



Healer



A Guide to Medical Cannabis and Hemp for Healthcare Providers

Dear Healthcare Provider,

This document provides a succinct overview of the clinical information you'll need to safely care for patients who elect to use medical cannabis and hemp CBD products. If you're interested in learning more about the emerging field of cannabinoid medicine, please visit Healer.com.

Sincerely,

Dustin Sulak, D.O.

Co-Founder, Healer

Healer.com

These statements and this guide have not been evaluated by the Food and Drug Administration. The information in this guide is for educational purposes only and is not to be used or relied on for any diagnostic or treatment purposes. It is not intended to be patient education, does not create a patient-physician relationship, and should not be used as a substitute for professional diagnosis or treatment. Dr. Sulak is an equity owner of Healer, a company he co-founded to provide access to trusted and effective cannabis education and products.

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MEDICAL CANNABIS SAFETY PROFILE: NON-LETHAL, NON-TOXIC

- Effective oral dosing range of plant-based cannabinoids in humans: 0.05 - 25 mg/kg/day¹
- No deaths occurred in monkeys treated acutely with THC 9,000 mg/kg PO² or for 28 days at 250 mg/kg/day PO
- Acute fatal cases in humans have not been substantiated.³ Six case reports on 13 patients have been published linking recent use of cannabis with sudden death.⁴
- Myocardial infarction may be triggered by inhaled THC due to effects on circulation in individuals who are unable to tolerate orthostatic hypotension or tachycardia.⁵

DRUG INTERACTIONS

- CYP450 inhibition⁶
 - THC: & CBN: 2C9, 3A4
 - CBD: 2C19, 3A4
 - Note – Cannabis is included in most online drug interaction checkers. Additionally, THC can be checked using “Dronabinol” and CBD can be checked using “Epidiolex”.
- Cannabis smoking may induce CYP1A2, similar to tobacco smoking, which can increase clearance of theophylline.⁷
- Case reports involving Warfarin suggest a risk for interaction with cannabis via inhibition of hepatic CYP2C9.⁸
- Cannabinoid-opioid interactions: ^{9, 10, 11}
 - Synergistic analgesia with greater-than-additive effects
 - No enhancement of cardiorespiratory suppression with combination treatment due to very low density of CB receptors in brainstem cardiorespiratory centers
 - Minimal pharmacokinetic interactions in humans with morphine, none with oxycodone
 - Chronic combination-treated animals demonstrate avoidance of opioid tolerance, retention of antinociceptive effect, and upregulation of spinal cord opioid receptor proteins. Clinical evidence suggests these findings translate to humans.
 - Adding low dose cannabinoids to opioids widens the therapeutic window and reduces the need for opioid dose-escalation.
- Alcohol and benzodiazepines: potentiation of sedation¹²
- Cholinergic drugs can modulate the effects of cannabis. Anticholinergic drugs may increase adverse psychoactive effects.¹³
- Most statins, including Simvastatin, Lovastatin, and Atorvastatin, are metabolized by CYP3A4, and the risks of adverse effects, such as myopathy, increase when they are taken with drugs that inhibit CYP3A4.¹⁴ Fluvastatin is primarily metabolized by CYP2C9 and may similarly interact with cannabis. Pravastatin is unlikely to have pharmacokinetic interactions with cannabis.¹⁵



- Indomethacin has been shown to attenuate some of the effects of THC.¹⁵
- Due to the anti-inflammatory and immunomodulating effects of cannabis, caution should be used in combination with immunotherapies designed to increase immune activity. For example, clinical data has demonstrated a possible reduction in response rate to nivolumab in cannabis users compared to non-users.^{16, 17}

ADVERSE EFFECTS

The adverse effects of medical cannabis are within the range tolerated for other medications.¹⁸ A 2008 review found that in 23 RCTs there was no higher incidence of serious adverse events following medical cannabis use compared with control, while non-serious adverse events were significantly higher in the cannabinoid groups (RR 1.86).¹⁹ Other common adverse effects include:

- A 2015 systematic review of randomized clinical trials found the most common adverse effects, in order of incidence, were disorientation, dizziness, euphoria, confusion, drowsiness, dry mouth, and somnolence.²⁰
- Cannabis-naïve patients demonstrate more frequent adverse effects,²¹ while regular users experience less psychotomimetic, perceptual altering, and amnesic effects.²² THC can broaden its own therapeutic window over time due to heterogeneous tolerance-building to various effects,²³ with therapeutic effects more resistant to tolerance development than side effects.²⁴ Adverse effects can typically be prevented or mitigated with individualized dosing and titration. The guidance of a cannabis clinician and access to diverse formulations and delivery methods allow for personalized treatments that offer an improved adverse effect profile compared to those seen in most controlled clinical trials. Our experience with 18,000 cannabis-using patients in New England has demonstrated that appropriate dosage, delivery method and constituent profile of the product can alleviate many or all the adverse effects.
- The adverse effects of medical cannabis cannot be equated with the effects of illicit cannabis use or abuse. For example, a standardized oromucosal extract spray combining THC, CBD, and other cannabis components has not been abused or diverted to any degree in more than 30,000 patient-years of recorded usage.¹ Long term cognitive impairment associated with adult illicit cannabis use has been shown to be completely reversible after a period of abstinence.²⁵ Conversely, medical cannabis users demonstrate improvement in cognitive tasks after 3 months of treatment.²⁶
- While smoking is usually not the preferred delivery method for medical use, even long-term heavy cannabis smokers have no increased incidence of lung cancer,²⁷ although they can suffer from reversible pulmonary symptoms.²⁸
- Adverse effects of hemp-based products containing CBD and/or CBDA are rarely reported in common dosing ranges (<200 mg daily). Based on the clinical experience of my colleagues and myself, the most common adverse effects of CBD are appetite loss, nausea, diarrhea, sleep disturbance, and restlessness. Higher doses of CBD (1500 mg daily) have been shown to increase liver enzymes in some healthy subjects.²⁹



THERAPEUTIC POTENTIAL

Cannabinoids have demonstrated therapeutic effects in a broad range of conditions due to the widespread distribution of cannabinoid receptors throughout the body. The endocannabinoid system (ECS) is a regulator of physiologic homeostasis and is an exciting target of pharmacotherapy.

Modulating the activity of the ECS has proven effective in human and/or preclinical studies on mood and anxiety disorders, movement disorders, neuropathic pain, epilepsy, multiple sclerosis, spinal cord injury, cancer, atherosclerosis, myocardial infarction, stroke, hypertension, glaucoma, obesity/metabolic syndrome, insomnia, drug addiction, Alzheimer's disease, and osteoporosis, to name just a few.³⁰ The vast majority of human research has focused on spasticity, nausea and vomiting, anorexia, and chronic pain.³¹

Some conditions, such as migraine, fibromyalgia, and IBS have pathophysiological patterns that suggest an underlying clinical endocannabinoid deficiency, which may be suitably treated with cannabinoid medicines.³²

CLINICAL EVIDENCE

A 2017 report from the National Academies of Sciences, Engineering, and Medicine found conclusive or substantial evidence that cannabis or cannabinoids are effective:

- For the treatment of chronic pain in adults
- As antiemetics in the treatment of chemotherapy-induced nausea and vomiting
- For improving patient-reported multiple sclerosis spasticity symptoms

The report also found moderate evidence that cannabis or cannabinoids are effective for: Improving short-term sleep outcomes in individuals with sleep disturbance associated with obstructive sleep apnea syndrome, fibromyalgia, chronic pain, and multiple sclerosis.³³

Increasing but limited clinical data demonstrates that cannabinoids are safe and effective in the treatment of seizure disorders,³⁴ Tourette syndrome,³⁵ and several geriatric conditions.³⁶

Distinct from non-medical use, studies involving the therapeutic use of cannabis demonstrate improvements in anxiety, depression, and neurocognition.^{37, 38}



ENTOURAGE EFFECTS

Cannabis is known to contain hundreds of physiologically active compounds, primarily phytocannabinoids, terpenoids and flavonoids. Whole plant cannabis medicines tend to exhibit superior therapeutic effects and less adverse effects than isolated or synthetic cannabinoids.³⁹ Currently, the most clinically useful strategy lies in the combination of THC and cannabidiol (CBD), which can be achieved by selecting specific cannabis chemovars (chemical varieties of the plant) or combinations thereof. CBD has been shown to antagonize the undesirable effects of THC, such as intoxication, sedation and tachycardia, while enhancing the analgesic and antiemetic effects. Many patients who experience adverse effects with THC-dominant cannabis are able to better tolerate combination treatment with THC and CBD.

HEMP-BASED PRODUCTS

Until recently, “hemp” varieties of cannabis were grown for non-medical crops, including fiber, hurd (the center of the stalk), and seed; these varieties do not produce high quality medicine. Most countries have regulations that limit the THC content (e.g., 0.3% by weight) of dietary hemp products, such as seed and seed oil.

Due to the exploding popularity of cannabidiol (CBD) following CNN’s 2013 documentary, *Weed*, which followed the story of a 4-year-old girl whose treatment-resistant seizures were relieved by a non-impairing, CBD-dominant variety of cannabis, cannabis breeders have developed type III, CBD-rich flowers with ultra-low THC content, in an effort to qualify as a hemp product. In 2018, the FDA approved Epidiolex, a highly purified liquid CBD extract, for the treatment of two rare seizure disorders, Lennox-Gastaut syndrome and Dravet syndrome, and in 2020 for tuberous sclerosis. In recent years, demand for CBD products has grown immensely, with a 2019 analysis reporting 6.9% of Americans were using CBD products at that time.⁴⁰

Over 65 distinct pharmacologic targets for CBD have been identified on the basis of in vitro studies, including receptors, ion channels, enzymes, and transporters.⁴¹

While the activity at many of these targets requires concentrations that are unlikely to occur in vivo, CBD is strongly pleiotropic, yet it is remarkably safe and well-tolerated. CBD has broad therapeutic applications including the following effects:⁴²

- anticonvulsive
- anti-inflammatory
- analgesic
- antioxidant
- antifibrotic
- anxiolytic
- antipsychotic
- procognitive
- neuroprotective



Cannabidiolic acid (CBDA), the precursor to CBD synthesized by the cannabis plant, is a promising therapeutic agent due to its overlapping pharmacological properties with CBD but superior bioavailability and efficacy at lower doses. For example, both CBD and CBDA are antiemetics via activation of the 5-HT_{1A} serotonin receptor in rodent models of nausea, but while CBD demonstrated antiemetic effects at 5 mg/kg ip, CBDA was effective at 0.0005 mg/kg ip.⁴³ Similarly, in a rodent model of carrageenan-induced hyperalgesia, orally administered CBD was effective at preventing hyperalgesia at 10 mg/kg, while oral CBDA was effective at 0.1 mg/kg.⁴⁴ In a rodent model of the seizure disorder Dravet syndrome, CBD reduced seizures at 100 mg/kg, while CBDA was effective at 10 mg/kg.⁴⁵ In humans, the oral bioavailability of CBDA is higher than that of CBD in decoction and oil by 5- and 11-fold, respectively.⁴⁶ Overall, early results with CBDA indicate promising therapeutic attributes that warrant more investigation.

Patients are increasingly turning to hemp products CBD and CBDA for relief of, most often, anxiety and pain. Though some early clinical evidence supports safety and efficacy for these conditions^{47, 48, 49, 50, 51} more research is needed and underway.

FOR MORE INFORMATION

The Society of Cannabis Clinicians (cannabisclinicians.org)

Handbook of Cannabis for Clinicians by Dustin Sulak, D.O. Norton Professional, 2021

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Introduction to Cannabis Dosage Program

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Do you require more and more cannabis to get the same relief? This is a sign of cannabis tolerance. Learn how to use less, feel more, and experience superior medical benefits. [Learn more](#)

Switching to a Cannabis Tincture Dosage Program

Learn how to use a tincture to prevent your symptoms rather than chasing and treating them with inhalation after they occur. Use less medicine and experience improved results. [Learn more](#)

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Dr. Sulak provides you with a number of strategies to help you get all the health benefits of cannabis without getting high or impaired. [Learn more](#)

Endocannabinoid Diet & Activities Dosage Program

Dr. Sulak outlines how specific foods and simple activities can help the endocannabinoid system function optimally, which is essential to improving your health. [Learn more](#)

A Guide to Medical Cannabis and Hemp for Healthcare Providers

Dr. Sulak's succinct overview of the clinical information your medical providers will need to know to safely care for you and other patients who elect to use medical cannabis. [Learn more](#)

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A NOTE FROM DR. SULAK

We created Healer Cannabis and Hemp products because I needed high quality, dependable, pure, and effective products for my patients, colleagues, family, friends, and for you. The most effective cannabis products retain the widest range of medicinal compounds. Healer's patented nano-filtration process both removes impurities and delivers more of the plant's entourage of medicinal compounds.

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