Vol. 8, Issue 10
November 2016

CANNABINOID CHRONICLES

Medical Cannabis News and Information

Is CBD Really Non-Psychoactive?

Cannabidiol (CBD) and tetrahydrocannabinol (THC) have similar molecular structures, but CBD does not directly stimulate CB1 and CB2, the cannabinoid receptors, like THC does. THC, cannabis' principal psychoactive component, makes a person feel high by binding to CB1, the most abundant protein receptor in the brain and central nervous system.

Since the CB1 receptor was discovered in 1988, it's been an article of faith among cannabinoid researchers that CBD, unlike THC, has little binding affinity for CB1.

New data emerging from the international cannabinoid research community indicates that CBD interacts directly with the CB1 receptor in ways that are therapeutically relevant. But CBD parks at a different docking site on CB1 that is functionally distinct from THC's primary, or orthosteric, binding site. CBD attaches to what is known as an "allosteric" binding site on the CB1 receptor.

When CBD, an allosteric modulator of CB1, docks at the receptor, it does not initiate a signaling cascade. But it does impact how the CB1 receptor responds to stimulation by THC and the endogenous cannabinoids. Allosteric modulation of CB1 changes the conformation (shape) of the receptor, and this can have a dramatic impact on the efficiency of cell signaling.

Every cell membrane has lots of receptors for many types of messenger molecules, which influence the activity of the cell. The orthosteric site is the switch that a drug turns on, whereas an allosteric modulator can either amplify or decrease a receptor's ability to transmit a signal depending on how the allosteric modulator changes the conformation of the receptor. To use a lock-and-key metaphor: If the orthosteric binding site is the lock on a door, then the allosteric binding site, when activated, makes the lock easier or more difficult to open.

As a negative allosteric modulator of the CB1 receptor, CBD shows particular promise for treating conditions associated with endocannabinoid excess or over-activity (obesity, metabolic disorders, liver disease, cardiovascular issues), whereas a positive allosteric modulator that enhances CB1 receptor signaling could be helpful for diseases linked to endocannabinoid deficits (such as anorexia, migraines, irritable bowel, fibromyalgia, and PTSD).

It should be noted that allosteric modulators typically are unable to alter receptor conformation unless the orthosteric binding site is also stimulated. CBD can modulate CB1 receptor signaling only when THC or another cannabinoid compound is active at the orthosteric binding site. In terms of whole plant cannabis therapeutics, CBD's efficacy as an allosteric modulator requires the co-presence of THC.

Scientists have identified more than 60 different molecular pathways through which CBD operates. It is known, for example, that CBD acts through multiple receptor-independent channels and it also binds to various receptors in the brain.

Researchers have demonstrated that CBD confers antipsychotic, anxiolytic (anxiety-reducing), and antidepressant effects. If CBD can relieve anxiety or depression or psychosis, then obviously cannabidiol is a profound mood-altering substance, even if it doesn't deliver much by way of euphoria. Perhaps it would be better to say that CBD is "not psychoactive *like* THC," rather than repeating the familiar and somewhat misleading refrain that "CBD is not psychoactive."

Source: https://www.projectcbd.org/article/cbd-really-non-psychoactive

International Association for Cannabinoid Medicines (IACM) Bulletin

Human: In US states with medical cannabis laws there is a greater workforce participation and an improvement in overall health of older individuals

States that passed medical cannabis laws saw a significant boost to older Americans' workforce participation, according to a new working paper from researchers at Johns Hopkins and Temple University (USA). States with medical cannabis laws also saw improvements in overall health for older men, although the health effects for older women were more mixed. The study compared what happened in medical cannabis states before and after the passage of medical cannabis provisions, and compared them to trajectories in similar states that did not implement medical cannabis. The data comes from the Health and Retirement study, a survey of the health and economic well-being of older American adults.

The study found that, among individuals age 50 and older, "passage of [a medical marijuana law] leads to a 9.4 percent increase in the probability of employment and a 4.6 percent to 4.9 percent increase in hours worked per week." The reason is that overall health appeared to be better in states with medical cannabis laws. In those states, older men were 5% more likely to say they were in "very good" or "excellent" health. And part of the reason men rated their health better is because they were in less pain: the passage of a medical cannabis law led to roughly a 10% drop in the percent of men saying they experienced pain. However, in women the probability of reporting pain increased by 3.8%, while as with men they were about 5% more likely to report "very good" or "excellent" health after the passage of medical cannabis.

Source: http://www.nber.org/papers/w22688

Human: Cannabidiol improves severe form of childhood epilepsy in controlled clinical trial

The manufacturer of the CBD extract Epidiolex, GW Pharmaceuticals, reported of positive results of the second placebo-controlled Phase 3 clinical trial of this preparation for the treatment of seizures associated with Lennox-Gastaut syndrome, a rare and severe form of childhood-onset epilepsy.

Patients taking Epidiolex in the higher dose achieved a median reduction in monthly drop seizures of 42% compared with a reduction of 17% in patients taking placebo, and patients taking Epidiolex in the lower dose achieved a median reduction in monthly drop seizures of 37%. "The positive outcome in this second trial of Epidiolex in patients with Lennox-Gastaut syndrome demonstrates the effectiveness of this product in this particularly difficult to treat, childhood-onset epilepsy."

Source: http://www.gwpharm.com/PR260916.aspx

Human: Cannabis use during pregnancy is not associated with adverse birth outcome

According to a review of studies on effects of cannabis use on pregnancy outcome there was no increased risk for low birth weight and preterm birth. Authors concluded that "maternal marijuana use during pregnancy is not an independent risk factor for adverse neonatal outcomes after adjusting for confounding factors."

Source: https://www.ncbi.nlm.nih.gov/pubmed/27607879

Cells: Cannabinoids reduce viability of stomach cancer cells

In a study with adenocarcinoma cells of the stomach of humans several cannabinoids (CP 55,940, anandamide and methanandamide) reduced their viability. Authors wrote that their results "support and confirm the therapeutic potential that cannabinoid receptor agonists exert in gastric cancer cells."

Source: https://www.ncbi.nlm.nih.gov/pubmed/27640887

Animal: Activation of the CB2-receptor may be useful in the treatment of complex regional pain syndrome type 1

Complex regional pain syndrome type 1 (CRPS-I) remains one of the most clinically challenging neuropathic pain syndromes. In a rat model of CRPS-1, a synthetic cannabinoid (MDA7), which selectively activates the CB2-receptor, reduced pain and inflammation in this syndrome.

Source: https://www.ncbi.nlm.nih.gov/pubmed/27717112

Cells: THC reduces permeability of airway epithelial cells

In a study with bronchial epithelial cells THC reduced permeability after exposure to pro-inflammatory cytokines by activation of the CB2 receptor. Authors wrote, that THC "beneficial in the prevention of inflammation-induced changes in airway epithelial cell permeability, an important feature of airways diseases."

Source: https://www.ncbi.nlm.nih.gov/pubmed/27641813

Human: CB1 receptor blockade increases inflammation

In 20 obese patients with polycystic ovary syndrome blockade of the CB1 receptor by rimonabant increased signs of inflammation, namely the concentrations of VEGF (vascular endothelial growth factor) and interleukin 8, pro-inflammatory cytokine.

Source: https://www.ncbi.nlm.nih.gov/pubmed/27651218

Human: Allergies against cannabis on the rise

Allergies against cannabis seem to be on the rise. Both active and passive exposure to cannabis allergens may trigger the allergy.

Source: https://www.ncbi.nlm.nih.gov/pubmed/27590896

Cannabis Use Remains Consistent

Harvard economist Jeffrey Miron and co-authors have released a report examining how drug use patterns have changed in Colorado, Washington, Oregon and Alaska following the legalization of cannabis.

Using the federally funded National Survey on Drug Use and Health, the study shows the proportion of respondents who report having used cannabis in the past year has remained basically stable since 2002, at 55% to 60% in each state. Although there are few data points since the first legalizations in 2012, there has been no observable increase in use.

Miron and company suggest that a long-running trend of increasing exposure to cannabis among the adult population has reduced its stigma and generated the cultural acceptance that leads to legalization in the first place. "In essence," they say, "rising marijuana use may not be a consequence of legalization, but a cause of it."

They also address the impact of legalization on measures of public health, crime, road safety, educational outcomes, the economy, and state fiscal health.

The data shows no observable trends in public health following legalization. Records from the Denver police department show no change in overall crime rates following legalization, and in Seattle, crime "has neither soared nor plummeted in the wake of legalization."

Economic gains are overblown. "Analysis show little evidence of significant Gross Domestic Product increases after legalization in any state."

In all, Miron and company conclude, "…state marijuana legalizations have had minimal effect on marijuana use and related outcomes. We cannot rule out small effects of legalization, and insufficient time has elapsed since the four initial legalizations to allow strong inference. On the basis of available data, however, we find little support for the stronger claims made by either opponents or advocates of legalization."

Source: http://www.mapinc.org/drugnews/v16/n651/a04.html?204

Petition to the Government of Canada

There is an E-petition underway, (e-500) calling upon the federal government to cover the cost of cannabis extracts supplied by Licensed Producers for military veterans. The government presently only covers dried cannabis, although extracts have been legally permitted for a nearly a year. The petition is open for signature until December 2, 2016, at 1:50 pm (EDT). Visit:
https://petitions.parl.gc.ca/en/Petition/Details?Petition=e-500

Cannabis Testing Available for Some

It's a small step forward but Health Canada will now allow accredited labs to test cannabis products submitted by some patients. The changes were announced two weeks after a Globe and Mail investigation this summer called into question Health Canada's long-held rules that prevented patients from having medical cannabis screened, even when their health was at stake.

For now, only people with a certificate from Health Canada that lets them grow their own cannabis or buy it from a designated grower can access the country's top labs. Patients wanting to submit products from a federally licensed producer, or one of the hundreds of storefront dispensaries that have proliferated across the country this year, are technically still barred from doing so.

By definition, that excludes many people who are using cannabis for medical purposes outside of Health Canada's Access to Cannabis for Medical Purposes Regulations (ACMPR). However, labs point out they have no way of distinguishing where the product comes from, so several of those facilities told The Globe & Mail that they will test anything that comes their way provided the patient has the proper certificate (presumably a valid ACMPR licence, or a grandfathered licence from the old MMAR protected under the Allard injunction).

This is welcome news for parents such as Mandy McKnight who has been administering cannabis oil to her severely epileptic son. After prescription drugs failed to control his up to 80 seizures a day, Ms. McKnight tried cannabis oil. Her son's seizures subsided and it was 10 *days* before he had another seizure. Armed with a prescription to allow her to access cannabis for medical purposes, Ms McKnight makes the cannabis oil at home. Until Health Canada changed the rules, it was illegal for her to get the product tested. A humanitarian lab accommodated her requests, but Mandy was always looking behind her back and expecting child-protection services to yank her son away.

The limited selection of cannabis oils from Licensed Producers means that some people are still going to storefront dispensaries for the strains they need.

Source: www.mapinc.org/drugnews/v16/n638/a05.html?180

Cannabis Oil Extraction Methods

Concentrated cannabis extracts, also known as cannabis oils because of their sticky and viscous appearance, are becoming increasingly popular among self-medicating patients as a claimed cure for cancer. As discussed in a previous issue of *Cannabinoid Chronicles*, there is a lot of anecdotal evidence that this is the case, but little hard clinical research exists.

Recognizing the need for more information, a research paper from 2013 evaluated several different extraction techniques to determine the content of cannabinoids, terpenes, and residual solvent components. Solvents used include ethanol, naphtha, petroleum ether, and olive oil. The obtained results were not intended to support or deny the therapeutic properties of these products, but may be useful for better understanding the experiences of self-medicating patients through chemical analysis of this popular medicine.

The report concluded that it is not feasible to perform decarboxylation of cannabinoids without significant loss of terpene components. Retaining the full spectrum of terpenes present in fresh cannabis material should therefore be a major focus during optimal cannabis oil production.

When comparing five methods of cannabis oil preparation, some interesting differences were observed between the resulting extracts. "Rick Simpson" oil, a popularized form that uses naptha as the solvent, has produced "cancer-curing" claims. Chemical analysis of the laboratory samples, as well as a sample obtained from a patient, showed that the heavy fraction (components with high boiling point) of naphtha indeed remains in the extract despite the recommended evaporation step.

It should be noted that the more concentrated an extract becomes, the more difficult it will be to remove the residual solvent from it. In such a case, applying more heat will increase evaporation, but simultaneously more terpenes will be lost as well. Especially under conditions where cannabis oil is prepared by simple household methods, there will always be a trade-off between residual solvents and terpene content. For this reason, the use of non-toxic solvents should always be advised, so that potential residues are not harmful to health.

Ethanol and olive oil were shown to perform much better as extraction solvents, extracting all terpenes and cannabinoids tested very efficiently. Additionally, these solvents are not harmful. Unfortunately, pure ethanol efficiently extracts chlorophyll from cannabis, which will give the final extract a distinct green colour, and often unpleasant taste. Removing chlorophyll by filtering the ethanol extract over activated charcoal was found to be very effective, but it also removed a large proportion of cannabinoids and terpenes, and is therefore not advised.

Of the solvents tested, this leaves olive oil as the most optimal choice for preparation of cannabis oils for self-medication. Olive oil is cheap, not flammable or toxic, and the oil needs to be heated up only to the boiling point of water so no over-heating of the oil may occur. After cooling down and filtering the oil, the product is immediately ready for consumption. As a trade-off, however, olive oil extract cannot be concentrated by evaporation, which means patients will need to consume a larger volume of it in order to get the same therapeutic effects.

[Note: CO_2, a non-toxic solvent, is gaining traction as a cannabis oil solvent. The cost of CO_2 extraction equipment keeps it out of most kitchens. It is claimed to retain more of the terpenes than other techniques.]

Source: Romano, L., Hazekamp A. ***Cannabis Oil - Chemical evaluation of an upcoming cannabis-based medicine***. May 5, 2013. Available online at www.cannabis-med.org

RESOURCE DIRECTORY:

AIDS Vancouver Island
3rd Fl- 713 Johnson St, Victoria
250-384-2366

VIPWA
101-1139 Yates Street, Victoria
250-382-7927

The Action Committee of People with Disabilities
948 View Street, Victoria
250-383-4105

MS Society of Canada
1004 North Park Street, Victoria
(250) 388-6496

HepC BC
2642 Quadra Street, Victoria
250- 595-3892

BC Cancer Agency
2410 Lee Ave, Victoria
(250) 519-5500

Canadians for Safe Access
www.safeaccess.ca

John W. Conroy, Q.C.
1-877-852-5110 (toll free)
www.johnconroy.com

Kirk Tousaw, Barrister
604-836-1420
www.tousawlaw.ca

DrugSense
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
www.drugpolicy.org

Media Awareness Project
www.mapinc.org

Together Against Poverty Society
302-895 Fort Street, Victoria
250-361-3521

"I'm hitting a lick for peace, and every time I'm in Georgia I eat a peach for peace."

-- Duane Allman (musician extraordinaire, 1946 - 1971)