



# Effects of Cannabis-Based Medications on Cognitive Functions in Multiple Sclerosis: An Updated Systematic Review and Meta-analysis of Clinical Trials

Sina Pakkhesal<sup>1</sup>, Amirreza Naseri<sup>1</sup>, Amir Mohammad Sharafi<sup>1</sup>, Rasa Beheshti<sup>1</sup>, Saman Baharomid<sup>1</sup>, Zahra Koochaki<sup>1</sup>, Fatemeh Amiri<sup>1</sup>, Mahnaz Talebi<sup>2</sup>, Sarvin Sanaei<sup>2\*</sup>

<sup>1</sup>Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>2</sup>Neurosciences Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

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### \*Corresponding Author:

Neurosciences Research  
Center, Tabriz University of  
Medical Sciences, Tabriz, Iran

## ABSTRACT

**Introduction:** Cognitive impairment, as a common symptom of multiple sclerosis (MS), significantly impacts the quality of life of MS patients. In this context, cannabis-based medications (CBMs) have been investigated as a therapeutic option for managing various symptoms of MS, including cognitive dysfunction. Previous systematic reviews provided limited conclusions regarding cognitive outcomes. The present study aimed to provide an updated systematic review and meta-analysis of the existing clinical evidence on the effects of CBMs on cognitive functions in individuals with MS.

**Methods and Materials:** A comprehensive literature search was conducted in May 2024 in major electronic databases, including Web of Science, Embase, Scopus, PubMed, and clinicaltrials.gov, with no time limit. A search strategy based on the terms of randomized-controlled trials (RCTs) evaluating the impact of CBMs on cognitive outcomes/adverse effects in MS patients was considered. Risk-of-bias was assessed using the Cochrane RoB2 tool. Meta-analysis was conducted using Comprehensive Meta-Analysis v3, and a fixed-effects model was used to estimate the pooled effect size. The whole process was according to PRISMA.

**Results:** From 1,274 primary results, 10 RCTs were included in the qualitative review, and 13 RCTs were included in test-based (331 patients) and event-based (1,232 patients) analyses. The event-based meta-analysis of the attention disturbances showed a significant decline among MS patients receiving CBMs compared to the placebo group (odds-ratio = 2.853, CI 95%: [1.41, 5.77],  $p = 0.004$ ,  $I^2 = 0.00$ ). The test-based meta-analysis of the Paced Auditory Serial-Addition Test (PASAT) showed a significant difference between CBM and placebo (standardized-mean-difference = 0.387, CI95%: [0.17, 0.61],  $p = 0.001$ ,  $I^2=38.87$ ), favoring placebo. Five studies reported no significant effects on processing speed, executive function, and measures of attention and concentration. In contrast, one study observed reduced complex attention and processing speed after acute cannabis administration. Regarding psychomotor skills, three studies indicated impairment. At the same time, the results for multiple domain screenings were mixed, with one study showing a reduction in Short-Orientation-Memory-Concentration Test (SOMC) with THC and another finding no differences between groups.

**Conclusion and Discussion:** This study suggests that CBM may have adverse effects on attention and processing speed in MS patients; however, overall cognitive impacts of CBM appear complex and dependent on factors such as dosage, duration of exposure, and specific cognitive domains assessed.

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