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# CANNABINOID CHRONICLES

## Medical Cannabis News and Information

### *Simplified Cannabinoid Guidelines for Canadian MDs Fall Short*

A recent paper published in *Canadian Family Physician* titled "Simplified Guideline for Prescribing Cannabinoids in Primary Care" has come down on the side of conservative, pharmaceutical-based solutions for only a handful of medical conditions. (Not a surprise.)

The conditions that the researchers feel have the most to benefit from cannabinoids are: chronic pain, nausea and vomiting, and spasticity. They "recommend against use of medical cannabinoids for most medical conditions owing to lack of evidence of benefit and known harms."

"The guideline suggests that clinicians could consider medical cannabinoids for refractory neuropathic pain and refractory pain in palliative care, chemotherapy-induced nausea and vomiting, and spasticity in multiple sclerosis and spinal cord injury after reasonable trials of standard therapies have failed. If considering medical cannabinoids and criteria are met, the guideline recommends nabilone *[Cesamet]* or nabiximols *[Sativex]* be tried first. Harms are generally more common than benefits are,.." (Really? Compared to what?)

In several cases, the paper suggests that cannabinoids only be used if the condition has not responded to attempted forms of treatment, also known as refractory. Therefore, cannabinoids are only recommended for chemotherapy induced nausea and vomiting (CINV) if the condition has not responded to other treatments and is now considered 'refractory CINV'. It's seen as a last resort medicine, so to speak, and all too commonly.

When one looks at the existing knowledge about, and the increasing amount of research on cannabinoids, whether whole plant or not, this basically amounts to "covering-our-butts because we don't know enough."

The relative safety profile of cannabis compared to other pharmaceuticals appears to have been understated (yet again). When looking at neuropathic pain, cannabinoids are compared against amitryptyline and high-dose opioids. What are *their* side effects? The level of harm? Too much high-dose opioids will kill you. Amitryptyline is an anti-depressant and could possibly kill you if taken in combination with, for example, another type of anti-depressant called MOA inhibitor. Pregabalin, a type of anti-epileptic medication, has been associated with increased risk of suicidal thinking and behavior.

There are no recorded deaths from cannabis ingestion alone; research has found that there may even be benefits from combining cannabis with other pharmaceuticals. Early evidence suggests that cannabis and opioid-based pain therapy can have a synergistic and positive effect, resulting in reduced opioid usage, improved pain management and a healthier digestive tract. Other evidence suggests that there is more drug-substitution and/or co-use of pharmaceuticals and/or other drugs (i.e. alcohol) with cannabis than is known or admitted. Perhaps we need further research into these phenomena.

Cannabis does have side effects, but they need to be compared against other drug side effects; the relative safety profile of cannabinoids is one of the reasons why doctors, without 'sufficient' research, are recommending cannabis as a treatment for their patients.

Perhaps, due to its gentler nature, whole-plant cannabis should be offered up first, not last.

**Source:** http://www.cfp.ca/content/64/2/111


**Image:** https://greenrushdaily.com/

### *Human: Heavy cannabis use in patients with HIV is associated with improved immune function*

In a study with 198 patients with HIV, who are treated with antiretroviral medication (ART), heavy use of cannabis was associated with reduction in systemic inflammation and immune activation. This is the result of research by scientists of the University of Washington and other universities across the USA. The study investigated the impact of cannabis use on immune cell frequency in the blood, their activation, and function.

Authors reported, that they "found that heavy cannabis use ... in HIV-infected, ART-treated individuals was associated with lower frequencies of activated CD4 and CD8 T cells compared to frequencies of these cells in non-cannabis using individuals. This novel finding is important given that elevated levels of T-cell activation have been associated with lower CD4 T-cell gains following ART (anti-retroviral therapy) and with mortality in this population. "They concluded from their work, that "while the clinical implications are unclear, our findings suggest that cannabis use is associated with a potentially beneficial reduction in systemic inflammation and immune activation in the context of antiretroviral-treated HIV infection."

**Source:** http://www.ncbi.nlm.nih.gov/pubmed/29471387

### *Human: Cannabis enhances the pain reducing effects of the opioid oxycodone according to experimental study*

According to an experimental study with healthy cannabis users, the combination of the opioid oxycodone and cannabis reduced pain assessed using the Cold-Pressure Test. Participants received either 2.5 or 5 mg of oxycodone or a placebo together with smoked cannabis with 5.6 % THC or no THC and immersed one hand in cold water. Researchers of the New York State Psychiatric Institute and Department of Psychiatry of the Columbia University, USA, measured the time to report pain (pain threshold) and to withdraw the hand from the water (pain tolerance).

Alone, 5.0 mg oxycodone increased pain threshold and tolerance. Although active cannabis and 2.5 mg oxycodone alone failed to elicit analgesia, combined they increased pain threshold and tolerance. authors concluded that "cannabis enhances the analgesic effects of sub-threshold oxycodone, suggesting synergy."

**Source:** http://www.ncbi.nlm.nih.gov/pubmed/29463913

### *Cells: CBD induces cell death in endometrial cancer*

In cell experiments, CBD and the endocannabinoid anandamide reduced cell viability and increased apoptosis (programmed cell death) in endometrial cancer cells by activation of the vanilloid 1 receptor (TRPV1).

**Source:** https://www.ncbi.nlm.nih.gov/pubmed/29441458

### *Human: Cannabis may have a beneficial effect on patients with fibromyalgia*

A group of Israeli scientists analysed data of 2970 cancer patients treated with medical cannabis between 2015 and 2017 and found beneficial effects across many symptoms. Average age was 59.5 years and 54.6% were women. About one quarter (26.7%) had previous experience with the drug. The most frequent types of cancer pertained to breast (20.7%), lung (13.6%), pancreas (8.1%) and bowel (7.9%).

After six months of follow up, 902 patients died and 682 stopped the treatment. Of the remaining, 1211 (60.6%) responded and 95.9% reported an improvement in their condition from the use of cannabis, 45 patients (3.7%) reported no change and four patients (0.3%) reported deterioration in their medical condition. The main symptoms were sleep problems (78%), pain (78%), weakness (73%), nausea (65%) and lack of appetite (49%). Authors concluded that cannabis "as a palliative treatment for cancer patients seems to be a well tolerated, effective and safe option to help patients cope with the malignancy related symptoms."

**Source:** http://www.ncbi.nlm.nih.gov/pubmed/29482741

### *Human: A high number of patients with spinal cord injury and traumatic brain injury use cannabis*

In a survey with 116 patients suffering from either spinal cord injury or traumatic brain injury, many used cannabis. Among the respondents with spinal cord injury, the most common reasons for use were to reduce spasticity (70%), recreation (63%), and to improve sleep (63%). Among those with traumatic brain injury, reasons were recreational (72%), reducing stress/anxiety (62%), and improving sleep (55%).

**Source:** http://www.ncbi.nlm.nih.gov/pubmed/29524396

### *Human: Cannabis may have a beneficial effect on patients with fibromyalgia*

In a study with 26 patients with fibromyalgia, who had been treated at two hospitals in Israel (Laniado Hospital in Kiryat Sanz and Nazareth Hospital in Nazareth) cannabis improved their symptoms. Their mean age was 37.8 years and mean dosage of cannabis was 26 gr. per month. All participants completed a questionnaire for the assessment of fibromyalgia severity (Revised Fibromyalgia Impact Questionnaire).

After commencing treatment with cannabis, all the patients reported a significant improvement in every parameter on the questionnaire, and 13 patients (50%) stopped taking any other medications for fibromyalgia. Eight patients (30%) experienced very mild adverse effects.

**Source:** http://www.ncbi.nlm.nih.gov/pubmed/29461346

## *9 Ways That Scientists Are Targeting the Endocannabinoid System*

The endocannabinoid system (ECS), a major biochemical signaling system in the human body, plays a pivotal role in regulating a wide range of physiological processes that affect our mood, our blood pressure, our bone density, our metabolism, our intestinal fortitude, our energy level, how we experience pain, stress, hunger, and more.

Described by Israeli scientist Raphael Mechoulam as "a medicinal treasure trove," cannabis contains over 60 unique biologically active compounds known as cannabinoids, including tetrahydrocannabinol (THC) and cannabidiol (CBD). Both have important therapeutic attributes.

Here are nine strategies that scientists are currently pursuing in an effort to harness the healing potential of the endocannabinoid system:

1. Single-molecule plant cannabinoids - such as Marinol (THC) or soon to be approved Epidiolex (CBD).

2. Synthetic cannabinoid analogs - such as Nabilone, a synthetic THC analog, and investigations into cannabinoid agonists and antagonists.

3. Synthetic cannabinoid antagonists - e.g. synthetic CB1 antagonist (aka Rimonabant) that caused many side effects and provided vivid evidence that a well-functioning endocannabinoid system is essential for good health.

4. Peripherally restricted CB1 agonists - researchers have created peripherally-restricted CB1 agonists that only activate CB1 receptors outside the central nervous system, but don't cross the blood-brain barrier, therefore avoiding disconcerting dysphoria.

5. Selective CB2 agonists - try to synthesize clinically effective CB2-selective compounds to reduce side effects.

6. Water-soluble cannabinoids - to increase bio-availability.

7. Allosteric cannabinoid receptor modulators - synthetic compounds that change the shape of the CB1 receptor and influence how it signals without causing a THC-like high.

8. Inhibitors of endocannabinoid metabolizing enzymes - indirect modulation of endocannabinoid signaling could become a treatment option for various inflammatory conditions and stress-related disorders.

9. Endocannabinoid reuptake inhibitors - Enhancing endocannabinoid tone via reuptake inhibition may be a key mechanism whereby plant cannabinoids confer protective effects against seizures and neuro-degeneration.

Synthetic CBD analogs are also in development. By tweaking the mother molecule and removing, adding or editing a molecular side chain, pharmaceutical researchers hope to create a marketable compound that is more potent and more effective than botanical CBD.

But a CBD isolate is not inherently superior to a whole plant CBD-rich extract. Preclinical studies that compare the efficacy of single-molecule CBD and full spectrum CBD-rich oil concentrates indicate that CBD solo is effective only at precise, high doses – whereas whole plant CBD-rich extracts have a much wider and safer therapeutic window and are effective at significantly lower doses. Problematic drug interactions are also much likelier with high dose single-molecule CBD.

Regulatory policy should not privilege single-molecule meds over full spectrum cannabis remedies. Patients are best served by having access to a wide range of cannabinoid-based therapeutic options, including artisanal whole-plant preparations and synthetic isolates, if and when they become available.

**Notes:**

1. Only four cannabis compounds bind directly to either one or both cannabinoid receptors. THC activates CB1 and CB2. Cannabinol (CBN), a THC breakdown component, activates the CB1 receptor, though with less potency than THC. Tetrahydracannabivarin (THCV), the propyl variant of THC, binds to both cannabinoid receptors, activating CB2 while blocking CB1. And beta caryophyllene, an aromatic terpene found in many cannabis strains, green leafy vegetables, and common kitchen spices, activates CB2. Other cannabinoids, including CBD, interact with the endocannabinoid system indirectly without binding like lock and key to a cannabinoid receptor.

2. Developed as a research tool to study that endocannabinoid system, JWH-018 is a synthetic cannabinoid compound that activates the CB1 receptor but not CB2. After the formula for this potent CB1 agonist was published in the scientific literature, JWH-018 surfaced as a street drug known as "Spice" or "K2." Media accounts typically mischaracterize Spice as "synthetic marijuana."

3. U.S. government scientists have not given up entirely on Rimonabant. The fact that this compound blocks the euphoric effects of cannabis is a big plus to the National Institute on Drug Abuse, which has sponsored research on utilizing CB1 blockers to treat various addictions, including "cannabis dependence."

4. Canadian scientists have identified CBD as a "negative allosteric modulator" of the CB1 receptor based on in vitro research. This means that CBD, when administered in combination with THC, will alter the shape of the CB1 receptor in a way that weakens its binding affinity for THC. As a negative allosteric modulator of CB1, CBD lowers the ceiling on THC's psychoactivity, which might be why people don't feel as high when using CBD-rich cannabis as compared to a THC-infused product.

**Source:** https://www.projectcbd.org/about/cannabis-pharmacology/treasure-hunt

## *Statistics Canada's Cannabis Study*

Statistics Canada, the national statistics agency, has released the results of a wide-ranging study that looked at the Canadian cannabis sector from 1961 to 2017.

Released on January 25, 2018, the study examined data from data such as consumption, domestic production, the size of the US market, the Canadian share of the American market, and seizure data at the border in both directions. They also reached out to Canadians via anonymous web-based surveys, seeking input on cannabis' regional purchase price, quantity, quality, and division between medical and recreational use.

In 2017, for example, Canadians spent an estimated $5.7 billion on cannabis. This came from some 4.9 million Canadians, about 14% of the country's total population, 90% of which was for recreational purposes. This is roughly $1,160 per cannabis consumer.

However, in 2016, Canadians spent just over $22 billion on alcohol and $16 billion on tobacco products in 2016.

Much of the tobacco and alcohol consumed in Canada is imported - not so with cannabis. In 2014, the domestic cannabis-producing industry was valued at $3.4 billion, whereas the tobacco industry was valued at $1 billion and the brewery industry at $2.9 billion.

The price of a gram of cannabis declined between 1989 and 2016, from $12 to $7.50, even though Canadians have been spending increasingly more on cannabis overall.

Between 2000 and 2017, 40% of Canadian cannabis purchases were made by citizens aged 25 to 44, 33% were made by those aged 18 to 24, 18% were made by those aged 15 to 17, and 9% were made by those aged 45 to 64.

Cannabis consumption among middle-aged Canadians, those between 45 and 64 years old, has been increasing in recent years. In 1975, they accounted for 4% of cannabis purchases. By 2017, the percentage was 23%.

In 2017, 20% of Canada's cannabis production, about $1.2 billion worth of it, was illegally sold outside the country - that is a 900% increase from 1961.

**Sources:** https://www.leafly.com/news/canada/7-takeaways-from-statistics-canadas-cannabis-stats-hub

http://www.statcan.gc.ca/pub/13-610-x/13-610-x2018001-eng.htm


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***"I believe alien life is quite common in the universe, although intelligent life is less so. Some say it has yet to appear on planet Earth."***

***-- Stephen Hawking (theoretical physicist, cosmologist, author, Jan. 8, 1942 - Mar. 14, 2018)***