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CANNABINOID CHRONICLES

Medical Cannabis News and Information

Cannabinoids and Breast Cancer

Cannabis is being used by people with cancer to help manage pain, fatigue, nausea, and other side effects of chemotherapy. Less well known is the fact that extensive preclinical research shows that phytocannabinoids - most notably, tetrahydrocannabinol (THC) and cannabidiol (CBD) - produce anti-tumour responses in various animal models of cancer.

The vast majority of this preclinical research has examined the anticancer activity of pure compounds, mainly THC isolates. But medical cannabis patients aren't using pure, single-molecule THC to battle cancer. Instead, they are consuming whole plant cannabis oil extracts that include hundreds of compounds, some of which also have therapeutic properties.

Thus far, however, few rigorous studies have analyzed the effects of whole plant cannabis extracts. So a team of Spanish researchers, led by Cristina Sanchez at Complutense University in Madrid, decided to compare the efficacy of pure THC isolates and THC-rich oil extracts in a series of preclinical experiments that focused on breast cancer. The researchers also investigated the effects of pure THC and an artisanal THC-rich oil formulation when each was combined with standard chemotherapy drugs.

Their findings ("Appraising the 'Entourage Effect': Antitumor action of a pure cannabinoid versus a botanical drug preparation in preclinical models of breast cancer") were published last year in the journal *Biochemical Pharmacology*. The phrase "entourage effect" in this context refers to the full-spectrum synergistic interplay between numerous cannabis compounds - cannabinoids, terpenes and flavonoids - that impart a therapeutic impact that's greater than the sum of the plant's individual components.

It is estimated that one in eight women will develop breast cancer. Breast cancer is tricky to treat because there

are few biomarkers that signal when someone has the disease, and many patients show or develop resistance to current therapies. Moreover, several specific types of breast cancer respond poorly to modern treatment.

Two biomarkers frequently used to diagnose breast cancer are hormonal receptors (the estrogen receptor and progesterone receptor) and the HER2 oncogene (a gene which can transform a normal cell into a tumor cell). But a more aggressive malignancy, known as "triple-negative breast cancer," doesn't express hormonal receptors or the HER2 oncogene. No targeted therapy exists for triple-negative breast cancer, so patients are treated with harsh chemotherapies that indiscriminately kill proliferating cells, whether cancerous or not.

Three types of cancer were used as models in the study:

Hormone-sensitive breast cancer - whole plant extract was found to be 15-25% more potent than THC alone. When the cannabinoid preparations were added to tamoxifen, a standard chemotherapy drug, in a cell plate, the combined therapy was about 20-25% more effective than chemotherapy alone. But these results were not replicated in live-animal trials.

In hormone-sensitive breast cancer, it appears that THC produces effects via interaction with the CB2 cannabinoid receptor.

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ANNOUNCEMENT

The VICS is sad to report that we will be closing our doors at 6 pm, July 5, 2019, in order to pursue a BC retail license, as voted on by the members.

See you again soon!

Human: MS patients taking cannabis were able to reduce intake of opioids and benzodiazepines

According to a retrospective chart review of 77 patients diagnosed with multiple sclerosis (MS), treatment with cannabis allowed one-third to reduce the intake of other medications, including opioids. Scientists of Dent Neurologic Institute Amherst in New York, USA, published their study results in the *Journal Neurology*. Subjective improvement endorsed by patients was extensive, with alleviation of pain (71%), spasticity (43%), and sleep (42%). In addition, 34% of patients were able to decrease or discontinue other medications including opioids, stimulants, and benzodiazepines. A low rate of discontinuation (14%) was observed, most frequently due to cost (36%) and lack of efficacy (36%).

Source: https://n.neurology.org/content/92/15_Supplement/P5.2-106

Human: The endocannabinoid system shows a reduced activity in patients with post-traumatic stress disorder

In a study with 20 patients suffering from post-traumatic stress disorder, and healthy controls, researchers investigated blood levels of the endocannabinoids anandamide (AEA), 2-AG (2-arachidonoylglycerol) and oleylethanolamide following exercise and psychosocial stress. Only healthy controls exhibited a significant increase in the levels of 2-AG following exercise and psychosocial stress. Researchers wrote that these data provide preliminary evidence that the endocannabinoid system “is hypoactive in PTSD following exposure to physical and psychosocial stressors.”

Dept. of Kinesiology, U. of Wisconsin-Madison, USA.

Source: <https://www.ncbi.nlm.nih.gov/pubmed/30978371>

Human: Endocannabinoids contribute to the mood improving effects of exercise in patients with major depression

Blood was taken from 17 women with major depressive disorder before and 10 minutes after exercise. There were significant elevations in anandamide and oleylethanolamide levels, and there were negative associations between changes in anandamide and mood states. Researchers concluded that the endocannabinoid system “contributes to the mood-enhancing effects of prescribed acute exercise” in major depressive disorder.

Source: <https://www.ncbi.nlm.nih.gov/pubmed/30973483>

Human: The risk for problematic use of cannabis depends on reason for use

In a study with 468 adults, the main reasons for using cannabis were to heighten positive feelings (35%), habit (29%) and to cope with negative feelings (25%). Coping with negative feelings was associated with the highest risk for problematic cannabis use.

Source: <https://www.ncbi.nlm.nih.gov/pubmed/31018002>

Human: CBD had no effect on psychomotor impairment by THC

In a simulated driving test with 14 healthy volunteers, there was no significant effect of CBD on impairment by THC. Participants inhaled 125 mg of cannabis with 11% THC and less than 1% CBD, and at another time the same amount of cannabis with 11% THC and 11% CBD. Authors wrote that subjective “drug effects (e.g., “stoned”) and confidence in driving ability did not vary with CBD content.” Peak blood plasma THC concentrations were higher following THC/CBD equivalent cannabis relative to THC-dominant cannabis, “suggesting a possible pharmacokinetic interaction.” Lambert Initiative for Cannabinoid Therapeutics, Australia.

Source: <https://www.ncbi.nlm.nih.gov/pubmed/31044290>

Human: CBD and palmitoylethanolamine may be helpful in inflammatory bowel disease

A randomized, double-blind, controlled-trial assessed the effect of palmitoylethanolamine (PEA) or CBD on the absorption of lactulose and mannitol in humans taking 600 mg of aspirin. In vivo, aspirin caused an increase in the absorption of lactulose and mannitol, which were reduced by PEA or CBD. Authors concluded that both substances “reduce permeability in the human colon. These findings have implications in disorders associated with increased gut permeability, such as inflammatory bowel disease.

Source: <https://www.ncbi.nlm.nih.gov/pubmed/31054246>

Animal: High doses of CBD may have negative effects on the liver

Mice treated with high oral doses of CBD (up to 2560 mg per kilogram bodyweight) showed signs of liver toxicity. Authors noted that their observation may be relevant to patients receiving up to 20 mg CBD per kilogram bodyweight. They noted that “involvement of numerous pathways associated with lipid and xenobiotic metabolism raises serious concerns about potential drug interactions as well as the safety of CBD.”

Source: <https://www.ncbi.nlm.nih.gov/pubmed/31052254>

Animal: The endocannabinoid system modulates symptoms of schizophrenia

In a mouse model of schizophrenia characterised by increased locomotor activity and memory impairment, increasing the levels of endocannabinoids influenced the symptoms in a dose dependent manner. A low dose of an inhibitor of endocannabinoid degradation (URB 597) reduced memory impairment, while a higher dose increased memory impairment.

Source: <https://www.ncbi.nlm.nih.gov/pubmed/31004320>

More info: www.cannabis-med.org/

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HER2-positive breast cancer - whole plant extract was found to be significantly more potent than THC for HER2-positive breast cancer cells. Both single-molecule THC and whole plant extract showed antitumor effects when the experiment was replicated in mice. Additionally, both THC and the whole plant extract amplified the anticancer effects of lapatinib, the standard chemotherapy drug for HER2 breast cancer.

As with hormone-sensitive breast cancer, THC's antitumoral effect in HER2-positive breast cancer experiments was shown to be mediated by the CB2 cannabinoid receptor.

Triple-negative breast cancer - triple-negative, the breast cancer subtype with the worst prognosis, does not generally respond well to chemotherapy. But the Spanish group found that THC and THC-rich cannabis oil both offer some hope in improving treatment outcomes for this highly aggressive cancer. Again, the whole plant extract was found to be more effective than THC alone in decreasing the viability of cancer cells *in vitro* as well as in mouse model studies.

In all models of breast cancer studied, *in vitro* as well as *in vivo*, the whole plant extract was significantly more effective at producing anticancer effects than single-molecule THC. These results were largely consistent for type of cancer and type of model.

The Spanish breast cancer study underscores the importance of the entourage effect by demonstrating that full spectrum artisanal cannabis oil extract with numerous components is more effective than pure THC.

The Spanish scientists emphasize that the whole plant cannabis drug preparation "did not, in any case, diminish the antitumor efficacy of any of the standard treatments." That's good news for cancer patients who use cannabis to manage the adverse side effects of chemo. Cannabis is very likely a safe add-on therapy for treating pain and nausea and for appetite stimulation. And it may also increase the efficacy of standard chemotherapy treatments, which means that chemo could be more effective - requiring lower and less toxic doses - when used in combination with cannabis.

The authors note that the whole plant cannabis oil extract used in the study also contained measurable amounts of cannabigerol (CBG) and tetrahydrocannabinolic acid (THCA; non-decarboxylated precursor to THC). CBG has demonstrated effectiveness against colon cancer in preclinical models, and THCA is known to interact with a PPAR (nuclear) receptor that mediates apoptosis (cell death) in cancer cell lines. A combination of all these compounds may be required to achieve the antitumoral response observed in the Spanish breast cancer study.

A recent study, published in *Hormone-Dependent Cancers: New Aspects on Biochemistry and Molecular Pathology (II)*, found that cannabinoids provide relief for tumour-associated symptoms (including nausea, anorexia, and neuropathic pain) in the palliative treatment of cancer patients. Additionally, they may decelerate tumor progression in breast cancer patients. Indeed, THC, CBD, and other cannabinoids inhibited disease progression in breast cancer models.

Sources: <https://www.ncbi.nlm.nih.gov/pubmed/29940172>
<https://www.projectcbd.org/medicine/thc-versus-breast-cancer>
<https://www.mdpi.com/1422-0067/20/7/1673/htm>

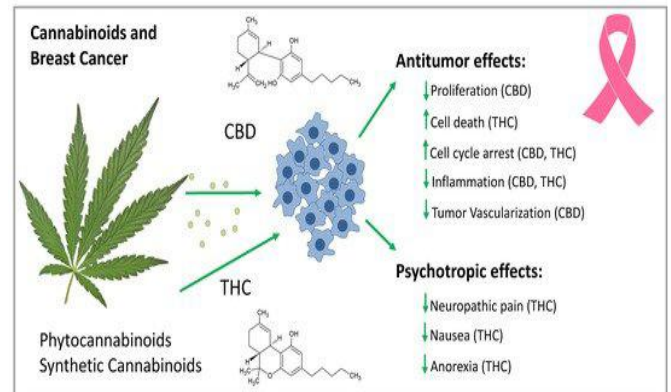


Image: https://www.mdpi.com/ijms/ijms-20-01673/article_deploy/html/images/ijms-20-01673-ag-550.jpg

Commission Recommends Against Δ 9-THC Threshold in Michigan USA

A new report in Michigan State on cannabinoid concentrations in the blood and impairment has found that Michigan should not set a legal driving limit for THC in the blood.

Studies show that, while cannabis use does impair critical driving skills, the blood level does not correlate with impairment. Peak THC levels drop quickly, but impairment happens more slowly and peaks later. Impairment levels also vary by driver.

"Due to the initial rapid elimination phase of Δ 9-THC followed by the long terminal elimination phase, blood-plasma concentrations of Δ 9-THC are indicative of *exposure*, but are not a reliable indicator of whether an individual is *impaired*."

"Therefore, because there is a poor correlation between Δ 9-THC bodily content and driving impairment, the Commission recommends against the establishment of a threshold of Δ 9-THC bodily content for determining driving impairment and instead recommends the use of a roadside sobriety test(s) to determine whether a driver is impaired."

Sources: <https://www.wilx.com/content/news/New-report-says-Michigan-shouldnt-set-driving-limit-for-marijuana-507658461.html>
http://media.graytvinc.com/documents/Michigan+Impaired_Driver_Report_1553554601148_79160282_ver1.02.pdf

Ontario Pharmacists Must Complete Mandatory Cannabis Education Course

The Ontario College of Pharmacists has informed its members that they must complete a mandatory cannabis education course to continue practicing in the province. The regulatory body began offering a cannabis education class online last month and will require pharmacists to complete an accredited course by March 27, 2020.

The College of Pharmacists class covers the benefits, risks, and side effects of cannabis, and explores a pharmacist's legal, ethical, and professional responsibilities involved in its use by patients. Although pharmacists do not dispense cannabis, regulators believe that they will be likely to encounter consumers curious about medicinal uses or risks of using marijuana products.

A statement from the college acknowledges that many patients want reliable information on how cannabis interacts with their medications. But while much is known about health effects of alcohol use, for instance, information about recreational pot is far less understood and available, notes the college.

In June 2018, the college released *A Cannabis Strategy for Pharmacy: Enhancing Knowledge, Protecting Patients* consisting of four priorities to serve and maintain the public interest. The priorities include developing and maintaining competency in cannabis, providing patient care, health information and advice, documenting, developing and tracking data, and preventing harm.

"The legalization of recreational cannabis is an extraordinary public policy shift that has a significant impact on the health and safety of Canadians and increases the potential for more open use among the public and pharmacy patients".

The move makes Ontario the only province to require pharmacists to complete a cannabis course. Regulatory bodies in other provinces have taken a more hands-off approach.

University of Waterloo pharmacy associate professor

Michael Beazely, who helped put together Ontario's course, said many pharmacists are frustrated that concrete data is hard to come by.

"The clarity of how (cannabis) should be used is less black-and-white than many prescription drugs," notes Beazely, whose course also breaks down the differences and similarities between recreational and medical cannabis products.

Ideally, pharmacists should know about all of a patient's drug use, whether it be over-the-counter, natural health products, vitamin supplements, prescription drugs or recreational drugs, legal and illegal, says Beazely.

Sources: <https://hightimes.com/news/ontario-pharmacists-must-now-complete-mandatory-cannabis-education-course/>
<https://globalnews.ca/news/5207085/ontario-pharmacists-cannabis-course-education/>
<http://www.ocpinfo.com/practice-education/practice-tools/support-materials/cannabis-training-requirements-courses/>



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BC Cancer Agency
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www.drugsense.org

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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

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"The reasonable man adapts himself to the world; the unreasonable one persists in trying to adapt the world to himself. Therefore, all progress depends on the unreasonable man."

-- George Bernard Shaw (1856 - 1950, Irish playwright, critic, and political activist)