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# Medical Cannabis in the Treatment of Multiple Sclerosis: A Review of Current Evidence

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## ABSTRACT

Multiple sclerosis (MS) is a long-term autoimmune disease where the immune system attacks the protective covering of nerves. This causes inflammation and damage, leading to symptoms like muscle stiffness, pain, and trouble with balance. Standard medications such as baclofen or tizanidine can help, but they don't always work for everyone and often come with unwanted side effects. Medical cannabis has been gaining attention as an alternative way to manage MS symptoms, especially spasticity. The body's endocannabinoid system plays a big role in multiple sclerosis, helping to protect nerves, calm inflammation, and keep the immune system in check. One of the most common cannabis-based treatments is nabiximols, a mouth spray that contains a balanced mix of THC ( $\Delta$ -9-tetrahydrocannabinol) and CBD (cannabidiol). Research shows it can help reduce how stiff or painful muscles feel, particularly for people who haven't had much success with regular treatments. It may also improve sleep, though the improvements measured in clinical tests are sometimes modest. Cannabis-based treatments are generally well tolerated. The most common side effects, like dizziness or tiredness, are usually mild. Still, it's important to watch for potential interactions with other medications and to be cautious if someone has heart or mental health issues. Overall, cannabinoids offer a useful option for people with MS who are struggling with symptoms that don't respond to conventional treatments.

**Keywords:** Medical Cannabis, Multiple Sclerosis (MS), Spasticity, Cannabinoids, and Nabiximols

## 1. INTRODUCTION

Multiple sclerosis (MS) is a long-term disease in which the immune system attacks the protective layer around nerves. Because of this damage, messages between the brain and the rest of the body do not work properly (Haki et al., 2024). People with MS can experience many different symptoms. Muscles may become stiff, movement can be painful, balance may be poor, and sensations such as touch or temperature can change. These problems may appear from time to time or slowly get worse over the years. One of the most difficult symptoms is spasticity, which makes moving harder, affects everyday activities, and often becomes more difficult to control with time. Some medications, such as baclofen or tizanidine, help certain patients, but

they are not effective for everyone. In addition, many people stop using them because of side effects (Sacco et al., 2024). For this reason, medical cannabis has gained more attention as another option. Cannabis contains many active substances, but the most studied ones are THC and CBD (Bridgeman & Abazia, 2017).

THC acts on the body's endocannabinoid system and may help reduce pain, muscle stiffness, and inflammation. Medical cannabis is different from recreational use because the doses are controlled, the composition is standardized, and the aim is symptom relief rather than intoxication. One of the most commonly used cannabis-based treatments for MS is nabiximols. It is a mouth spray that contains THC and CBD in a fixed ratio. Research studies and real-life clinical experience show that it can reduce spasticity and related symptoms, such as pain or bladder problems, even in patients who do not respond well to standard treatments (Sacco et al., 2024). Because many traditional therapies are not fully effective, cannabinoids are increasingly seen as a useful add-on or alternative option. This paper reviews current evidence on the use of cannabinoids in MS. It focuses on their safety and their effectiveness in managing spasticity. By looking at recent studies, it aims to assess whether these treatments can help fill the gap left by standard medications.

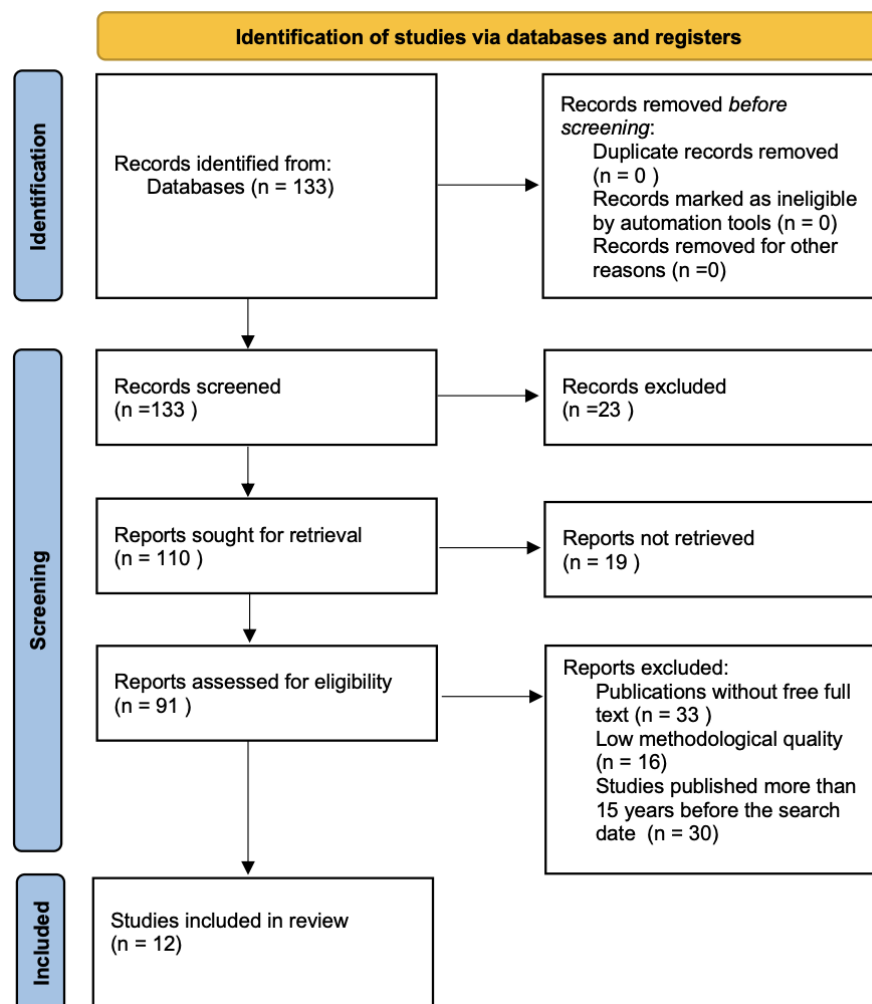


Figure 1: PRISMA chart

## 2. REVIEW METHODS

**Search Strategy:** A systematic literature search was performed in electronic databases. The search strategy utilized keywords: "Medical Cannabis", "Multiple Sclerosis" (MS), "Spasticity", "Cannabinoids", and "Nabiximols".

**Inclusion & Exclusion:** We included full-text publications in English published within the last 15 years. The review focused on systematic reviews, meta-analyses, and clinical studies concerning the efficacy, safety, mechanisms of action, and injection protocols of cannabinoids in multiple sclerosis. Publications without free full-text access, studies characterized by low methodological quality, and articles published more than 15 years before the search date were excluded.

*Study Selection:* The authors conducted the selection and data extraction process. In cases of disagreement, a consensus was reached. The final selection process resulted in 12 studies included in the review, as illustrated in the PRISMA diagram (Figure 1).

### 3. RESULTS & DISCUSSION

#### *The role of the endocannabinoid system and the mechanisms of action of cannabinoids in the pathophysiology and treatment of multiple sclerosis*

The endocannabinoid system, or ECS, is a network in the body made up of CB1 and CB2 receptors, natural endocannabinoids, and the enzymes that regulate them (Lu & Mackie, 2021). In multiple sclerosis, the ECS plays an important role in protecting nerve cells and controlling inflammation (Nouh et al., 2023). When the disease is active, the body appears to activate this system. Researchers have found higher levels of a substance called anandamide (AEA) and a greater number of receptors in patients, which suggests that the body is trying to protect and repair itself in a natural way (Pagano et al., 2022).

#### *Modulation of synaptic transmission and neuroprotective*

The main idea behind this system is that it helps “quiet down” nerve cells to protect them. When this pathway is active, it blocks calcium channels and reduces the release of chemicals called neurotransmitters, which keeps cells from getting overloaded and damaged (Lu & Mackie, 2021). This is really important in multiple sclerosis because both CB1 receptors and certain enzyme blockers, like MAGL inhibitors, can help prevent nerve cell damage and slow down the loss of myelin, the protective coating around nerves (Nouh et al., 2023; Pagano et al., 2022).

#### *Anti-inflammatory and immunomodulatory action*

Cannabinoids can strongly affect the immune system through CB2 receptors. These receptors are found on many immune cells, such as microglia and T cells. Studies using EAE models show that cannabinoids, especially THC, can slow down T cells and stop them from moving into the central nervous system. As a result, inflammation in the white matter is reduced. CBD also helps reduce inflammation. It changes the way the immune system sends signals by lowering substances that increase inflammation and boosting those that calm it. By limiting the entry of immune cells into the brain, they reduce the risk of new inflammatory areas forming (Nouh et al., 2023).

#### *Alleviating the symptoms of multiple sclerosis*

For people with multiple sclerosis (MS) who don't get much help from usual treatments, cannabinoids are often used to help with symptoms. Still, they don't work the same for everyone, and results depend on the symptom and how it is measured. One big problem in MS is spasticity, which makes muscles stiff, movement hard, and can cause pain. How well cannabinoids work for spasticity depends on how it's measured (Filippini et al., 2022). When patients report their own symptoms using simple rating scales, there is good evidence that nabiximols (Sativex) work better than a placebo. In fact, out of 1,000 people treated, about 216 more feel relief compared to those who don't get it (Filippini et al., 2022). This is supported by studies focused on people whose spasticity doesn't respond to regular treatments (Solmi et al., 2023; Nouh et al., 2023). But when researchers measure muscle stiffness with the Ashworth scale, improvements are very small (Filippini et al., 2022; Solmi et al., 2023). Many say this scale doesn't capture what patients actually feel (Filippini et al., 2022). There isn't a lot of data on complete pain relief, but research suggests that cannabinoids, including synthetic THC and nabiximols, work better than placebos to reduce overall symptoms. For bladder problems, nabiximols didn't reduce the total number of accidents, but patients still felt better overall and had fewer trips to the bathroom at night (Filippini et al., 2022). Sleep is often a problem in MS, and here the results are more promising: cannabinoids, especially nabiximols, seem to improve sleep quality better than placebos (Filippini et al., 2022; Solmi et al., 2023).

#### *Forms of cannabinoid preparations and their safety profile in multiple sclerosis therapy*

Contemporary pharmacotherapy for multiple sclerosis (MS) increasingly includes cannabinoid-based drugs, which come in various forms, from plant extracts to synthetic analogues. The most widely used and best-studied preparation registered for the treatment of spasticity in MS is nabiximols (Sativex). This form avoids the first-pass effect in the liver, which is important compared to oral forms of cannabinoids, which are characterized by variable bioavailability (Legare et al., 2022). Patients usually titrate the dose of nabiximols themselves, starting with one spray and increasing it to a maximum of 12 doses per day over two weeks (Salehi et al., 2022). Studies indicate that nabiximol is likely to reduce the severity of spasticity as assessed by patients in the short term (up to 14 weeks) (Filippini

et al., 2022). In addition to plant extracts, synthetic preparations are also available for medical use. Legare et al., (2022) and Salehi et al., (2022) list agents such as dronabinol and nabilone. Dronabinol (e.g., Marinol, Syndros) consists of synthetic THC provided in oral solutions or capsules, whereas nabilone (e.g., Cesamet) is classified as a synthetic THC analog. Pharmaceutical raw material in the form of dried inflorescences (e.g., products from Bedrocan) is also available on the market (e.g., in the Netherlands), which has a standardized THC and CBD content and a full terpene profile (Salehi et al., 2022). Conversely, the inhalation of combusted dried material lacks dosing accuracy and introduces the hazard of respiratory health problems (Legare et al., 2022). Hoch et al., (2025) consider the safety of cannabis-based medicines to be generally good. Most patients tolerate these preparations well. Still, side effects occur. They are usually mild to moderate. The most common reports involve dry mouth, fatigue, nausea, dizziness, drowsiness, or imbalance (Filippini et al., 2022; Legare et al., 2022). Because of this, the dropout rate is slightly higher than with a placebo (Filippini et al., 2022). Serious effects are much rarer. These can include palpitations or blood pressure changes. Chronic use of products with high THC content may lead to the development of tolerance and cannabis use disorder (CUD), although this risk is considered low in the case of medical use of nabiximols (Salehi et al., 2022; Hoch et al., 2025). An important clinical aspect is the interaction of cannabinoids with other drugs, which results from their hepatic metabolism. Cytochrome P450 enzymes, mainly CYP3A4 and CYP2C9, are responsible for the metabolism of THC and CBD in the body (Stella, 2023; Salehi et al., 2022). A significant problem is the fact that CBD strongly blocks (is an inhibitor of) the action of CYP3A4, which creates a risk of interaction with other drugs. For example, Stella (2023) points out that drugs like clobazam may accumulate due to this pathway blockage, resulting in stronger clinical effects. In addition, the simultaneous use of THC and/or CBD with serotonin reuptake inhibitors (SSRIs) may increase the concentration of antidepressants in the blood, which in adolescents has been associated with coughing, diarrhea, dizziness, and fatigue (Hoch et al., 2025). Due to these interactions, the introduction of cannabinoid therapy in MS patients taking other medications requires monitoring for potential changes in the pharmacokinetics of the pharmaceuticals used. Key studies are discussed and summarized in Table 1.

**Table 1.** Efficacy and safety of cannabinoids for symptomatic management of multiple sclerosis: evidence from meta-analyses and systematic reviews

Author (year)	Study type	Intervention	Symptom assessed	Main findings	Clinical implications
Filippini et al., 2022	Meta-analysis (Cochrane Review)	Nabiximols, THC, synthetic cannabinoids	Spasticity	Significant improvement in patient-reported spasticity; no clinically meaningful improvement on the Ashworth scale	Cannabinoids are effective mainly for subjective relief of spasticity; limited impact on objective measures
Filippini et al., 2022	Meta-analysis	Nabiximols, THC	Pain	Small but statistically significant reduction in pain compared with placebo	Potential role in the management of treatment-resistant pain
Filippini et al., 2022	Meta-analysis	Nabiximols	Sleep disturbances	Significant improvement in sleep quality compared with placebo	Beneficial effect in patients with MS-related sleep disorders
Solmi et al., 2023	Umbrella review of meta-analyses	Various cannabinoid preparations	Spasticity, sleep	Moderate efficacy confirmed for spasticity and sleep quality; outcomes dependent on assessment methods	Clinical benefits may outweigh risks in carefully selected patients
Nouh et al., 2023	Systematic review	THC, CBD, nabiximols	Spasticity, inflammation, neuroprotection	Reduction of inflammatory activity and improvement of spasticity in clinical studies and EAE models	Cannabinoids may serve as adjunctive therapy in patients refractory to standard treatment

Hoch et al., 2025	Systematic review	Cannabinoids (various forms)	Safety profile	Adverse events mostly mild to moderate (dizziness, somnolence, dry mouth)	Overall favorable safety profile; caution advised in patients with psychiatric or cardiovascular comorbidities
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#### 4. CONCLUSION

The current approach to the symptomatic treatment of multiple sclerosis includes the use of cannabinoids in various pharmaceutical forms, the leading one being nabiximols – a standardized extract of *Cannabis sativa* administered as an aerosol to the oral mucosa. In addition to plant extracts, synthetic THC analogues such as dronabinol and nabilone, as well as standardized plant material, are also used in therapy, although each of these forms has different pharmacokinetics and risk profiles. Although the safety profile is generally good and adverse effects (mainly involving the central nervous system and stomach) are mild, the therapy is associated with certain risks. The main clinical concerns are metabolic interactions (P450 enzymes) and risks for patients with cardiac or psychiatric conditions.

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#### Authors' Contributions

Conceptualization: Agnieszka Kowalska, Michał Wójcicki.

Methodology: Milena Kędzierska, Michał Biernacki.

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Visualization: Agnieszka Kowalska, Milena Kędzierska.

All authors have read and agreed with the published version of the manuscript.

#### Informed consent

Not applicable.

#### Ethical approval

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#### Conflict of interest

The authors declare that they have no conflicts of interest, competing financial interests or personal relationships that could have influenced the work reported in this paper.

#### Data and materials availability

All data associated with this study will be available based on reasonable request to the corresponding author.

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