MS INFO CHANNEL

Knowledge & evidence

Cannabis, Terpenes and the Entourage Effect in MS

The in-depth guide, based on the evidence



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Orientation

Important notes first

Not a substitute for medical advice

This booklet reports the published evidence. It makes no diagnosis and recommends no product or dose. Whether cannabis is an option for you is a decision for you and your neurologist. Never stop or change prescribed medicines on your own.

What this is about. Cannabis is one of the most debated topics in MS. Online, miracle claims sit next to blanket bans, and terms like *terpenes* and *entourage effect* are used heavily in marketing. This booklet sorts things out: what is proven, what is a plausible hypothesis, what is plain advertising? It is written for people with MS, their relatives and anyone interested in the evidence.

Our yardstick. We name studies with authors and year and say how strong the evidence is. Findings from cell culture and animal studies are labelled as such. Where no MS study exists, we say so. Cannabis is a word without taboo here, but also without romance.

How to use this booklet

- **Quick start:** read the summary on the next page, then the chapters that interest you most.
- **In depth:** chapters 1 to 4 build on each other (basics, studies in MS, terpenes, entourage effect).
- **For your appointment:** chapters 5 to 7 cover practice, risks and legal matters, chapters 8 and 9 help you judge studies and myths, chapter 10 offers templates to fill in and print.
- **Look things up:** the glossary explains technical terms, the reference list gives every study by number.

The summary in ten sentences

1. Cannabis contains over a hundred cannabinoids; for MS mainly THC and CBD have been studied.
2. Our body has its own endocannabinoid system, which these plant compounds dock onto.
3. The best evidence is for spasticity: cannabinoids probably improve it, especially as people experience it themselves [1].
4. For nerve pain, bladder, sleep and tremor the evidence is thin or inconsistent.
5. There is no evidence that cannabis slows the course of MS [4].
6. Side effects such as tiredness, dizziness and poor concentration are common; serious events are rare in the trials [1].
7. Terpenes are the plant’s scent compounds. Some have interesting properties in the lab or in animals, including MS models [12].
8. The entourage effect says the plant’s ingredients act differently together than THC alone. It is a plausible but unproven hypothesis [7, 9].

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BASICS

Chapter 1: Cannabis and the endocannabinoid system

The plant and its compounds

The hemp plant *Cannabis sativa* forms a sticky resin in the glandular hairs of its flowers. It holds three large groups of compounds: **cannabinoids** (over a hundred described), **terpenes** (scent and aroma compounds) and **flavonoids** (pigments and protective compounds). The effects on humans are mainly due to the cannabinoids. In the fresh plant they occur mostly as acids (THCA, CBDA). Only heat, for example when drying, vaporising or baking, turns them into the active forms THC and CBD.

Compound	Short profile	Research in MS
THC (delta-9-tetrahydro cannabinol)	Partial agonist at CB1 and CB2; responsible for the high, but also for muscle-relaxing and pain-dampening effects.	Best studied for spasticity and pain (dronabinol, extracts, nabiximols).
CBD (cannabidiol)	No high; binds only weakly to CB1/CB2, affects many other targets and may soften THC effects [15].	As a single compound hardly any convincing MS trials; studied as part of nabiximols.
CBN (cannabinol)	Forms when THC degrades; weakly active, often advertised as “sleepy”.	No MS trials.
CBG (cannabigerol)	Precursor of the other cannabinoids; studied in lab and animals.	No MS trials in humans.
CBC, THCV	Further minor cannabinoids with their own targets.	No MS trials in humans.

The endocannabinoid system (ECS)

Cannabis works at all because your body has its own system for similar compounds. Mechoulam and Gaoni isolated THC in 1964 [25]; from 1988 the matching receptors were found, and in 1992 anandamide, the first of the body’s own counterparts [26]. The ECS has three parts:

- **Receptors:** CB1 sits mainly on nerve cells in brain and spinal cord (movement, pain, memory, mood). CB2 is found mainly on immune cells and microglia.
- **The body’s own messengers:** anandamide and 2-AG. They are made on demand and quickly broken down.
- **Enzymes:** FAAH and MAGL break the messengers down; other enzymes make them.

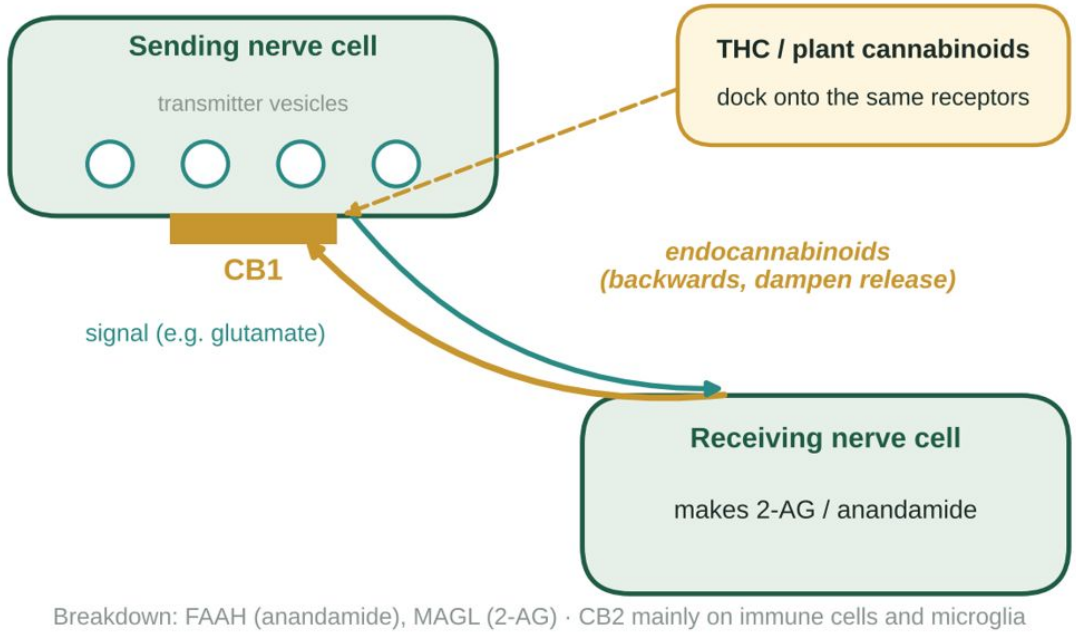


Figure 1: The endocannabinoid system: the body's own cannabinoids act "backwards" and dampen the release of transmitters. THC and other plant compounds use the same receptors.

Why is this interesting for MS?

In MS, inflammation and myelin loss throw signal transmission out of rhythm. Spasticity, pain, bladder irritation and sleep problems are linked to overactive nerve circuits. The ECS dampens such overexcitation. In animal models of MS (EAE), spasticity and tremor get worse when the ECS is blocked and better when it is activated. CB2 also sits on immune cells, which raises the hope that cannabinoids could dampen inflammation. In humans, such an effect on the disease course is **not** proven (chapter 2).

> **Remember**
> THC is a partial agonist at CB1 and CB2, CBD binds only weakly and acts more indirectly [15, 31]. That is why preparations with both compounds can act differently from pure THC.