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# CANNABINOID CHRONICLES

## Medical Cannabis News and Information

### **Cannabis Therapeutics and the Future of Neurology** *by Ethan Russo*

Neurological therapeutics have been hampered by its inability to advance beyond symptomatic treatment of neurodegenerative disorders into the realm of actual palliation, arrest or reversal of the attendant pathological processes. While cannabis-based medicines have demonstrated safety, efficacy and consistency sufficient for regulatory approval in spasticity in multiple sclerosis (MS), and in Dravet and Lennox-Gastaut Syndromes (LGS), many therapeutic challenges remain. This review will examine the intriguing promise that recent discoveries regarding cannabis-based medicines offer to neurological therapeutics by incorporating the neutral phytocannabinoids tetrahydrocannabinol (THC), cannabidiol (CBD), their acidic precursors, tetrahydrocannabinolic acid (THCA) and cannabidiolic acid (CBDA), and cannabis terpenoids in the putative treatment of five syndromes, currently labeled recalcitrant to therapeutic success, and wherein improved pharmacological intervention is required: intractable epilepsy (seizure threshold mediated by endocannabinoid system (ECS)), brain tumors (cytotoxic benefit of phytocannabinoids), Parkinson disease (PD) (nabiximols, i.e. Sativex, reduce neurofibrillary tangles), Alzheimer disease (AD) (benefits target symptoms: e.g. agitation, anxiety, psychosis, insomnia, aggression, depression), and traumatic brain injury (TBI)/chronic traumatic encephalopathy (CTE) (phytocannabinoids are neuroprotective). Current basic science and clinical investigations support the safety and efficacy of such interventions in treatment of these currently intractable conditions. The inherent polypharmaceutical properties of cannabis botanicals offer distinct advantages over the current single-target pharmaceutical model and portend to revolutionize neurological treatment into a new reality of effective interventional and even preventative treatment.

Source: [www.frontiersin.org/articles/10.3389/fnint.2018.00051/full](http://www.frontiersin.org/articles/10.3389/fnint.2018.00051/full)

### **Endocannabinoid System and the Treatment of Skin Disorders**

The skin is the largest organ of the body and has a complex and very active structure that contributes to homeostasis; it also provides the first line of defense against injury and infection. It has become evident that the endocannabinoid system (ECS) plays a relevant role in healthy and diseased skin. This research paper reviews how the dysregulation of ECS has been associated to dermatological disorders such as atopic dermatitis, psoriasis, scleroderma and skin cancer. The druggability (term used to describe a biological target, such as a protein, that is known to or is predicted to bind with high affinity to a drug) of the ECS could open new research avenues for the treatment of the pathologies mentioned above. Numerous studies have reported that phyto-cannabinoids and their biological analogues modulate a complex network pharmacology involved in the modulation of the ECS, focusing on classical cannabinoid receptors, transient receptor potential channels (TRPs), and peroxisome proliferator-activated receptors (PPARs).

Source: [www.sciencedirect.com/science/article/abs/pii/S0006295218303484](http://www.sciencedirect.com/science/article/abs/pii/S0006295218303484)

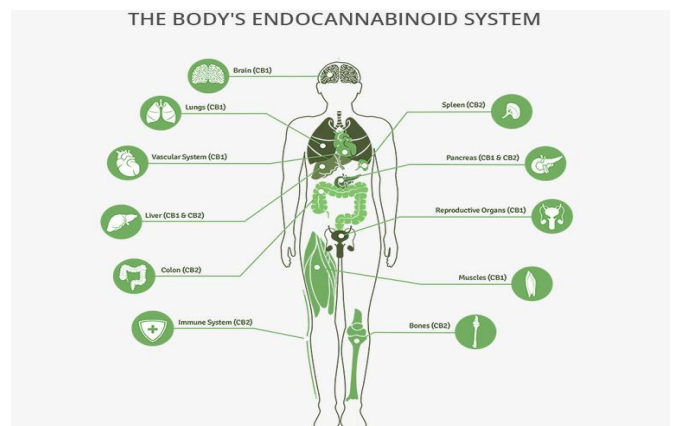


Image: <https://theorganicgrocer.ca/wp-content/uploads/2018/09/endocannabinoid-system-1.jpg>

## ***Human: Cannabis may be helpful in bipolar disorder***

For some patients suffering from bipolar disorder, cannabis may result in partial alleviation of symptoms. This is the result of research at the McLean Hospital in Belmont, USA. Twelve patients with bipolar disorder who used cannabis, 18 bipolar patients who did not use the drug, 23 cannabis users and 21 healthy controls completed a neuropsychological battery. Further, participants rated their mood three times daily as well as after each instance of cannabis use over a four-week period.

Results revealed that although the cannabis users and patients with bipolar disorder exhibited some degree of cognitive impairment relative to healthy controls, there was no evidence of an additive negative impact of bipolar disorder and cannabis use on cognition. Additionally, momentary assessment analyses indicated alleviation of mood symptoms in the group with bipolar disorder and cannabis use. They experienced a substantial decrease in mood symptoms. Authors concluded that “findings suggest that for some bipolar patients, marijuana may result in partial alleviation of clinical symptoms. Moreover, this improvement is not at the expense of additional cognitive impairment.”

**Source:** <https://www.ncbi.nlm.nih.gov/pubmed/27275781>

## ***Human: Running and singing may increase endo-cannabinoid blood levels***

Circulating levels of endocannabinoids in 9 healthy female volunteers were measured before and immediately after 30 min of dance, reading, singing or cycling in a fasted state. Authors concluded, that “increases in endocannabinoids may underlie the rewarding and pleasurable effects of singing and exercise, and ultimately some of the long-term beneficial effects on mental health, cognition and memory.”

**Source:** [www.frontiersin.org/articles/10.3389/fnbeh.2018.00269/abstract](http://www.frontiersin.org/articles/10.3389/fnbeh.2018.00269/abstract)

## ***Human: Differences between medical and recreational cannabis users with regard to withdrawal***

According to a survey of 2905 cannabis users, relative to recreational users, medical users were less likely to report undesirable acute effects but were more likely to report undesirable withdrawal symptoms. Older (50+) individuals reported fewer undesirable acute effects and withdrawal symptoms compared with younger users (18-29). University of California San Diego, USA.

**Source:** <https://www.ncbi.nlm.nih.gov/pubmed/30383388>

## ***Animal: THC and gabapentin act synergistically against neuropathic pain***

In a study with mice with neuropathic pain, the combination of THC and gabapentin was beneficial in reducing allodynia (pain response to usually non-painful stimuli). **Source:** <https://www.ncbi.nlm.nih.gov/pubmed/30312630>

## ***Science: New journal on cannabis and cannabinoid research***

BioMed Central (BMC) announced the publication of a new journal. “We are delighted to announce that *Journal of Cannabis Research* is now accepting submissions. Published in partnership with the Institute of Cannabis Research, *Journal of Cannabis Research* is an innovative open access journal covering all aspects of research related to cannabis and its constituents.” The new journal is the third in the field of cannabis research, following “*Cannabis and Cannabinoid Research*” and “*Medical Cannabis and Cannabinoids*.”

**Sources:** <http://j cannabisresearch.biomedcentral.com/>  
<https://www.csupueblo.edu/institute-of-cannabis-research/index.html>

## ***Human: Cannabis reduces risk of liver cirrhosis in patients with hepatitis C virus infection***

In a study with 188,333 patients with a positive diagnosis of hepatitis C virus infection, those with cannabis use had a 19% decreased risk of liver cirrhosis compared to non-users. Among those with cannabis use people with cannabis dependence had a 38% decreased risk compared to non-dependent users. Authors wrote that their “findings suggest that cannabis use is associated with decreased incidence of liver cirrhosis, but no change in mortality (...) among HCV patients.”

**Source:** <https://www.ncbi.nlm.nih.gov/pubmed/30345261>

## ***Human: Cannabis may be helpful in the treatment of children with autism in an open study***

Cannabis with a ratio of CBD to THC of 20:1 and 6:1 was beneficial in children with autism spectrum disorder (ASD). Results of this research by doctors of the Neuropediatric Unit of the Shaare Zedek Medical Centre in Jerusalem, Israel, were published in the *Journal of Autism and Developmental Disorders*. Sixty patients aged 5 to 18 years received up to 10 mg/kg bodyweight of CBD and 0.5 mg/kg of THC. In 29 patients with an insufficient response to the extract with the 20:1 ratio higher THC doses were given. Mean total daily dose was 3.8 mg/kg CBD and 0.29 mg/kg THC (13:1 ratio). Following cannabis treatment, behavioural outbreaks were much improved or very much improved in 61% of patients. Authors wrote, that “this preliminary study supports feasibility of CBD-based cannabis trials in children with ASD.” However, the denomination of the extract as “cannabidiol-rich” may be questionable since a daily dose of 0.3 mg/kg THC may be a considerable dose for children, which is underlined by a transient serious psychotic event in one patient. Thus, treatment effects may not be based on CBD but on THC.

**Source:** <https://www.ncbi.nlm.nih.gov/pubmed/30382443>

**More info: [www.cannabis-med.org/](http://www.cannabis-med.org/)**

## Sex, Drugs and Hormones

Cannabis use is riding high on a decade-long wave of decriminalization, legalization and unregulated synthetic substitutes. As society examines the impact, an interesting disparity has become apparent: the risks are different in females than in males.

A new review of animal studies says that sex differences in response to cannabis are not just socio-cultural, but biological too. Published in *Frontiers in Behavioral Neuroscience*, it examines the influence of sex hormones like testosterone, estradiol (estrogen) and progesterone on the endocannabinoid (ECS) system (networks of brain cells which communicate using the same family of chemicals, aka cannabinoids, found in cannabis).

"It has been pretty hard to get laboratory animals to self-administer cannabinoids like human cannabis users," says study co-author Dr Liana Fattore, Senior Researcher at the National Research Council of Italy and President of the Mediterranean Society of Neuroscience. "However, animal studies on the effects of sex hormones and anabolic steroids on cannabinoid self-administration behavior have contributed a lot to our current understanding of sex differences in response to cannabis."

So how does cannabis affect men and women differently? Besides genetic background and hormonal fluctuations, the paper highlights a number of important sex differences.

Men are up to four times more likely to try cannabis - and use higher doses, more frequently.

"Male sex steroids increase risk-taking behavior and suppress the brain's reward system, which could explain why males are more likely to try drugs, including cannabis" explains Fattore. "This is true for both natural male sex steroids like testosterone and synthetic steroids like nandrolone."

But despite lower average cannabis use, women go from first hit to habit faster than men. In fact, men and women differ not only in the prevalence and frequency of cannabis use, pattern and reasons of use, but also in the vulnerability to develop cannabis use disorder.

"Females seem to be more vulnerable, at a neurochemical level, in developing addiction to cannabis," explains Fattore.

"Studies in rats show that the female hormone estradiol affects control of movement, social behavior and filtering of sensory input to the brain - all targets of drug taking - via modulation of the endocannabinoid system, whose feedback in turn influences estradiol production." "Specifically, female rats have different levels of endocannabinoids and more sensitive receptors than males in key brain areas related to these functions, with significant changes along the menstrual cycle. As a result,

the interactions between the endocannabinoid system and the brain level of dopamine - the neurotransmitter of "pleasure" and "reward" - are sex-dependent."

The inconsistency of conditions in these studies greatly complicates interpretation of an already complex role of sex hormones in the endocannabinoid system and cannabinoid sensitivity.

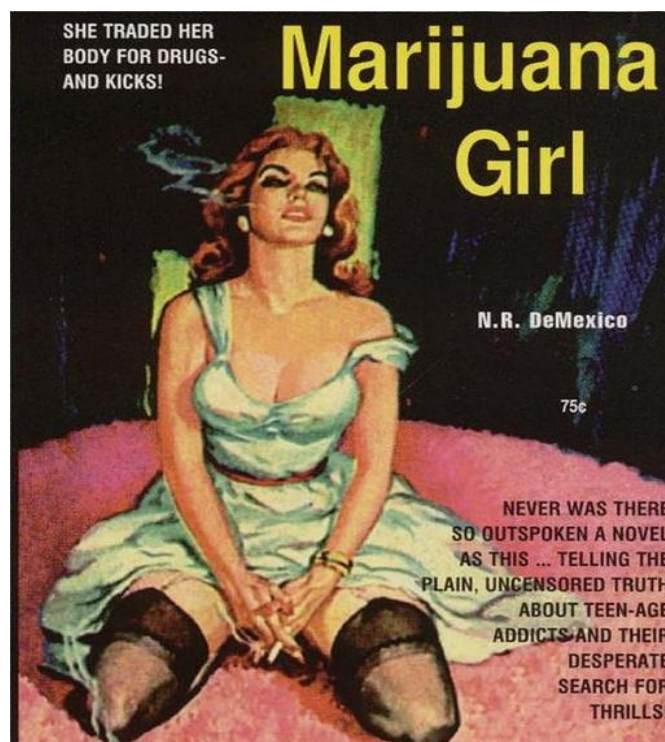
"The effects varied according [to] the specific cannabinoid studied, as well as the strain of animals tested and duration of hormone exposure," admits Fattore. However, the human data so far are consistent with the idea that estradiol regulates the female response to cannabinoids. As in animals, human males and females are diverse in their genetic and hormonally driven behaviour and they process information differently, perceive emotions in different ways and are differently vulnerable to develop drug addiction.

"Blood levels of enzymes which break down cannabinoids fluctuate across the human menstrual cycle, and imaging studies show that brain levels of cannabinoid receptors increase with aging in females - mirroring in each case changes in estradiol levels."

Fattore believes that deepening our understanding of the interactions between cannabinoids and sex steroids is crucial in assessing the impact of increasing cannabis use, and tackling the fallout.

"Gender-tailored detoxification treatments and relapse prevention strategies for patients with cannabis addiction are increasingly requested; optimizing personalized evidence-based prevention and treatment protocols demands further research on the source of sex disparities in cannabis response."

Source: [www.sciencedaily.com/releases/2018/10/181026102627.htm](http://www.sciencedaily.com/releases/2018/10/181026102627.htm)



## **Cannabidiol (CBD) Holds Promise for Smoking Cessation**

Cannabidiol (CBD), a non-intoxicating cannabinoid, may be a promising novel smoking cessation treatment due to its anxiolytic properties, minimal side-effects and research showing it may modify drug cue salience. The research team used an experimental medicine approach with dependent cigarette smokers to investigate if (1) overnight nicotine abstinence, compared with satiety, will produce greater attentional bias (AB), higher pleasantness ratings of cigarette-related stimuli and increased craving and withdrawal; (2) CBD in comparison to placebo, would attenuate AB, pleasantness of cigarette-related stimuli, craving and withdrawal and not produce any side-effects.

The study is a randomized, double-blind crossover study with a fixed satiated session followed by two overnight abstinent sessions. Thirty non-treatment seeking, dependent cigarette smokers were recruited from the community, and given either 800mg oral CBD or a matched placebo (PBO).

When participants received placebo, tobacco abstinence increased AB compared with satiety. However, CBD reversed this effect, such that automatic AB was directed away from cigarette cues and no longer differed from satiety. Compared with placebo, CBD also reduced explicit pleasantness of cigarette images. Craving and withdrawal were unaffected by CBD, but greater in abstinence compared with satiety. Systolic blood pressure decreased under CBD during abstinence.

The study concluded that a single 800mg oral dose of cannabidiol (CBD) reduced the salience and pleasantness of cigarette cues, compared with placebo, after overnight cigarette abstinence in dependent smokers. CBD did not influence tobacco craving or withdrawal or any subjectively rated side-effects.

**Sources:** <https://www.ncbi.nlm.nih.gov/pubmed/29714034>  
<https://onlinelibrary.wiley.com/doi/full/10.1111/add.14243>



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***“Stop thinking and talking about it and there is nothing you will not be able to know.”***

**-- Zen Paradigm**