



Vol. 7, Issue 3  
April 2015

# CANNABINOID CHRONICLES

## Medical Cannabis News and Information

### **CBD-Rich Cannabis Extract More Effective Than Pure CBD**

Cannabidiol (CBD) is a major cannabinoid found in cannabis that is not psychoactive and has been found to be effective at treating a wide variety of medical conditions, including neurological disorders, convulsions, inflammation, anxiety, and nausea, to name a few. Its neuroprotective and neurogenic effects, and anti-cancer properties, are currently the focus of research, most of which have used single-molecule, purified CBD.

Enter three researchers in Israel who have recently published a study in the journal *Pharmacology & Pharmacy* (Feb. 2015) that examines the effectiveness of pure CBD versus CBD-rich, whole-plant cannabis extract when treating inflammation. The researchers noted that during the past fifteen years numerous preclinical studies had focused on the anti-inflammatory effects of pure, single-molecule CBD in animal models of various pathologies, including rheumatoid arthritis, inflammatory bowel disease, MS, and diabetes. These studies showed that administration of pure, single-molecule CBD resulted in a bell-shaped dose-response curve, meaning that when the amount of CBD exceeded a certain point its therapeutic impact declined dramatically. This characteristic of single-molecule CBD imposes serious obstacles that limit its usefulness in a clinical context.

Their search to find a CBD source that could eliminate the bell-shaped dose-response of purified CBD led them to a high-CBD, low-THC cannabis strain from which they produced a whole-plant extract (17.9% CBD, 1.1% THC, 1.1% cannabichromene (CBC), 0.2% cannabigerol (CBG), and “traces” of cannabinol (CBN) and cannabivarol (CBDV)). This extract was administered to mice in order to evaluate its anti-inflammatory and painkilling effect.

For comparative purposes, they administered pure, synthetic CBD to another group of mice. They also compared the extent to which single-molecule CBD and whole-plant CBD inhibited the production of tumor necrosis factor alpha (TNF $\alpha$ ), a systemic inflammatory signaling molecule. Dysregulation of TNF- $\alpha$  production has been implicated in several diseases.

Once again, the synthetic CBD produced a bell-curve response but the whole plant CBD-rich extract caused a direct, dose-dependent inhibition of pain, inflammation, and TNF $\alpha$  production. “In stark contrast to purified CBD,” the Israeli team reported, “the clone extract...provided a clear correlation between the anti-inflammatory and anti-nociceptive (reduce pain sensitivity) responses and the dose, with increasing responses upon increasing doses, which makes this plant medicine ideal for clinical uses.” Moreover, the Israeli researchers found that a small amount of CBD in the plant extract was needed for significant pain relief compared to the much larger amount of pure CBD required to achieve the same analgesic effect.

The greater efficiency of the whole-plant extract might be explained by additive or synergistic interactions between CBD and dozens of minor phytocannabinoids and hundreds of non-cannabinoid plant compounds, also known as the “entourage effect”.

**Source:** [www.scirp.org/journal/PaperInformation.aspx?PaperID=53912#.VPmnKjSG\\_1U%204](http://www.scirp.org/journal/PaperInformation.aspx?PaperID=53912#.VPmnKjSG_1U%204) AND [www.projectcbd.org/news/whole-plant-cbd-rich-cannabis-better-medicine-than-single-molecule-cbd/](http://www.projectcbd.org/news/whole-plant-cbd-rich-cannabis-better-medicine-than-single-molecule-cbd/)

**Image courtesy:** [http://www.askdrgarland.com/wp-content/uploads/2014/12/cbd-oil-spoon-and-plant\\_580x-e1417832423820.jpg](http://www.askdrgarland.com/wp-content/uploads/2014/12/cbd-oil-spoon-and-plant_580x-e1417832423820.jpg)



## **International Association for Cannabinoid Medicines (IACM) Bulletin**

### ***Cannabis use is associated with a reduced risk of diabetes in patients infected both with HIV and HCV***

Diabetes and insulin resistance are frequent in patients who are both infected with the HI virus [HIV] and the hepatitis C virus [HCV]. Researchers from several French institutes found that, among 703 patients infected with both viruses, the 319 (45%) participants who reported cannabis use in the 6 months before the first study visit were less likely to have insulin resistance.

With insulin resistance, cells fail to respond to the normal actions of the hormone insulin. The body produces insulin, but the cells in the body become resistant to insulin and are unable to use it as effectively, leading to type 2 diabetes. Authors concluded that “the benefits of cannabis-based pharmacotherapies for patients concerned by increased risk of insulin resistance and diabetes need to be evaluated in clinical research and practice. “

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25778750>

### ***THC may safely be used in older persons with dementia***

Only a few of the 98 patients (with a mean age of 77 years) suffering from dementia who received THC experienced side effects, researchers wrote in the journal *Psychopharmacology*. In a random order they received a placebo for six weeks and 0.75 to 1.5 mg THC twice daily for another six weeks in a trial conducted by scientists of the Department of Psychogeriatric Medicine, Vincent van Gogh Institute in Venray, The Netherlands. In the past year these researchers had published results of a smaller trial with twelve participants.

Only 6 of the 98 participants reported adverse events related to THC. Psychotropic effects, diastolic blood pressure and other measures were not significantly different between THC and the placebo. THC was rapidly absorbed and had dose-linear pharmacokinetics with considerable variation between different subjects. Authors wrote that “pharmacodynamic effects, including adverse events, were minor.”

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25752889>

### ***Patients use cannabis to substitute other medicinal drugs***

According to a survey conducted among 200 patients of a cannabis dispensary centre in Rhode Island, the majority report having used it as an alternative to conventional prescription drugs. Most participants (69%) used it against chronic pain. Over 90% of respondents reported that cannabis was associated with fewer side effects than conventional pain medications. Brown University School of Public Health, Providence, USA.

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25715068>

### ***The endocannabinoid system is tonically active in pain***

Rats received injections of formalin into their paws to cause pain. This pain was increased by the administration of antagonists (blockers) of the CB1 and CB2 receptor. Researchers concluded that the results “indicate that CB1 and CB2 receptors mediate a tonically inhibitory action on formalin-induced inflammatory pain.” This means that the body tries to counteract pain itself by an activation of the endocannabinoid system.

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25687494>

### ***Endocannabinoids prevent damage caused by nonsteroidal anti-inflammatory drugs***

Unlike nonsteroidal anti-inflammatory drugs such as diclofenac, a blocker of endocannabinoid degradation (ARN2508) caused no gastric damage and even protected the gastrointestinal tract from damage in a study with mice.

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25757568>

### ***CBD may safely be co-administered together with fentanyl***

In a clinical study with healthy volunteers, CBD in doses of 400 or 800 mg did not influence effects of the opioid fentanyl. Authors wrote that “coadministration of CBD and opioids was safe and well tolerated.”

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25748562>

### ***The activation of the CB2 receptor reduced rejection of transplanted organs***

Studies with mice revealed that the CB2 receptor influences mechanisms associated with the rejection of transplanted organs. Authors wrote that their experiments “suggest that CB2 may be a promising therapeutic target in organ transplantation.”

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25744392>

### ***CB2 receptor activation was effective against a certain severe form of breast cancer***

Triple-negative breast cancer represents a subtype of breast cancer characterized by high aggressiveness. Researchers showed that activation of the CB2 cannabinoid receptor induced death of cells of this type of cancer.

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25671648>

### ***Activation of the CB2 receptor was effective against colitis***

A synthetic CB2 receptor agonist protected mice against experimental colitis (inflammation of the colon). Université de Lille Nord de France, Lille Cedex, France.

Source: <http://www.ncbi.nlm.nih.gov/pubmed/25699149>

**For more info visit: [www.cannabis-med.org](http://www.cannabis-med.org)**

## **Medical Cannabis Insurance Coverage Awarded To Student**

In a possible precedent-setting decision in Ontario, Jonathan Zaid, a student at the U. of Waterloo, has been granted insurance coverage for his MD-recommended medical cannabis, and a vaporizer.

Zaid was initially refused by the insurer, Sun Life, with his request for reimbursement for his cannabis costs under the student health service plan. Using a “restricted drug use” clause that he had used before to successfully claim for an alternative headache medicine, Zaid was successful in convincing the committee to cover his costs. Zaid has also been reimbursed \$300 for the cost of the document from his doctor because the College of Physicians and Surgeons of Ontario have recently banned that particular fee (see below).

**Source:** [http://www.huffingtonpost.ca/2015/03/16/medical-marijuana-insurance-sun-life-jonathan-zaid\\_n\\_6881578.html](http://www.huffingtonpost.ca/2015/03/16/medical-marijuana-insurance-sun-life-jonathan-zaid_n_6881578.html)

## **College of Physicians and Surgeons of Ontario Medical Cannabis Policy**

The College of Physicians and Surgeons of Ontario (CPSO) have released an updated policy regarding medical cannabis. The policy, while not endorsing nor prohibiting the use of medical cannabis, refers to the federal MMPR and legal precedents to permit their doctors to prescribe it “in accordance with their own clinical and professional judgment.” And since the federal MMPR only recognizes dried cannabis (at the present), it is the only form the CPSO policy paper considers at this point in time.

The College is taking a novel position in Canada stating that “the medical document required under the *MMPR* is equivalent to a *prescription* (emphasis added).” As such, physicians will have to prescribe a specific quantity of cannabis and indicate the THC-percentage. To limit “euphoria and cognitive impairment”, the College also directs MDs to prescribe low-THC strains ( $\leq 9\%$  THC) to start with. The policy has nothing to say about other cannabinoids, more specifically CBD-rich strains that are less psychoactive.

Another key feature is that the College, by recognizing the doctor’s document as a prescription, requires that “physicians *must not charge* (emphasis added) patients or licensed producers of dried marijuana for completing the medical document, or for any activities associated with completing the medical document.” It is hoped that other medical colleges and health agencies across Canada adopt this measure as it can be an expensive and unfair burden for sick Canadians.

**Source:** <http://www.cpso.on.ca/policies-publications/policy/medical-marijuana>

## **Conversion and Transfer of Cannabinoids in a Joint**

A group in California believe that they are the first to study the total mass balance of THC, CBD, THCA and CBDA in the smoke stream, sidestream smoke and ash of a cannabis cigarette, or joint.

Dr. Jeffrey Raber and colleagues in Pasadena found that the average joint smoker inhales a little more than one third of the cannabinoids present in the plant material prior to burning, and that THC/CBD ratios remained constant upon combustion.

The paper, “The Conversion and Transfer of Cannabinoids from Cannabis to Smoke Stream in Cigarettes”, was published in the journal *Natural Products Chemistry and Research* in January 2015.

Dried cannabis contains cannabinoids primarily in an acidic form; when heated these acidic cannabinoids, designated in this case as THCA and CBDA, are converted, or decarboxylated, to their neutral equivalents THC and CBD respectively. In this example, the difference is the removal of  $\text{CO}_2$ . When decarboxylated, cannabinoids are more readily absorbed by the body.

The cannabis used in the study had varying cannabinoid levels; 4.5 to 18.6%  $\text{THC}_{\text{max}}$ , and 2.7 to 7.6%  $\text{CBD}_{\text{max}}$ . The term ‘max’ is the sum of THC and THCA, or CBD and CBDA, corrected for the loss of  $\text{CO}_2$  due to combustion. Each joint weighed around 0.8 grams. Less than 0.5% of the originally present  $\text{THC}_{\text{max}}$  or  $\text{CBD}_{\text{max}}$  was recovered as carboxylic acids in the mainstream smoke, sidestream smoke and ash. This indicates almost complete decarboxylation of the cannabinoid acids during cannabis smoking.

The recovery of  $\text{THC}_{\text{max}}$  as THC in the smoke stream averaged 36.9% over all the experiments; the recovery of  $\text{CBD}_{\text{max}}$  as CBD showed similar results with an average of 38.4%.

The THC/CBD ratios remained constant upon combustion. This could be of importance for future studies in which the interaction between THC and CBD is investigated.


On average over all of the experiments, 9.2% of the  $\text{THC}_{\text{max}}$  could be recovered as THC in the sidestream smoke and 5.6% could be found in the ashes. For  $\text{CBD}_{\text{max}}$  11.0% could be recovered in the side stream smoke and 4.1% in the ash.

On average a little over 50% of the  $\text{THC}_{\text{max}}$  and  $\text{CBD}_{\text{max}}$  present in the plant material could be recovered in mainstream smoke, sidestream smoke and ash.

**Source:** <http://esciencecentral.org/journals/the-conversion-and-transfer-of-cannabinoids-from-cannabis-to-smoke-stream-in-cigarettes-2329-6836.1000163.php?aid=36397>



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## Cannabis as a Bronchodilator

Asthma is one of the more common chronic inflammatory diseases; it affects roughly 2.4 million people in Canada (2013). The disease is typically caused by inflammation of the bronchial tubes. Anti-inflammatory drugs (e.g. corticosteroids) are the most popular treatment, inhaled either through an inhaler or nebulizer. The steroid acts as a bronchodilator, working to open airway passages.

Contrary to the perception that cannabis smoke is detrimental to the pulmonary system, research has re-affirmed that cannabis may improve lung function and act as a bronchodilator. In the 19th century, one of the medicinal uses of cannabis was bronchial asthma therapy. One study from the 1970s found that THC acted as a bronchodilator from 2 hours (smoked) up to 4 hours (oral). Another 1970s study stated, "Marihuana smoke, unlike cigarette smoke, causes bronchodilatation rather than bronchoconstriction and, unlike opiates, does not cause central respiratory depression [i.e. a decrease in breathing]." And a long-term study from 1985 to 2006 examined 5,000 subjects from three American cities. The researchers found that at low to moderate levels of cannabis smoking, lung volume and air flow rates both increased with each "joint year" (365 joints), up until seven joint-years (or 2,555 joints).

Vaporization is certainly one route to reduce harm and obtain valuable cannabinoids. Oral cannabis ingestion also holds promise. A 1984 study found that oral THC (delta-9, to a lesser extent delta-8), but not CBD or CBN, acted as a bronchodilator. Some have found Marinol helpful to combat asthma but it is more psychoactive and has more side effects than whole-plant cannabis. Ingestion of cannabis via edible products or tinctures may also be beneficial due to its anti-inflammatory properties.

**Sources:** [www.medicaljane.com/2013/02/02/asthma-and-cannabis-marijuana-shown-to-manage-asthma-symptoms/](http://www.medicaljane.com/2013/02/02/asthma-and-cannabis-marijuana-shown-to-manage-asthma-symptoms/)

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1004 North Park Street, Victoria  
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2642 Quadra Street, Victoria  
250- 595-3892

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**DrugSense**  
[www.drugsense.org](http://www.drugsense.org)

**BC Coalition of People  
With Disabilities**  
1-800-663-1278

**Health Canada**  
<http://www.hc-sc.gc.ca/dhp-mps/marihuana/index-eng.php>

**Drug Policy Alliance**  
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**Media Awareness Project**  
[www.mapinc.org](http://www.mapinc.org)

**Together Against Poverty  
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***"Truth resides in every human heart, and one has to search for it there, and to be guided by truth as one sees it. But no one has a right to coerce others to act according to his own view of truth."***

***-- Mahatma Gandhi (Indian politician, 1869-1948)***