



# HEALER



## Medical Cannabis Healthcare Provider Info

### **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. If you're interested in learning more about the emerging field of cannabinoid medicine, please visit **Healer.com**.

Sincerely,

Dustin Sulak, D.O.  
*Founder, Healer.com*

[www.Healer.com](http://www.Healer.com)



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

- Effective oral dosing range of plant based cannabinoids in humans: 0.05 -25mg/kg/day<sup>1</sup>
- No deaths occurred in monkeys treated acutely with THC 9,000mg/kg PO.<sup>2</sup>
- Acute fatal cases in humans have not been substantiated.<sup>3</sup>
- Myocardial infarction may be triggered by inhaled THC due to effects on circulation in individuals who are unable to tolerate orthostatic hypotension or tachycardia.<sup>4</sup>

## DRUG INTERACTIONS:

- CYP<sub>450</sub> inhibition<sup>5</sup>
  - THC: & CBN: 2C<sub>9</sub>, 3A<sub>4</sub>
  - CBD: 2C<sub>19</sub>, 3A<sub>4</sub>
  - Note - cannabis is included in Medscape's drug interaction checker.
- Cannabinoid-opioid interactions:<sup>6,7</sup>
  - 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.
  - Adding low dose cannabinoids to opioids widens the therapeutic window and reduces the need for opioid dose-escalation.
- Alcohol and benzodiazepines: potentiation of sedation<sup>8</sup>
- NSAIDs, particularly indomethacin, can partially antagonize the effects of THC.<sup>9</sup>
- Cholinergic drugs can modulate the effects of cannabis. Anticholinergic drugs may increase psychoactive side effects.<sup>10</sup>



## ADVERSE EFFECTS

The adverse effects of medical cannabis are within the range tolerated for other medications.<sup>11</sup> 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). Dizziness was the most common non-serious adverse effect.<sup>12</sup> Other common adverse effects seen in our practice include:

- Euphoria, altered consciousness
- Acute panic or paranoid reaction
- Altered motivation
- Impaired attention, memory, and psychomotor performance
- Tachycardia, orthostatic hypotension
- Xerostomia
- Increased appetite

Cannabis-naïve patients demonstrate more frequent adverse effects,<sup>13</sup> while regular users experience less psychotomimetic, perceptual altering, and amnesic effects.<sup>14</sup> THC can broaden its own therapeutic window over time due to heterogeneous tolerance-building to various effects,<sup>15</sup> with therapeutic effects more resistant to tolerance development than side effects.<sup>16</sup> Our experience with 17,000 cannabis-using patients in New England has shown that appropriate dosage, delivery method, and ratio of cannabinoids can mitigate many of the adverse effects.

The adverse effects of medical cannabis cannot be equated with the effects of illicit marijuana 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.<sup>1</sup> Long term cognitive impairment associated with adult illicit cannabis use has been shown to be completely reversible after a period of abstinence.<sup>17</sup> And while smoking is not the preferred delivery method for medical use, even long-term heavy cannabis smokers have no increased incidence of lung cancer,<sup>18</sup> although they can suffer other pulmonary symptoms.<sup>19</sup>

Caution should be used in patients with active liver fibrosis. CB1 receptor agonists, such as THC, likely hasten the formation of fibrosis,<sup>20</sup> while CB2 agonists and cannabidiol (CBD) exert antifibrotic and hepatoprotective effects.<sup>21,22</sup>



## 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.<sup>23</sup> The vast majority of human research has focused on spasticity, nausea and vomiting, anorexia, and chronic pain.<sup>24</sup> 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.<sup>25</sup>

## ENTOURAGE EFFECTS

Cannabis is known to contain hundreds of physiologically active compounds, primarily phytocannabinoids and terpenoids. Whole plant cannabis medicines tend to exhibit superior therapeutic effects and less adverse effects than isolated or synthetic cannabinoids.<sup>26</sup> Currently, the most clinically useful strategy lies in the combination of THC and CBD, which can be achieved by selecting specific cannabis chemotypes (plant strains). CBD has been shown to antagonize the undesirable effects of THC, such as intoxication, sedation and tachycardia, while enhancing the analgesic, anti-emetic, and anti-carcinogenic properties of THC.<sup>27</sup> The psychoactive side effects of THC are rarely noticeable when the CBD:THC ratio exceeds 4:1.



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- <sup>3</sup>Grotenhermen, Franjo. "Pharmacology of cannabinoids." *Neuroendocrinology Letters* 25.1/2 (2004): 14-23.
- <sup>4</sup>Mittleman, Murray A., et al. "Triggering myocardial infarction by marijuana." *Circulation* 103.23 (2001): 2805-2809.
- <sup>5</sup>Stout, Stephen M., and Nina M. Cimino. "Exogenous cannabinoids as substrates, inhibitors, and inducers of human drug metabolizing enzymes: a systematic review." *Drug metabolism reviews* 46.1 (2013): 86-95.
- <sup>6</sup>Cichewicz, Diana L. "Synergistic interactions between cannabinoid and opioid analgesics." *Life sciences* 74.11 (2004): 1317-1324.
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- <sup>14</sup>D'Souza D, et al. Blunted psychotomimetic and amnestic effects of  $\Delta$ -9- tetrahydrocannabinol in frequent users of cannabis. *Neuropsychopharmacol* 2008;33(10):2505-16.
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- <sup>18</sup>Hashibe, Mia, et al. "Marijuana use and the risk of lung and upper aerodigestive tract cancers: results of a population-based case-control study." *Cancer Epidemiology Biomarkers & Prevention* 15.10 (2006): 1829-1834.
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