Interference Journal
ISSN 2009-3578
DOI
A2 QUALIS SUCUPIRA 2017-2020

ENDOCANNABINOID SYSTEM AND NEUROCARDIOLOGY: IMPACTS ON AUTONOMIC REGULATION AND CARDIOVASCULAR OUTCOMES IN PATIENTS WITH NEUROLOGICAL DISORDERS

Arthur Junqueira Ferreira Santos, Loren Ferrarezi, Rodolfo de Oliveira Medeiros, Guilherme de Lúcio Consalter, Camila Menon Oliveros, Sofia Leoncini de Almeida, Sophia Evaristo Coércio, Renato Augusto Paro Lima, Gabriel Baraldi Labegalini, João Victor Cardoso Casarin

https://doi.org/10.36557/2009-3578.2025v11n2p3664-3678
Artigo recebido em 25 de Julho e publicado em 25 de Setembro de 2025

REVISÃO INTEGRATIVA DA LITERATURA

ABSTRACT

This study aimed to examine the influence of the endocannabinoid system (ECS) on autonomic regulation and cardiovascular outcomes in patients with neurological disorders. An Integrative Literature Review (ILR) was conducted across SciELO, LILACS, PubMed, and ScienceDirect databases, covering the period from 2018 to 2025, and including original articles published in Portuguese and English. The synthesis of findings highlighted the distinct roles of CB_1 and CB_2 receptors, whose effects ranged from protective actions to potential risks for autonomic and cardiovascular stability. The CB_2 receptor demonstrated a relevant role in reducing vascular inflammation and protecting against ischemic events, whereas CB_1 was associated both with nitric oxide–mediated hypotensive effects and with episodes of tachycardia and autonomic instability. In the field of neurocardiology, the reviewed studies suggest that the ECS modulates norepinephrine release from sympathetic fibers, directly influencing hemodynamic control. Recent clinical trials reported that cannabidiol (CBD) may lower blood pressure and improve autonomic variability parameters, particularly in hypertensive patients or under stress conditions. However, these findings remain limited by small sample sizes, methodological heterogeneity, and the scarcity of large-scale randomized clinical trials. It is concluded that the ECS represents a promising biological axis for understanding the interface between neurological diseases, autonomic dysfunction, and cardiovascular risk. Nonetheless, further targeted investigations are required to confirm the efficacy and safety of cannabinoid use in specific clinical contexts. The integration of neuroscience, cardiology, and pharmacology may pave the way for innovative therapeutic approaches aimed at preventing cardiovascular complications in neurological patients.

Keywords: Endocannabinoid system; Autonomic regulation; Neurological disorders.

Instituição afiliada – Universidade de Marília (UNIMAR)

Autor correspondente*: Rodolfo de Oliveira Medeiros e-mail: rodolfomedeiros@unimar.br*

1- INTRODUCTION

The endocannabinoid system (ECS) is a signaling network that comprises endogenous molecules such as anandamide (AEA) and 2-AG, as well as CB_1 and CB_2 receptors and the enzymes involved in their synthesis and degradation. Recent studies highlight its broad distribution across the nervous, respiratory, and cardiovascular systems, with regulatory implications for various physiological processes (Krzyżewska et al., 2025). The expanded concept of the "endocannabinoidome" underscores the scope and complexity of this system, moving beyond the classical view limited to receptor activity (Fonseca et al., 2025).

In the cardiovascular context, evidence suggests that the ECS is often modulated in pathological states, with CB_2 receptors playing a protective role, particularly in atherosclerosis and ischemic events, while CB_1 receptors appear to exert more ambiguous effects (Fulmer; Thewke, 2018). Moreover, in adverse conditions such as shock or hypertension, the ECS displays hypotensive effects via CB_1 activation and vasorelaxant actions mediated through multiple mechanisms, including nitric oxide and ion channel modulation (O'Sullivan, 2015).

Within neurocardiology, autonomic modulation through endocannabinoid receptor activation presents biphasic features: at lower doses, anti-inflammatory and sedative effects; at higher doses, an increased risk of tachycardia, hypertension, and autonomic instability, a critical concern for individuals predisposed to arrhythmias (Šoša, 2025). Furthermore, the ECS influences autonomic neurotransmission by reducing norepinephrine release from sympathetic fibers, a modulation that may alter cardiovascular regulation (Matei et al., 2023).

Given this scenario, a systematic synthesis is essential, particularly in populations with neurological disorders such as epilepsy, multiple sclerosis, Parkinson's disease, or traumatic brain injury, where dysautonomia and cardiovascular risks are often interconnected with ECS imbalances. Therefore, the aim of this study is to examine the influence of the endocannabinoid system on autonomic regulation and cardiovascular outcomes in patients with neurological disorders, seeking to identify knowledge gaps and potential clinical implications.

2- METHOD

This study consists of an Integrative Literature Review (ILR) aimed at identifying scientific evidence regarding the influence of the endocannabinoid system on autonomic regulation and cardiovascular outcomes in patients with neurological disorders. The ILR is a systematic and comprehensive research method, grounded in the principles of Evidence-Based Practice (EBP), which enables the inclusion of studies with different methodological designs. This approach allows for a critical synthesis of available knowledge and the identification of gaps for future research (Souza; Silva, Carvalho, 2010; Ganong, 1987).

This method encompasses empirical research with diverse methodologies, while respecting their specificities, and requires that the analysis and synthesis of data be conducted systematically to ensure reliability and consistency in interpreting the results. The development of this review followed the stages proposed by Ganong (1987) and updated by Lockwood et al. (2020): (1) formulation of the research question; (2) definition of inclusion and exclusion criteria, followed by a systematic search of databases; (3) extraction of relevant information from the selected studies; (4) critical analysis and categorization according to levels of scientific evidence; (5) discussion of the findings in light of the relevant literature; and (6) presentation of the final synthesis.

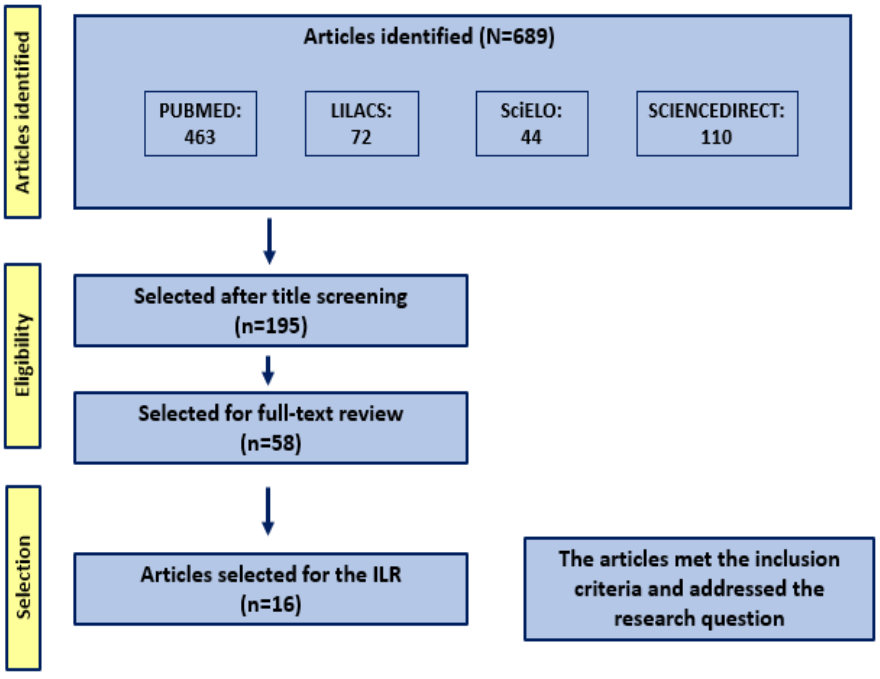
The guiding research question was structured using the PICo strategy, where P corresponds to the population (patients with neurological disorders), I to the phenomenon of interest (endocannabinoid system and autonomic cardiovascular regulation), and Co to the context (cardiovascular clinical outcomes) (Stern; Jordan, McArthur, 2014). Accordingly, the following question was established: What is the influence of the endocannabinoid system on autonomic regulation and cardiovascular outcomes in patients with neurological disorders?

The search was conducted in the Scientific Electronic Library Online (SciELO), Latin American and Caribbean Health Sciences Literature (LILACS), PubMed, and ScienceDirect databases, considering publications from 2018 to 2025, in both Portuguese and English. The descriptors used were: Endocannabinoid System, Autonomic Nervous System, Cardiovascular Diseases, and Neurological Disorders, combined with the Boolean operator AND. Original, full-text articles addressing the

relationship between the endocannabinoid system, autonomic regulation, and cardiovascular outcomes in neurological patients were included. Books, dissertations, theses, narrative reviews, and studies not aligned with the research question were excluded.

After applying the exclusion criteria and carefully reviewing the abstracts, eligible studies were read in full and comprised the final sample. The study selection process followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009), as outlined in the methodological flowchart below.

Figure 1. PRISMA flow diagram of the study selection process for the Integrative Literature Review



Adapted from: Moher et al., 2009

For data analysis and synthesis, a chart was developed to compile essential information from each selected study, including article title, lead author, journal, year of publication, country of origin, method, level of evidence, and objective. The classification of levels of evidence followed the criteria established by the Joanna Briggs

Institute (JBI) (Lockwood et al., 2020), organized hierarchically as follows: Level I (systematic reviews or meta-analyses of randomized controlled trials); Level II (experimental studies); Level III (quasi-experimental studies); Level IV (descriptive or observational studies, either qualitative or quantitative); Level V (case reports or experiential studies); and Level VI (expert opinions).

The results were organized descriptively to provide a comprehensive overview of the relationships among the endocannabinoid system, autonomic regulation, and cardiovascular outcomes in patients with neurological disorders, enabling a critical discussion and articulation with the clinical implications identified in the literature.

3- RESULTS

Based on the application of predefined inclusion and exclusion criteria, 16 articles composed the final sample of this review. The analyzed studies demonstrated, from different perspectives, the relationship between modulation of the endocannabinoid system (ECS), autonomic regulation, and cardiovascular outcomes in patients with neurological disorders. Publications were identified across diverse clinical and methodological contexts, ranging from preclinical research in animal models to human clinical trials and observational studies. This body of evidence enables the construction of a broader and more critical understanding of the ECS effects on the interplay between neurocardiology and autonomic dysfunction, while also highlighting important gaps in its clinical applicability.

Overall, the findings suggest that CB_1 receptor activation is associated with hypotensive effects mediated by vasodilation and nitric oxide, but may also trigger tachycardia and autonomic instability in certain contexts (Dragun et al., 2023; Šoša, 2025). Conversely, CB_2 receptors demonstrated a protective role against inflammatory and ischemic processes, particularly in conditions such as atherosclerosis or arrhythmias in neurological patients (Fulmer; Thewke, 2018; Batinic et al., 2023). In addition, recent evidence indicates that the ECS may modulate sympathetic neurotransmission by reducing norepinephrine release, with direct impact on cardiovascular control (Matei et al., 2023; Krzyżewska et al., 2025).

Despite these promising results, the critical analysis revealed important limitations. These include methodological heterogeneity, the limited number of randomized clinical trials, and the predominance of preclinical investigations - factors that hinder the consolidation of broader clinical recommendations (Fonseca et al., 2025; Dragun et al., 2023). These gaps underscore the need for further studies involving neurological patients at high cardiovascular risk in order to more consistently elucidate the influence of the ECS in this complex scenario.

To organize the findings, a summary table was developed, compiling the main characteristics of the included studies. This synthesis encompassed information regarding article title, lead author, journal and year of publication, study design, level of evidence, and key results.

Table 1. Synthesis of the studies included in the Discussion stage of the Integrative Review

Title	Lead Author	Journal / Year	Study Design / Level of Evidence	Main Findings
A meta-narrative review of channelopathies and cannabis: mechanistic, epidemiologic, and forensic insights into arrhythmia and sudden cardiac death	Šoša, I.	Int. J. Mol. Sci., 2025	Narrative review – Level VI	Cannabis may precipitate arrhythmias through ion channel alterations; evidence suggests cardiovascular risk in predisposed individuals.
The endocannabinoid system and heart disease: the role of cannabinoid receptor type 2	Fulmer, M.	Cardiovasc. & Hematol. Disord. Drug Targets, 2018	Narrative review – Level VI	CB_2 receptor exerts a protective role against vascular inflammation and atherosclerosis.
The endocannabinoid system: a potential target for the treatment of various diseases	Lowe, H.	Int. J. Mol. Sci., 2021	Narrative review – Level VI	ECS as a therapeutic target; CB_2 shows protective potential in chronic diseases.
The endocannabinoid system and physical exercise	Matei, D.	Int. J. Mol. Sci., 2023	Experimental study – Level II	Endocannabinoid activation reduces norepinephrine release, modulating autonomic response.

Cannabis and cannabinoids for symptomatic treatment for people with multiple sclerosis	Filippini, G.	Cochrane Database Syst. Rev., 2022	Systematic review – Level I	Cannabinoids relieve MS symptoms; cardiovascular impact still underexplored.
Clinical considerations for cannabis use and cardiovascular health	Sajdeya, R.	Med. Cannabis Cannabinoids, 2022	Narrative review – Level VI	Highlights benefits and cardiovascular risks of clinical cannabis use.
Arrhythmias and cannabis use: a comprehensive overview	Paulraj, S.	Heart Rhythm O2, 2024	Narrative review – Level VI	Cannabis may precipitate arrhythmias; caution recommended in vulnerable patients.
The influence of oral cannabidiol on 24-h ambulatory blood pressure and arterial stiffness in untreated hypertension	Dragun, T.	Adv. Ther., 2023	Pilot clinical trial – Level II	CBD reduced blood pressure and arterial stiffness in untreated hypertensive patients.
Trial of a novel oral cannabinoid formulation in patients with hypertension	Batinic, A.	Pharmaceuticals, 2023	Randomized clinical trial – Level II	CBD formulation reduced mean/diastolic BP; promising effect in autonomic dysfunction.
Neurological benefits, clinical challenges, and neuropathologic promise of medical marijuana in multiple sclerosis	Longoria, V.	Biomedicines, 2022	Narrative review – Level VI	CBD may improve MS symptoms; indirect cardiovascular impact.
Efficacy of cannabinoids compared to standard treatments in multiple sclerosis (CANSEP trial): protocol	Zertal, A.	Front. Neurol., 2024	RCT protocol – Level V	Ongoing trial; assessing cannabinoid efficacy versus standard therapies.
19 patients report seizure freedom with medical cannabis oil treatment for drug-resistant epilepsy	Chen, F.	Front. Neurosci., 2025	Case series – Level V	Cannabis oil promoted seizure control; cardiovascular effects not primary outcomes.
Cannabinoids and the endocannabinoid system in the regulation of cytochrome P450 metabolic activity	Fonseca, C.	Front. Pharmacol., 2025	Narrative review – Level VI	ECS interactions with drug metabolism; highlights caution for clinical use.

A systematic review and meta-analysis of randomized controlled trials of cardiovascular toxicity of medical cannabinoids	Watanabe, A.	J. Am. Pharm. Assoc., 2021	Systematic review and meta-analysis – Level I	Identified cardiovascular toxicity associated with cannabinoids; need for monitoring.
Acute effects of oral delta-9-tetrahydrocannabinol (THC) on autonomic cardiac activity	Pabón, E.	Psychophysiology, 2021	Human experimental study – Level II	THC increases heart rate and reduces heart rate variability; arrhythmia risk.
Cardiovascular complications of marijuana and related substances: a review	Singh, A.	Cardiol. Ther., 2018	Narrative review – Level VI	Links cannabis use to various cardiovascular complications.

Table 1. Summary of the 16 studies included in the Discussion stage, presenting title, lead author, journal and year of publication, study design, level of evidence (JBI classification), and main findings related to the endocannabinoid system, autonomic regulation, and cardiovascular outcomes in neurological patients.

4- DISCUSSION

This integrative review made it possible to compile and analyze evidence on the influence of the endocannabinoid system (ECS) on autonomic regulation and cardiovascular outcomes in patients with neurological disorders. The literature points to relevant but still fragmented advances, revealing both the therapeutic potential of cannabinoid compounds and the risks associated with their use in vulnerable populations. Accordingly, the discussion was structured into two analytical categories: (1) Endocannabinoid system, autonomic regulation, and neurocardiology; and (2) Therapeutic potential and clinical limitations of cannabinoid modulation in neurological patients.

4.1 Endocannabinoid system, autonomic regulation, and neurocardiology

Recent studies emphasize the importance of the ECS in modulating the cardiovascular autonomic response, particularly through the differential activation of CB_1 and CB_2 receptors. While CB_1 exerts vasodilatory and hypotensive effects mediated by nitric oxide and potassium channels, it may also trigger tachycardia and autonomic instability under adverse conditions (Šoša, 2025). Conversely, CB_2 is associated with protective effects against vascular inflammation and ischemic events, positioning it as a promising target for the prevention of cardiovascular complications (Fulmer; Thewke,

2018; Lowe et al., 2021).

In the field of neurocardiology, the ECS has proven relevant at the interface between the nervous system and hemodynamic regulation. Experimental studies show that endocannabinoid activation reduces norepinephrine release from sympathetic fibers, directly modulating autonomic response (Matei et al., 2023). This mechanism is particularly significant in conditions such as epilepsy and multiple sclerosis, where dysautonomia may exacerbate cardiovascular risk (Filippini et al., 2022). The analysis of these data suggests that ECS-mediated autonomic homeostasis is complex, oscillating between protective and destabilizing effects depending on intensity and clinical context.

Despite these advances, uncertainties remain regarding the clinical translation of these mechanisms in neurological patients. The methodological heterogeneity of the studies—ranging from animal models to small-scale clinical trials - limits the generalizability of findings. Recent reviews reinforce that ECS modulation of autonomic function requires further characterization in real clinical scenarios, with emphasis on the cardiovascular safety of individuals susceptible to arrhythmias or hemodynamic instability (Sajdeya et al., 2022; Paulraj et al., 2024).

4.2 Therapeutic potential and clinical limitations of cannabinoid modulation in neurological patients

In recent years, cannabidiol (CBD) has gained prominence as a therapeutic alternative with anti-inflammatory and anxiolytic effects, also associated with cardiovascular modulatory properties. Recent clinical trials have demonstrated that acute CBD administration can reduce blood pressure in hypertensive individuals, particularly under stress conditions (Dragun et al., 2023). Moreover, optimized formulations with higher bioavailability showed early reductions in mean and diastolic blood pressure, suggesting a promising effect for the management of autonomic dysfunction (Batinic et al., 2023).

In the neurological context, the literature also indicates possible benefits of CBD as an adjuvant in patients with multiple sclerosis and refractory epilepsy, in which impaired autonomic regulation contributes to increased cardiovascular risk (Longoria et al., 2022). However, it is important to emphasize that most available studies focus on

neurological symptoms, with few investigations directly correlating ECS modulation with cardiovascular outcomes in these patients (Zertal et al., 2024; Chen et al., 2025).

On the other hand, it is essential to acknowledge the limitations of clinical cannabinoid use. In addition to methodological variability, there is still a scarcity of randomized clinical trials confirming the long-term cardiovascular efficacy and safety of CBD and other ECS modulators (Fonseca et al., 2025; Watanabe et al., 2023). Furthermore, the literature warns of the potential risks of exposure to Δ9-THC, which has been associated with increased heart rate and reduced heart rate variability, potentially precipitating arrhythmias and adverse events in vulnerable populations (Pabón et al., 2021; Singh et al., 2018). This scenario reinforces the need for individualized approaches that consider not only therapeutic potential but also the inherent risks of clinical management.

5- FINAL CONSIDERATIONS

The aim of this study was to examine the influence of the endocannabinoid system (ECS) on autonomic regulation and cardiovascular outcomes in patients with neurological disorders. The synthesis demonstrated that the ECS acts as an essential modulator of neurocardiological homeostasis, revealing both protective effects - primarily mediated by CB_2 receptor activity - and risks associated with CB_1 receptor activation in certain clinical contexts. Despite the identified potential, the critical analysis highlighted methodological gaps and the need for higher-quality evidence to support consistent clinical recommendations.

In the field of neurocardiology, the findings indicate that dysautonomia, frequently observed in conditions such as epilepsy, multiple sclerosis, and traumatic brain injury, may be modulated by the ECS, directly influencing cardiovascular risks. Recent trials suggest that cannabidiol (CBD) has promising effects in reducing blood pressure and modulating autonomic function; however, these studies remain limited in number, scale, and methodological homogeneity. Moreover, the literature underscores the importance of distinguishing the beneficial effects of CBD from the cardiovascular risks associated with Δ9-THC, particularly in individuals predisposed to arrhythmias and autonomic instability.

Thus, this integrative review contributes by highlighting both the potential and the limitations of ECS modulators in neurological populations with cardiovascular risk. Moving forward, broader and methodologically rigorous clinical investigations are required to consolidate the safety and efficacy of such interventions. Integrating perspectives from neuroscience, cardiology, and pharmacology may open pathways for innovative therapeutic strategies aimed at promoting autonomic stability and preventing cardiovascular complications in neurological patients.

REFERENCES

BATINIC, A. et al. Trial of a novel oral cannabinoid formulation in patients with hypertension: a double-blind, placebo-controlled pharmacogenetic study. **Pharmaceuticals** (Basel), v. 16, n. 5, p. 645, 2023. DOI: 10.3390/ph16050645. Available at: https://doi.org/10.3390/ph16050645. Accessed on: Sept. 4, 2025.

CHEN, F. Y. et al. 19 patients report seizure freedom with medical cannabis oil treatment for drug-resistant epilepsy: a case series. **Frontiers in Neuroscience**, v. 19, 2025. DOI: 10.3389/fnins.2025.1570531. Available at: https://doi.org/10.3389/fnins.2025.1570531. Accessed on: Sept. 5, 2025.

DRAGUN, T. et al. The influence of oral cannabidiol on 24-h ambulatory blood pressure and arterial stiffness in untreated hypertension: a double-blind, placebo-controlled, cross-over pilot study. **Advances in Therapy**, v. 40, n. 8, p. 3495-3511, 2023. DOI: 10.1007/s12325-023-02560-8. Available at: https://doi.org/10.1007/s12325-023-02560-8. Accessed on: Sept. 5, 2025.

FILIPPINI, G. et al. Cannabis and cannabinoids for symptomatic treatment for people with multiple sclerosis. **Cochrane Database of Systematic Reviews**, v. 2022, n. 5, Art. No.: CD013444, 2022. DOI: 10.1002/14651858.CD013444.pub2. Available at: https://doi.org/10.1002/14651858.CD013444.pub2. Accessed on: Sept. 5, 2025.

FONSECA, C. D. F. et al. Cannabinoids and the endocannabinoid system in the regulation of cytochrome P450 metabolic activity – a review. **Frontiers in Pharmacology**, v. 16, June 5, 2025. Drug Metabolism and Transport section. DOI: 10.3389/fphar.2025.1599012. Available at: https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2025.1599012/. Accessed on: Sept. 2, 2025.

FULMER, M. L.; THEWKE, D. P. The endocannabinoid system and heart disease: the role of cannabinoid receptor type 2. **Cardiovascular & Hematological Disorders Drug Targets**, v. 18, n. 1, p. 34-51, 2018. DOI: 10.2174/1871529X18666180206161457. Available at: https://doi.org/10.2174/1871529X18666180206161457. Accessed on: Sept. 4, 2025.

GANONG, L. H. Integrative reviews of nursing research. **Research Nursing Health**, v. 10, n. 1, p. 01-10, 1987. Available at: https://pubmed.ncbi.nlm.nih.gov/3644366/. Accessed on: Sept. 4, 2025.

KRZYŻEWSKA, A. et al. Comprehensive mini-review: therapeutic potential of cannabigerol – focus on the cardiovascular system. **Frontiers in Pharmacology**, v. 16, Mar. 25, 2025. Experimental Pharmacology and Drug Discovery section. DOI: 10.3389/fphar.2025.1561385. Available at: https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2025.1561385/full?. Accessed on: Sept. 1, 2025.

LOCKWOOD, C. et al. Systematic reviews of qualitative evidence. In: AROMATARIS, E.; MUNN, Z. (Editors). **JBI Manual for Evidence Synthesis**. JBI, 2020. Available at: https://jbi-global-wiki.refined.site/space/MANUAL/355860482. Accessed on: Sept. 4, 2025.

LOCKWOOD, C.; MUNN, Z.; PORRITT, K. Qualitative research synthesis: methodological guidance for systematic reviewers utilizing meta-aggregation. **International Journal of Evidence-based Healthcare**, v. 13, n. 3, p. 179-187, 2015. Available at: https://pubmed.ncbi.nlm.nih.gov/26262565/. Accessed on: Sept. 4, 2025.

LONGORIA, V. et al. Neurological benefits, clinical challenges, and neuropathologic promise of medical marijuana: a systematic review of cannabinoid effects in multiple sclerosis and experimental models of demyelination. **Biomedicines**, v. 10, n. 3, p. 539, 2022. DOI: 10.3390/biomedicines10030539. Available at: https://doi.org/10.3390/biomedicines10030539. Accessed on: Sept. 5, 2025.

LOWE, H. et al. The endocannabinoid system: a potential target for the treatment of various diseases. **International Journal of Molecular Sciences**, v. 22, n. 17, p. 9472, 2021. DOI: 10.3390/ijms22179472. Available at: https://doi.org/10.3390/ijms22179472. Accessed on: Sept. 5, 2025.

MATEI, D. et al. The endocannabinoid system and physical exercise. **International Journal of Molecular Sciences**, v. 24, n. 3, p. 1989, 2023. DOI: 10.3390/ijms24031989. Available at: https://doi.org/10.3390/ijms24031989. Accessed on: Sept. 4, 2025.

MOHER, D. et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. **PLoS Med**., v. 6, n. 7, p. e1000097, 2009. Available at: https://pubmed.ncbi.nlm.nih.gov/19621072/. Accessed on: Sept. 4, 2025.

O'SULLIVAN, S. E. Endocannabinoids and the cardiovascular system in health and disease. **Handbook of Experimental Pharmacology**, v. 231, p. 393-422, 2015. DOI: 10.1007/978-3-319-20825-1_14. Available at: https://doi.org/10.1007/978-3-319-20825-1_14. Accessed on: Sept. 4, 2025.

PABON, E. et al. Acute effects of oral delta-9-tetrahydrocannabinol (THC) on autonomic cardiac activity and their relation to subjective and anxiogenic effects. **Psychophysiology**, v. 59, n. 2, e13955, 2022. DOI: 10.1111/psyp.13955. Available at: https://doi.org/10.1111/psyp.13955. Accessed on: Sept. 6, 2025.

PAULRAJ, S. et al. Arrhythmias and cannabis use: a comprehensive overview. **Heart Rhythm O2**, v. 6, n. 1, p. 78-85, 2024. DOI: 10.1016/j.hroo.2024.10.020. Available at: https://doi.org/10.1016/j.hroo.2024.10.020. Accessed on: Sept. 5, 2025.

SAJDEYA, R. et al. Clinical considerations for cannabis use and cardiovascular health. **Medical Cannabis and Cannabinoids**, v. 5, n. 1, p. 120-127, 2022. DOI: 10.1159/000526731. Available at: https://doi.org/10.1159/000526731. Accessed on: Sept. 4, 2025.

SINGH, A. et al. Cardiovascular complications of marijuana and related substances: a review. **Cardiology and Therapy**, v. 7, n. 1, p. 45-59, 2018. DOI: 10.1007/s40119-017-0102-x. Available at: https://doi.org/10.1007/s40119-017-0102-x. Accessed on: Sept. 6, 2025.

ŠOŠA, I. A meta-narrative review of channelopathies and cannabis: mechanistic, epidemiologic, and forensic insights into arrhythmia and sudden cardiac death. **International Journal of Molecular Sciences**, v. 26, n. 17, p. 8635, 2025. DOI: 10.3390/ijms26178635. Available at: https://doi.org/10.3390/ijms26178635. Accessed on: Sept. 4, 2025.

SOUZA, M. T.; SILVA, M. D.; CARVALHO, R. Integrative review: what is it? How to do it? **Einstein**, v. 8, n. 1, p. 102-106, 2010. Available at: https://www.scielo.br/j/eins/a/ZQTBkVJZqcWrTT34cXLjtBx/?format=pdf&lang=pt. Accessed on: Sept. 5, 2025.

STERN, C.; JORDAN, Z.; MCARTHUR, A. Developing the review question and inclusion criteria. **The American Journal of Nursing**, v. 14, n. 4, p. 53-56, 2014. Available at: https://pubmed.ncbi.nlm.nih.gov/24681476/. Accessed on: Sept. 4, 2025.

WATANABE, A. H.; CHAIYAKUNAPRUK, N. et al. A systematic review and meta-analysis of randomized controlled trials of cardiovascular toxicity of medical cannabinoids. **Journal of the American Pharmacists Association** (2003), v. 61, n. 5, p. e1-e13, 2021. DOI: 10.1016/j.japh.2021.03.013. Available at: https://doi.org/10.1016/j.japh.2021.03.013. Accessed on: Sept. 6, 2025.

ZERTAL, A. et al. Efficacy of cannabinoids compared to the current standard treatments on symptom relief in persons with multiple sclerosis (CANSEP trial): study protocol for a randomized clinical trial**. Frontiers in Neurology**, v. 15, 2024. DOI: 10.3389/fneur.2024.1440678. Available at: https://doi.org/10.3389/fneur.2024.1440678. Accessed on: Sept. 5, 2025.