1] PETER A. STE-MARIE,[1] WINFRIED HÄUSER,[2] DANIEL J. CLAUW,[3] SHAHIN JAMAL,[4] JACOB KARSH,[5] TARA LANDRY,[6] SHARON LECLERCQ,[7] JASON J. MCDOUGALL,[8] YORAM SHIR,[1] KAM SHOJANIA,[9] AND ZACH WALSH[4]

Objective. To assess the efficacy, tolerability, and safety of cannabinoids (phyto- and syntheto-) in the management of rheumatic diseases.

Methods. Multiple databases, including Medline, Embase, and CENTRAL, were searched. Randomized controlled trials with outcomes of pain, sleep, quality of life, tolerability (dropouts due to adverse events), and safety (serious adverse events), with comparison of cannabinoids with any type of control, were included. Study methodology quality was evaluated with the Cochrane risk of bias tool.

Results. In 4 short-term studies comprising 203 patients (58 with rheumatoid arthritis, 71 with fibromyalgia, and 74 with osteoarthritis [OA]), cannabinoids had a statistically significant effect on pain in 2, sleep in 2, and improved quality of life in 1, with the OA study prematurely terminated due to futility. The risk of bias was high for all 3 completed studies. Dizziness, cognitive problems, and drowsiness, as well as nausea, were reported for almost half of the patients. No serious adverse events were reported for cannabinoids during the study duration. No studies of herbal cannabis were identified.

Conclusion. Extremely small sample sizes, short study duration, heterogeneity of rheumatic conditions and products, and absence of studies of herbal cannabis allow for only limited conclusions for the effects of cannabinoids in rheumatic conditions. Pain relief and effect on sleep may have some potential therapeutic benefit, but with considerable mild to moderate adverse events. There is currently insufficient evidence to recommend cannabinoid treatments for management of rheumatic diseases pending further study.

Reference: Fitzcharles, M, et al. Efficacy, Tolerability, and Safety of Cannabinoid Treatments in Rheumatic Diseases: A systemic Review of Randomized Controlled Trials. Arthritis Care & Research. 2016; 68 (5): 681-688.

Arthritis Care & Research
Vol. 68, No. 5, May 2016, pp 681–688
DOI 10.1002/acr.22727

ORIGINAL ARTICLE

Efficacy, Tolerability, and Safety of Cannabinoid Treatments in the Rheumatic Diseases: A Systematic Review of Randomized Controlled Trials

- Qualitative Review included 4 studies
- Evaluation only of:
  - Nabiximols (combo of THC and CBD + trace minor phytocannabinoids)
    - 5 week study vs placebo for RA
    - 58 patients, randomized double blind
    - 28 (48%) reported improvement in pain, sleep quality, & disease activity score
  - Nabilone (synthetic analog of THC)
    - 2 studies focused on Fibromyalgia
      - 8 week study: 40 patients vs placebo, statistical improvement pain & QOL
      - 6 week study: 31 patients vs Amitriptyline (2 week each treatment), nabilone marginal advantage in Insomnia Severity Index.

Reference: Fitzcharles, M, et al. Efficacy, Tolerability, and Safety of Cannabinoid Treatments in Rheumatic Diseases: A systemic Review of Randomized Controlled Trials. Arthritis Care & Research. 2016; 68 (5): 681-688.

CLINICAL EXPERIENCE WITH CBD

CLINICAL EXPERIENCE WITH HEMP EXTRACT (CBD)

- 3+ years experience to date
- Positive results for:
  - Chronic Pain
  - Arthritis/joint pain
  - Insomnia
  - Anxiety (mild-moderate)
  - Autism (limited)
  - Severe ADHD (limited)
- Viable alternative to opioids, NSAIDs, Benzodiazepines

SAFETY INFORMATION

Neurotherapeutics (2015) 12:807–815
DOI 10.1007/s13311-015-0373-7

REVIEW

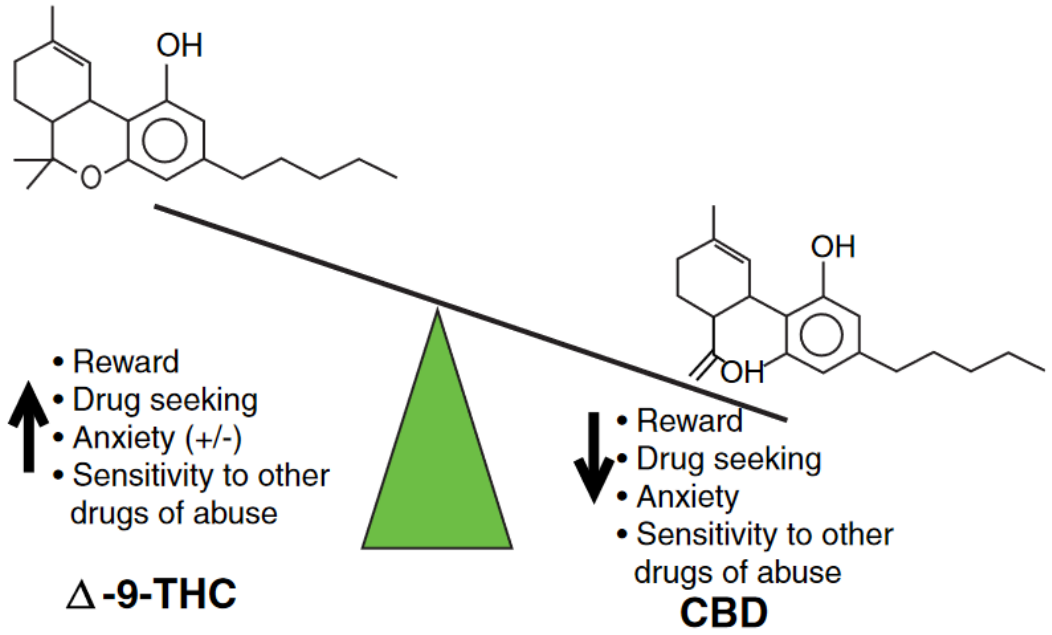
Early Phase in the Development of Cannabidiol as a Treatment for Addiction: Opioid Relapse Takes Initial Center Stage

Yasmin L. Hurd[1] · Michelle Yoon[1] · Alex F. Manini[2] · Stephanie Hernandez[2] · Ruben Olmedo[2] · Maria Ostman[3] · Didier Jutras-Aswad[4]

Reference: Hurd, et al. Early Phase in the Development of Cannabidiol as a Treatment for Addiction: Opioid Relapse Takes Initial Center Stage. *Neurotherapeutics*. 2015 (12): 807-815

CANNABIDIOL AND OPIOID ADDICTION

Fig. 2 Δ^9-tetrahydrocannabinol (THC) and cannabidiol (CBD) have opposing "yin/yang" effects on addiction-related behaviors. In contrast to THC that is rewarding and promotes drug use, CBD has low hedonic property and inhibits drug seeking



Springer

Reference: Hurd, et al. Early Phase in the Development of Cannabidiol as a Treatment for Addiction: Opioid Relapse Takes Initial Center Stage. *Neurotherapeutics*. 2015 (12): 807-815

SAFETY OF CBD USE WITH OPIOIDS

laboratory studies to begin to explore the potential of this cannabinoid as a medication for opioid craving. A critical first step was to document that CBD, if combined with a potent opioid, would be safe as there was always the chance for a lapse in abstinent heroin abusers. Our double-blind, placebo-controlled cross-over phase I study in healthy subjects demonstrated that CBD (400 mg and 800 mg; approximately 10–15 mg/kg) co-administered with intravenous fentanyl is well tolerated and does not exacerbate adverse effects associated with intravenous fentanyl administration such as respiratory depression or cardiovascular complications [82]. Measure-

Reference: Hurd, et al. Early Phase in the Development of Cannabidiol as a Treatment for Addiction: Opioid Relapse Takes Initial Center Stage. *Neurotherapeutics*. 2015 (12): 807-815

DRUG INTERACTIONS

- CYP 450 system
- Full spectrum vs isolates

DRUG SCREENING AND CBD

The New York Times

CBD or THC? Common Drug Test Can't Tell the Difference

Those cannabidiol-laced gummy bears may be entirely legal, but they could still get you arrested on marijuana possession charges.

By Amanda Chicago Lewis

Oct. 15, 2019

Research Letter

FREE

November 7, 2017

Labeling Accuracy of Cannabidiol Extracts Sold Online

Marcel O. Bonn-Miller, PhD[1]; Mallory J. E. Loflin, PhD[2]; Brian F. Thomas, PhD[3]; et al

» Author Affiliations | Article Information

JAMA. 2017;318(17):1708-1709. doi:10.1001/jama.2017.11909

Only 30% of the 84 products tested were accurate for labeled ingredients and concentrations.

FINDING QUALITY CBD PRODUCTS

MOSS COMPOUNDING PHARMACY
2500 Hoffmeyer Road, Florence, SC 29501
843.665.0289 (phone) / 843.667.9964 (fax)
www.mosscompounding.com

CBD Product Evaluation Checklist

Product Name/Strength _____

Manufacturer _____ Lot# _____

Evaluation Criteria	Yes/No
Contains expiration date and lot number	
Product labeled with concentration or strength per dose	
Product Grown and Produced in USA	
Potency testing available for specific lot	
Potency testing results matches with product labeling	
Testing for contaminations (ie. pesticides/fungicides) for specific lot	
Potency and Contamination testing completed by a qualified, third party lab	
Company/product previously cited by FDA or third party research lab for false labeling or medical claims	

QUESTIONS??

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