

**TrePsy**

# **Cannabinoids: What You Need To Know**

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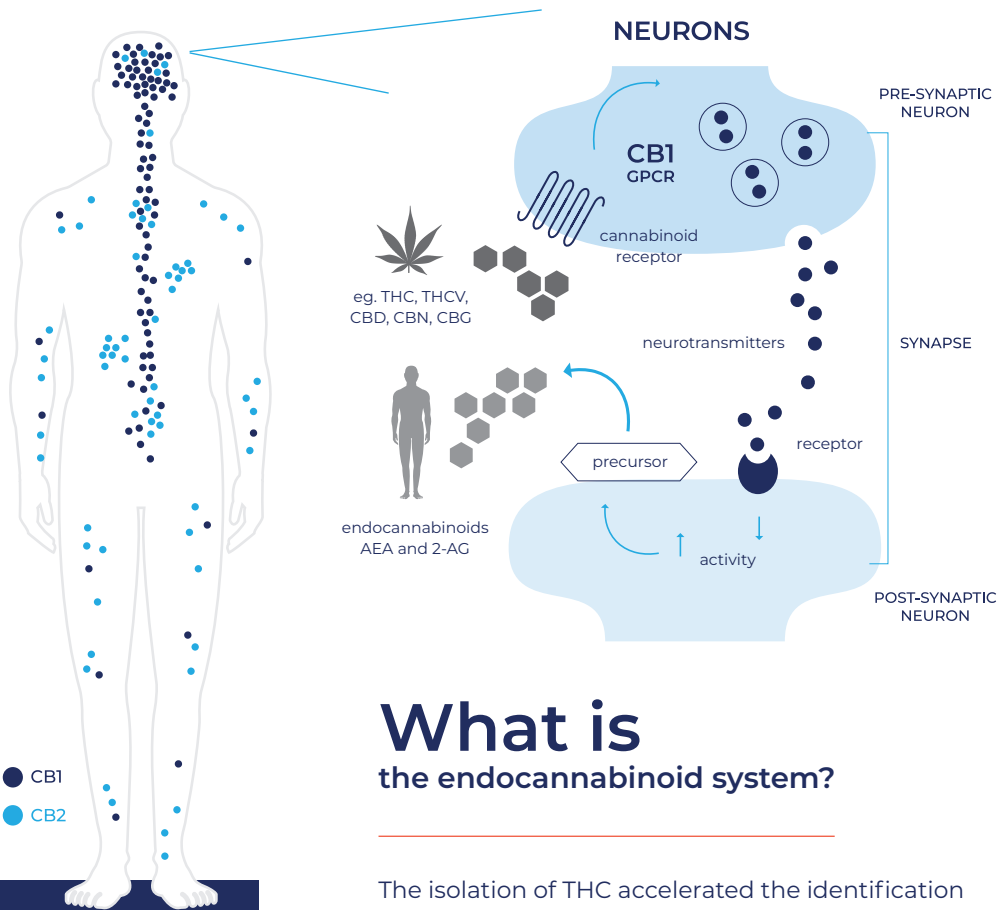
# What are cannabinoids?

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Cannabinoids, more specifically phytocannabinoids, are compounds found in the plant *Cannabis sativa* L.<sup>1</sup> More than 120 phytocannabinoids have been isolated and classified into 11 groups based on their chemical structure; among them, the best-known cannabinoids in *Cannabis sativa* L. are  $\Delta^9$ -trans-tetrahydrocannabinol (THC) and cannabidiol (CBD)<sup>2</sup>.



THC, the first cannabinoid to be identified and studied<sup>3,4</sup>, is the main psychotomimetic component of the plant. Depending on the dose, the pattern of administration and psychiatric vulnerability may cause psychosis-like behaviour and hallucinations. CBD is the second most abundant component in the *Cannabis sativa* L. plant. It was first synthesized by Roger Adams in 1942 and isolated from the plant by Mechoulam and Shvo in 1963<sup>5</sup>. CBD, contrary to THC, does not exhibit the same potential for abuse<sup>6</sup>.



## What is the endocannabinoid system?

The isolation of THC accelerated the identification of the endocannabinoid system, a ubiquitous lipid signalling system found throughout the body. It regulates the crosstalk between different neurotransmitter systems in the brain, mediating the central physiological processes that underlie learning and memory, anxiety, depression, addiction, appetite, pain and general neuronal excitability. The primary components of the endocannabinoid system are the two cannabinoid receptors CB1r and CB2r, endogenous cannabinoids (endocannabinoids) synthesized by various cell types in the body and the enzymes responsible for the synthesis and degradation of endocannabinoids.

# Are cannabinoids dangerous?



Consumption of cannabis produces a broad range of immediate effects, including euphoria, increased heart rate, perceptual alterations and impaired cognitive functions. Repeated use of cannabis has been reported to cause long-term cognitive impairments and increase the risk of developing psychotic outbreaks<sup>7</sup>.



**cannabis sativa L.**



**EUPHORIA**



**INCREASED HEART RATE**



**IMPAIRED COGNITIVE FUNCTIONS**



**PERCEPTUAL ALTERATIONS**



**2.5%** Population consumes cannabis

**24%** Patients entering substance abuse treatment use marijuana

According to the World Health Organization, 2.5% of the world's population consumes cannabis, and 24% of patients entering substance abuse treatment are diagnosed with marijuana use disorder<sup>8</sup>. In addition, a variety of synthetic cannabinoids are present in “designer” drugs of abuse. These compounds are particularly dangerous, as they usually have very poorly studied properties, are often toxic and cause severe adverse health effects.

# What are the medical uses of cannabinoids?



In recent years, there has been a growing interest in medical use of the *Cannabis sativa L.* plant due to its wide range of pharmacological properties. However, plant extracts have complex compositions, and their use is frequently associated with adverse effects. The complexity of these compounds and the diversity among diseases complicate the determination of the appropriate dosage to obtain the best benefit-risk ratio.

Studies in animal models have shown that purified or synthetic CBD displays anxiolytic, antidepressant, antipsychotic, antiepileptic, and neuroprotective properties, suggesting its potential therapeutic use in several psychiatric, neurological, and drug-use disorders.

The European Medicines Agency (EMA) has authorized the use of a CBD-based drug as part of the treatment for seizures associated with Lennox-Gastaut syndrome, Dravet syndrome and tuberous sclerosis complex in patients aged two years and older. Independent of clinical use, CBD has become a widely used food supplement and is frequently found in cosmetic formulations; however, its potential benefits remain uncertain.



**Purified or synthetic CBD**



**ANXIOLYTIC AND ANTIDEPRESSANT EFFECT**



**ANTIPSYCHOTIC EFFECT**



**ANTIEPILEPTIC EFFECT**



**NEUROPROTECTIVE EFFECT**

# Why research cannabinoids?

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Thus far, only a few rigorous clinical studies using cannabinoids in disease treatment have been completed, and the debate on the risks vs. benefits of their medical use continues. The great diversity of compounds found in the *Cannabis sativa* L. plant makes it difficult to assign the observed efficacy or adverse effect to a specific compound.

Therefore, if we want to advance the pharmacological use of cannabinoids in clinical practice, we must increase our knowledge of their pharmacological properties and therapeutic benefits. This will allow us to conduct clinical trials to test the efficacy and safety of active ingredients isolated from *Cannabis sativa* L., as has been done with a wide variety of drugs whose active ingredients were first derived from plants or trees, such as acetylsalicylic acid.



In parallel, a major effort is being aimed at developing synthetic cannabinoids that can be used for the treatment of chronic inflammation, pain or neuropsychiatric disorders without the potential for abuse or severe adverse effects. A major obstacle is the incomplete knowledge of the mechanisms of endogenous cannabinoid function, which limits the ability to design novel compounds and predict their properties.

Therefore, the goal of research into cannabinoids is to rigorously determine their clinical effectiveness and to carefully study the risks of abuse and their long-term effects on mental health.

## References:

1. Andre, C. M., Hausman, J.-F. & Guerriero, G. Cannabis sativa: The Plant of the Thousand and One Molecules. *Frontiers in Plant Science* 7, (2016).
2. Morales, P., Hurst, D. P. & Reggio, P. H. Molecular Targets of the Phytocannabinoids: A Complex Picture. *Prog Chem Org Nat Prod* 103, 103–131 (2017).
3. Gaoni, Y. & Mechoulam, R. Isolation, Structure, and Partial Synthesis of an Active Constituent of Hashish. *J. Am. Chem. Soc.* 86, 1646–1647 (1964).
4. Pertwee, R. G. Cannabinoid pharmacology: the first 66 years. *Br J Pharmacol* 147, S163–S171 (2006).
5. Mechoulam, R. & Shvo, Y. Hashish. I. The structure of cannabidiol. *Tetrahedron* 19, 2073–2078 (1963).
6. Viudez-Martínez, A. et al. Cannabidiol does not display drug abuse potential in mice behavior. *Acta Pharmacol Sin* 40, 358–364 (2019).
7. Di Forti, M. et al. The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study. *Lancet Psychiatry* 6, 427–436 (2019).
8. World Health Organization. The health and social effects of nonmedical cannabis use. (World Health Organization, 2016).

## Partners of the project



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