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CANNABINOID CHRONICLES

Medical Cannabis News and Information

CBD/THC Formulation Shows Promise for Treating Epilepsy

A cannabis oil formulation that consists of mostly cannabidiol (CBD) and a small amount of tetrahydrocannabinol (THC) (50:1 ratio) has been found to be safe and tolerated by children with Dravet syndrome, a rare genetic form of epilepsy that causes lifelong seizures. Researchers at the Hospital for Sick Children tested the cannabis oil in 19 children whose seizures were not well-controlled with standard anti-convulsant medications.

CBD-only formulations have been successful in treating certain conditions, but the research team wanted to assess the benefits of a preparation that also included THC, with a primary goal of determining a safe pediatric dose and any side-effects the drug caused.

Children with Dravet syndrome experience ongoing seizures - in some cases, more than a hundred a day - leading to developmental delays and significant learning disabilities. Dravet's is responsible for up to 30% of all cases of epilepsy; it is difficult to treat and has no cure.

"We saw an overall median reduction (in seizures) of 70%," said neurologist Dr. Blathnaid McCoy, lead author of the study published August 1st in the *Annals of Clinical and Translational Neurology*.

"And one of the things we tracked was seizure-free days ... which went from a mean of 11.8 days to 18.3 days, which is essentially an extra week (and) which is clinically very meaningful."

However, not all of the children responded positively: four saw their seizures increase in frequency while taking oral doses of the oil, a pharmacy-grade preparation produced by Tilray Inc. However, McCoy said that increased seizure activity could also be due to the nature of Dravet's, which is known to cause "peaks and troughs, even if we don't do anything."

For Laura Weightman, whose 16-year-old daughter Abigail had her first Dravet seizure at eight months old, the cannabis oil therapy has meant new hope for her child's future. Abigail had experienced about 100 seizures a month from about age three to five, a number that was subsequently reduced to about 10 to 20 per month with surgical and pharmaceutical interventions.

But since enrolling in the study in April 2017 and starting treatment with the cannabis oil, Abigail has had only three seizures in the last eight months, she said.

"This therapy has turned our lives around."

Much of the scientific evidence for cannabis' anti-seizure properties has come from research using a CBD-only product; research suggests that preparations that also contain THC may be superior.

McCoy said the next step is to design a larger study of at least 200 children with any kind of epilepsy to assess the effect of the CBD/THC oil in better controlling seizures.

Sources: <https://onlinelibrary.wiley.com/doi/full/10.1002/acn3.621>
<https://www.theglobeandmail.com/cannabis/article-thc-containing-cannabis-oil-shows-promise-for-treating-dravet-syndrome/>



Image: <http://cannabismedicalworld.blogspot.com/2013/05/epilepsy-seizures-cured-after-ingesting.html>

Human: Medical cannabis laws in the USA are associated with improved workplace safety

In a large study, scientists demonstrated that the legalization of the medical use of cannabis improved workplace safety for workers aged 25 to 44. Investigators at the US Department of Agricultural Economics and Economics of Montana State University in Bozeman, MT, analysed data of all 50 US states and the District of Columbia for the period 1992 to 2015.

Authors wrote: “Legalizing medical marijuana was associated with a 19.5% reduction in the expected number of workplace fatalities among workers aged 25-44 (...). The association between legalizing medical marijuana and workplace fatalities among workers aged 16-24, although negative, was not statistically significant at conventional levels. The association between legalizing medical marijuana and workplace fatalities among workers aged 25-44 grew stronger over time. Five years after coming into effect, MMLs [medical marijuana laws] were associated with a 33.7% reduction in the expected number of workplace fatalities.”

Source: <https://www.ncbi.nlm.nih.gov/pubmed/30092547>

Human: Human: Large study with CBD in patients with epilepsy demonstrates long-term safety of the medication

In an open study with 72 children and 60 adults with different forms of treatment-resistant epilepsy, adverse events decreased over time. Scientists of the Department of Neurology at the US University of Alabama in Birmingham, AL, wrote that their prospective, open-level safety study of CBD in treatment resistant epilepsy “provides evidence for significant improvements in AEP [adverse events profile], CSSS [Chalfont Seizure Severity Scale], and SF [seizure frequency] at 12 weeks that are sustained over the 48-week duration of treatment.”

Patients started with a dose of at 5 mg/kg/day and titrated it up to a maximum dosage of 50 mg/kg/day. Data were analysed for the enrolment and visits at 12, 24, and 48 weeks. For all participants, adverse events decreased between the start of the study and the 12-week visit with stable scores thereafter. Seizure frequency within 2 weeks decreased from a mean of 144.4 at entry to 52.2 at 12 weeks and remained stable thereafter.

Source: <https://www.ncbi.nlm.nih.gov/pubmed/30100226>

Human: Cannabinoids may be helpful in glioblastoma

Among natural products, which may have antitumor effects in glioblastoma (GBM), an aggressive brain tumour, are cannabinoids, terpenes and curcumin, because according to the authors “many have been shown to have a significant effect in decreasing the progress of GBM through known mechanisms.” Faculty of Sciences, Universidad Austral de Chile, Valdivia, Chile.

Source: <https://www.ncbi.nlm.nih.gov/pubmed/30109743>

Human: Patients with insomnia experience improved sleep by the use of cannabis

The use of cannabis flowers in 409 people with a specified condition of insomnia resulted in significant improvements of their sleep. The extent of therapeutic effects depended on the cannabis strain. These are the results of research conducted at the Department of Psychology of the University of New Mexico in Albuquerque, USA. Patients completed 1056 medical cannabis administration sessions during which they rated self-perceived insomnia severity levels prior to and following consumption.

Participants showed an average symptom severity reduction of -4.5 points on a 0 to 10 point visual analogue scale. Use of pipes and vaporizers was associated with greater symptom relief and more positive side effects as compared to the use of cannabis cigarettes, while vaporization was also associated with lower negative effects. CBD was associated with greater statistically significant symptom relief than THC. Flowers from cannabis sativa plants were associated with more negative side effects than flowers from cannabis indica or hybrid plant subtypes.

Source: <https://www.ncbi.nlm.nih.gov/pubmed/29997343>

Animal: The use of cannabidiol (CBD) in dogs with arthritis was effective and safe

In a placebo-controlled study with 22 dogs suffering from osteoarthritis, CBD in a dose of 2 mg/kg twice daily increased comfort and activity of the animals. No side-effects were reported by owners. Each treatment lasted for 4 weeks with a 2-week washout period. College of Veterinary Medicine, Cornell University, Ithaca, USA.

Source: <https://www.ncbi.nlm.nih.gov/pubmed/30083539>

Animal: Cannabidiol (CBD) and cannabidivarin (CBDV) may be helpful in muscular dystrophy

In muscle cells from patients with Duchenne muscular dystrophy, some cannabinoids (CBD, CBDV) promoted the formation of myotubes, developing skeletal muscle fibers. In a mouse model of muscular dystrophy, these cannabinoids prevented the loss of locomotor activity. Authors wrote that their research may lead to the prevention of muscle degeneration in patients with Duchenne muscular dystrophy.

Source: <https://www.ncbi.nlm.nih.gov/pubmed/30074247>

Animal: CBD increased the anti-cancer effects of gemcitabine against pancreatic cancer

In a study with mice with pancreatic cancer, a combination of CBD and gemcitabine increased survival nearly 3-fold compared to gemcitabine only. Antagonism (blocking) of the GPR55 receptor played a major role in this effect. CBD is a GPR55 receptor antagonist.

Source: <https://www.ncbi.nlm.nih.gov/pubmed/30061636>

Cannabinoids for the Treatment of Behavioral and Psychological Symptoms of Dementia (BPSD)

The term behavioral and psychological symptoms of dementia (BPSD) describes a group of important non-cognitive symptoms and behaviors that are often seen among individuals with dementia. BPSD tends to occur in 90% of the individuals with cancer. Available data indicates that BPSD can worsen cognition, cause functional decline, increase the rate of institutionalization, lower quality of life, increase caregiver burden and adds to the cost of caring for individuals with dementia.

Current evidence has demonstrated that both non-pharmacologic and pharmacologic treatments display some sort of benefit in the management of BPSD. Most treatment protocols recommend the use of non-pharmacologic treatments first before considering a combination of non-pharmacologic and pharmacologic treatments for more refractory symptoms.

Pharmacological agents that have been used for the treatment of BPSD include anti-psychotics, anti-depressants, anti-convulsants, and cognitive enhancers. Regrettably, the use of these medications is often associated with significant adverse effects among older patients with dementia. Hence, additional pharmacological strategies need to be identified that are more suitable for use among individuals with BPSD.

Cannabis is a plant that contains numerous psychoactive compounds. The primary psychoactive ingredient of cannabis is $\Delta 9$ -tetrahydrocannabinol ($\Delta 9$ -THC). The physiologic effects noted after the use of cannabis are directly related to the THC concentrations in the product. The term cannabinoid typically refers to compounds that activate the cannabinoid 1 (CB₁) and cannabinoid 2 (CB₂) receptors. More recently, other compounds with similar structures to THC that do not specifically activate these receptors have often been included under this term.

There is evidence to suggest that cannabinoids can reduce neuro-degeneration, neuro-inflammation, and have neuro-protective effects through the activation of the CB₁ and CB₂ receptors. The CB₁ receptors are present in great density in the cerebral cortex, hippocampus, basal ganglia, and cerebellum. In contrast, CB₂ receptor activation has been associated with reduced production of pro-inflammatory compounds and the removal of amyloid-beta (A β) plaques among humans. There is also evidence to suggest that cannabinoid receptor agonists, including WIN55,212-2 and arachidonyl-2-chloroethylamide, may reduce aggressive behaviours. Emerging evidence indicates that cannabinoids may also have some benefit in treatment of BPSD. A review of the

literature indicates that there is a total of eight reports on the use of cannabinoids for the treatment of BPSD. These studies included a total of 117 individuals with a diagnosis of dementia (67 with Alzheimer's-type dementia, 8 with vascular-type dementia, and 42 with unspecified dementia).

Sources: <https://doi.org/10.2217/nmt-2018-0019>
<https://www.ncbi.nlm.nih.gov/pubmed/30040030>

Cannabis Improves Pancreatic Survival Rates of Mice

Mice with pancreatic cancer that were treated with the cannabinoid cannabidiol (CBD) alongside chemotherapy, survived almost three times longer than those treated with chemotherapy alone, a new study reports.

The study is published in the journal *Oncogene* and was led by Queen Mary University of London and Curtin University, Australia. It tested the impact of CBD on the use of the commonly used chemotherapy medication Gemcitabine as a treatment for pancreatic cancer in mice. Presently, the five-year survival rate for people with pancreatic cancer is less than 7%.

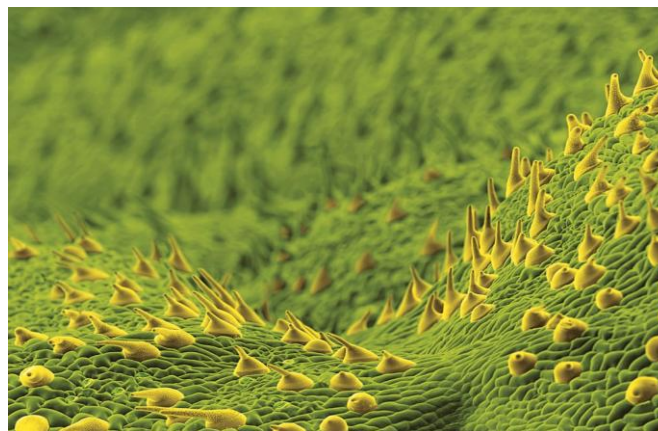
Lead researcher Professor Marco Falasca said: "This is a remarkable result. We found that mice with pancreatic cancer survived nearly three times longer if a constituent of medicinal cannabis was added to their chemotherapy treatment."

"Cannabidiol is already approved for use in clinics, which means we can quickly go on to test this in human clinical trials. If we can reproduce these effects in humans, cannabidiol could be in use in cancer clinics almost immediately, compared to having to wait for authorities to approve a new drug."

The researchers add that CBD is also known to improve the side effects of chemotherapy, including nausea, diarrhoea, vomiting, meaning it could also improve the quality of life of patients undergoing chemotherapy.

Sources: <https://medicalxpress.com/news/2018-07-cannabinoid-survival-mice-pancreatic-cancer.html>

<https://www.nature.com/articles/s41388-018-0390-1>



CANNABIS TRICHOMES UP CLOSE

Benefits of Three Terpenes: Myrcene, Linalool and Bisabolol

Terpenes are a large and varied class of organic compounds produced by a variety of plants (e.g. cannabis, conifers) and the odd insect. Terpenes have been found to be essential building blocks of complex plant hormones and molecules, pigments, sterols, and cannabinoids in cannabis. Terpenes also provide the plant with natural protection from bacteria and fungus, insects, and other environmental stresses.

Cannabis cannabinoids are odorless, so the terpenes, in various combinations, are largely responsible for the smell and the taste of cannabis. Different strains have distinctive aromas and flavours such as pine, diesel, pineapple and berry. Besides affecting aroma and flavour, there is some evidence suggesting that they may also modify cannabis's effects independent from the cannabinoids. The over 100 different terpenes contribute to a strain's particular influence - a phenomenon known as the entourage effect.

Myrcene (or β -myrcene) is a terpene that occurs often in highly fragrant plants and herbs such as mangoes, hops, bay leaves, thyme, lemongrass, and basil. Myrcene is the most abundant terpene in cannabis, and is produced by many different cannabis strains. Some have suggested that it lends sedative, indica-like effects to some strains. Found mainly in sativas, myrcene possesses muscle-relaxing, anti-depressant, anti-inflammatory, anti-mutagenic, and analgesic properties. Myrcene also has an effect on the permeability of cell membranes, and allows cannabinoids to more easily bridge the blood-brain barrier (BBB).

Linalool is a naturally occurring terpene found in many flowers and spices including lavender and coriander. Humans have inhaled the scent of certain plants, including many containing linalool, since ancient times to help lower stress levels, fight inflammation, and combat depression. A recent study, in which scientists allowed lab rats to inhale linalool while exposing them to stressful

conditions, reported that linalool returned elevated stress levels in the immune system to near-normal conditions.

Bisabolol is a fragrant chemical compound produced by the chamomile flower and other plants. It is also found in various cannabis strains. While it has long been widely used in the cosmetics industry, bisabolol has more recently become the subject of research for the medical benefits it displays in cannabis, possessing anti-inflammatory, anti-oxidant, anti-microbial and analgesic properties.

Sources: <https://pubs.acs.org/doi/abs/10.1021/jf900420g>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3165946/>
www.leafly.com/news/cannabis-101/myrcene-linalool-and-bisabolol-what-are-the-benefits-of-these-can



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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

Together Against Poverty Society
302-895 Fort Street, Victoria
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"There is no folly of the beasts of the earth which is not infinitely outdone by the madness of men."

-- Herman Melville (1819 - 1891, American writer, poet)