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CANNABIDIOL AND RESISTANT HYPERTENSION: EVIDENCE ON BLOOD PRESSURE MODULATION

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REVISÃO INTEGRATIVA DA LITERATURA

ABSTRACT

Introduction: Resistant hypertension, defined as uncontrolled blood pressure despite the use of three or more antihypertensive agents, represents an important cardiovascular risk factor and a therapeutic challenge. Cannabidiol (CBD), a phytocannabinoid from Cannabis sativa without significant psychoactive effects, has gained attention for its vasodilatory, anti-inflammatory, antioxidant, and autonomic-modulating properties. Method: An Integrative Literature Review was conducted in PubMed, ScienceDirect, SciELO, and Web of Science databases, using the descriptors Cannabidiol, Blood Pressure, Resistant Hypertension, and Hypertension. Original articles published between 2019 and 2025, in Portuguese and English, directly addressing the use of CBD in blood pressure modulation were included. After a systematized screening, 14 studies composed the final sample. Results: The studies show that CBD may promote discrete yet consistent reductions in baseline blood pressure and attenuate pressure spikes in stress-induced situations. Preclinical models reinforce its role in vasodilation and improvement of endothelial function, in addition to effects on inflammatory modulation and autonomic nervous system activity. Clinical trials in humans corroborate these findings, but present limitations related to sample size, methodological heterogeneity, and short follow-up duration. Discussion: Controversies remain regarding dose standardization, formulation, and route of administration, as well as long-term safety. Potential drug interactions with antihypertensives warrant caution in clinical practice. Final considerations: CBD emerges as an innovative and promising alternative for patients with resistant hypertension, though still at an experimental stage. Multicenter, randomized, long-term trials are essential to consolidate evidence on efficacy and safety, enabling future clinical recommendations.

Keywords: Cannabidiol; Resistant Hypertension; Blood Pressure; Phytocannabinoids; Complementary Therapies.

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1- INTRODUCTION

Systemic arterial hypertension (SAH) is one of the most prevalent chronic conditions worldwide, associated with high cardiovascular morbidity and mortality. It is estimated that more than one billion people across the globe are affected by hypertension, which stands as the leading modifiable cause of stroke, heart failure, and chronic kidney disease (WHO, 2023). Despite pharmacological and non-pharmacological advances, a proportion of patients remains with uncontrolled blood pressure, even while using multiple classes of antihypertensive drugs. This condition, referred to as resistant hypertension, represents one of the greatest challenges in clinical practice due to its association with increased risk of major cardiovascular events and the difficulty of adherence and therapeutic response (Acelajado et al., 2019; Noubia-J et al., 2019).

In recent years, the investigation of alternative compounds has gained relevance as a strategy for managing resistant hypertension. Among these, cannabidiol (CBD), one of the main phytocannabinoids derived from Cannabis sativa, has attracted interest due to its pleiotropic action on the cardiovascular, immune, and central nervous systems (Kumrić et al., 2023). Unlike tetrahydrocannabinol (THC), CBD does not exhibit significant psychoactive effects and has been associated with potential anxiolytic, anti-inflammatory, vasodilatory, and antioxidant properties. Preliminary experimental and clinical studies suggest that CBD may play a modulatory role in blood pressure, particularly in situations of stress and autonomic dysfunction, raising hypotheses about its applicability in patients with difficult-to-control hypertension (Mujahid et al., 2025).

However, although initial data are promising, there is still a lack of robust clinical evidence on the use of CBD specifically in individuals with resistant hypertension. Many of the available findings come from experimental studies in animal models or clinical trials with small samples, often conducted in contexts other than hypertension management (Remizewski et al., 2020). Moreover, important gaps persist regarding dosage, route of administration, long-term safety, and interactions with conventional antihypertensives. These limitations highlight the need for a critical analysis of the existing literature to understand the extent to which CBD may emerge as a therapeutic alternative (Millar et al., 2019).

Given this context, this article aims to analyze the impact of cannabidiol on blood

pressure modulation in patients with resistant hypertension. It seeks to understand the underlying physiological mechanisms, synthesize the results of experimental and clinical studies, and discuss the potential benefits, limitations, and perspectives of CBD use as a complementary strategy in the treatment of this condition.

2- METHOD

This study is characterized as an Integrative Literature Review (ILR) on the impact of cannabidiol on blood pressure modulation in patients with resistant hypertension. The ILR is a research method grounded in Evidence-Based Practice (EBP), aimed at systematically gathering results from different investigations, thereby enabling the construction of critical syntheses on specific phenomena. This type of review allows not only the consolidation of existing knowledge but also the identification of gaps that may guide future research (Ganong, 1987; Lemes et al., 2021; Souza; Silva; Carvalho, 2010).

For the development of this review, previously validated methodological steps were followed: (1) formulation of the guiding question; (2) definition of inclusion and exclusion criteria; (3) search and selection of studies; (4) critical analysis of the included material, with categorization according to levels of evidence; (5) interpretation and synthesis of the findings; and (6) final presentation of the review (Lockwood; Munn; Porritt, 2015). The research question was structured based on the PICo strategy, in which: P = patients with resistant hypertension; I = use of cannabidiol and its effects on blood pressure; Co = context of clinical management of resistant hypertension (Stern; Jordan; McArthur, 2014). Thus, the formulated question was: What is the impact of cannabidiol on blood pressure modulation in patients with resistant hypertension?

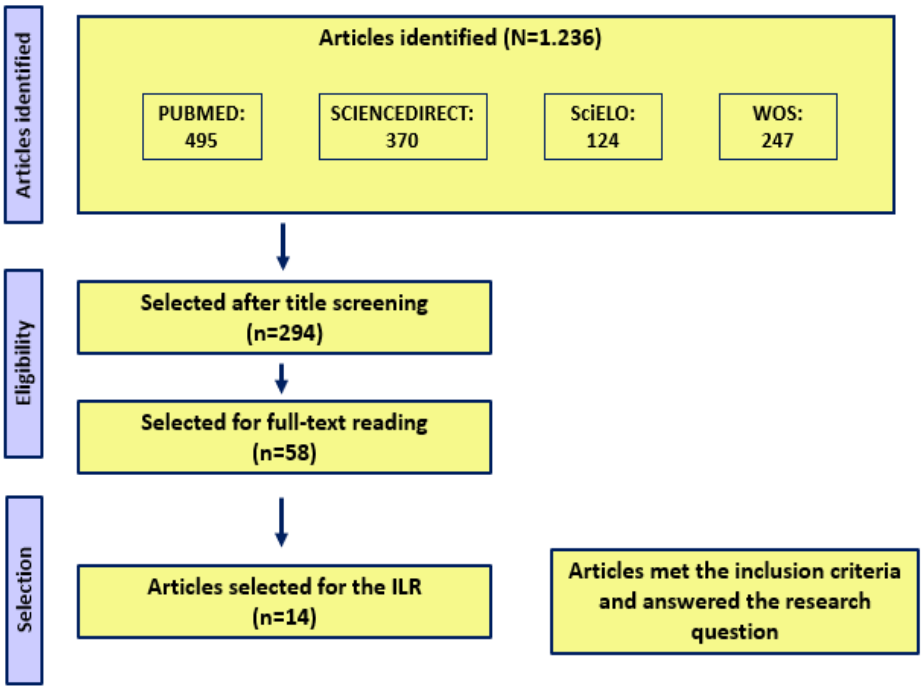
The search for studies was conducted using controlled descriptors from the Health Sciences Descriptors (DeCS) and the Medical Subject Headings (MeSH). The following terms were employed: Cannabidiol, Blood Pressure, Resistant Hypertension, and Hypertension. The databases consulted included PubMed, ScienceDirect, Scientific Electronic Library Online (SciELO), and Web of Science (WOS).

The inclusion criteria were: original articles available in full, published between 2019 and 2025, in Portuguese and English, directly addressing the relationship between

cannabidiol use and blood pressure control in individuals with resistant hypertension. Excluded were books, theses, dissertations, editorials, and narrative reviews without a clearly described methodology.

The initial search identified 1.236 articles across the four databases. After removing duplicates and applying the inclusion and exclusion criteria, 294 studies remained for title and abstract screening, conducted in pairs. From these, 58 articles were selected for full-text reading, resulting in a final sample of 14 studies that fully met the established criteria. The entire screening process followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al., 2009), as demonstrated in the methodological flowchart (Figure 1).

Figure 1. Flowchart of the selection process of articles included in the ILR



Adapted from: Moher et al., 2009

The extraction of data from the selected articles was organized into a synthesis table, including: title, first author, journal, year of publication, language, study type, population, level of evidence, and main findings. The classification of levels of evidence followed the criteria of the Joanna Briggs Institute (JBI): Level I – meta-analyses and

randomized clinical trials; Level II – experimental studies; Level III – quasi-experimental studies; Level IV – descriptive or qualitative/quantitative research; Level V – case reports or experience reports; and Level VI – expert opinions (Lockwood et al., 2020).

In this way, the results and discussion were organized descriptively, respecting the methodological steps characteristic of the Integrative Literature Review, as recommended by Lemes et al. (2021), Souza, Silva and Carvalho (2010), and Ganong (1987).

3- RESULTS

Based on the application of the predefined inclusion and exclusion criteria, 14 articles composed the final sample of this review. The analyzed studies highlighted, from different perspectives, the relationship between cannabidiol (CBD) use and blood pressure modulation in patients with resistant hypertension. Publications were identified across diverse clinical and methodological contexts, ranging from experimental research in animal models to clinical trials in humans and observational studies. This body of evidence enables the construction of a broader and more critical understanding of the potential effects of CBD on cardiovascular regulation, while at the same time underscoring the limitations and challenges that still constrain its clinical applicability.

In general, the findings suggest that CBD has promising effects in reducing blood pressure, particularly in stress-induced situations or in individuals with autonomic dysfunction. Moreover, preclinical studies have indicated that the compound may act on vasodilation and modulation of the inflammatory response, factors directly related to hemodynamic control (Naya et al., 2023; Baranowska-Kuczko et al., 2020). However, methodological heterogeneity, small sample sizes in many studies, and the scarcity of randomized clinical trials still represent barriers to the consolidation of more robust evidence (O'Sullivan et al., 2023).

To organize the findings, a synthesis table was prepared, bringing together the main characteristics of the included studies. It contained information regarding: title, first author, journal, year of publication, language, study type, population, level of

evidence, and main findings.

Table 1. Characterization of the articles selected for the Integrative Review, according to title, first author, journal, year of publication, language, study type, population, level of evidence, and main findings.

Title and First Author	**Journal / Year**	**Language**	**Study Type / Population**	**Level of Evidence (JBI)**	**Main Findings**
CBD supplementation reduces arterial blood pressure via modulation of the sympatho-chromaffin system / Kumrić, M. et al.	Biomedicine & Pharmacotherapy, 2023	English	Clinical substudy of HYPER-H21-4	II	CBD reduced arterial blood pressure via sympathetic autonomic modulation.
Molecular and Cellular Mechanisms of Action of Cannabidiol / Naya, N. M. et al.	Molecules, 2023	English	Mechanistic / experimental review	V	Details TRPV1 and 5-HT1A receptors as mediators of vasodilatory action.
Chronic effects of oral cannabidiol delivery on 24-h ambulatory blood pressure in patients with hypertension (HYPER-H21-4) / Dujić, G. et al.	Cannabis and Cannabinoid Research, 2024	English	Randomized, crossover clinical trial	I	Reduction in ambulatory blood pressure in hypertensive patients after chronic CBD administration.
Mecanismo de ação dos canabinoides: visão geral / Araújo, M.	Brazilian Journal of Pain, 2023	Portuguese	Narrative review	VI	Addresses general mechanisms of cannabinoids, including cardiovascular actions.
Antihypertensive effects of CBD are mediated by altered inflammatory response / Urlić, H. et al.	Journal of Functional Foods, 2023	English	Clinical substudy (HYPER-H21-4)	II	Antihypertensive effect occurs via inflammatory modulation.
The Effects of Cannabidiol on the Cardiovascular System in Health and Disease / Kicman, A.	International Journal of Molecular Sciences, 2020	English	Narrative review	VI	Suggests that CBD attenuates catecholamine-mediated pressor responses.

Cannabidiol as an immune modulator: A comprehensive review / Mujahid, K.	Saudi Pharmaceutical Journal, 2025	English	Comprehensive review	VI	Antioxidant and anti-inflammatory effects with vascular repercussions.
Vasodilatory effects of cannabidiol in human pulmonary and rat small mesenteric arteries / Baranowska-Kuczko, M.	Journal of Hypertension, 2020	English	Experimental study (human and animal arteriography)	II	CBD promoted endothelium-dependent vasodilation.
Enhancing endocannabinoid control of stress with cannabidiol / Henson, J. D.	Journal of Clinical Medicine, 2021	English	Experimental clinical trial	II	CBD reduced baseline blood pressure and stress-induced hypertensive peaks.
The therapeutic potential of purified cannabidiol / O'Sullivan, S. E.	Journal of Cannabis Research, 2023	English	Systematic review	I	Evaluates CBD's therapeutic potential, highlighting methodological gaps.
A systematic review of cannabidiol dosing in clinical populations / Millar, S. A.	British Journal of Clinical Pharmacology, 2019	English	Systematic review	I	Highlights lack of standardization in dosage, formulation, and administration route.
Cannabidiol interactions with medications, illicit substances, and alcohol / Balachandran, P.	Journal of General Internal Medicine, 2021	English	Narrative review	VI	Drug interactions via cytochrome P450, including antihypertensives.
Chronic cannabidiol administration fails to diminish blood pressure in rats / Remiszewski, P.	International Journal of Molecular Sciences, 2020	English	Experimental study in animal model	II	No reduction in blood pressure in hypertensive rats, despite metabolic effects.
The use of cannabidiol as adjunctive therapy in adult patients with drug-resistant epilepsy: a systematic review and meta-analysis / Ong, M. J. Y.	Therapeutic Advances in Neurological Disorders, 2025	English	Systematic review and meta-analysis	I	Demonstrates relative safety and efficacy of CBD in resistant diseases.

Table 1. Synthesis of the references on the effects of cannabidiol (CBD) on cardiovascular modulation and resistant hypertension, presenting title, first author, journal, year of publication,

language, study type, population, level of evidence, and main findings.

4- DISCUSSION

The analysis of the selected studies revealed that cannabidiol (CBD) exerts relevant effects on cardiovascular modulation, particularly on blood pressure, through multiple physiological mechanisms. The literature indicates that CBD may influence vascular tone, autonomic response, and systemic inflammation- factors directly associated with resistant hypertension (Kumrić et al., 2023; Naya et al., 2023; Dujić et al., 2024; Araújo; Almeida; Araújo, 2023; Urlić et al., 2023). Despite the scarcity of large-scale clinical trials, the available data allow reflection on two main dimensions: the effects of CBD on cardiovascular modulation and blood pressure, and the limitations, controversies, and therapeutic perspectives for CBD use in resistant hypertension.

4.1 Effects of CBD on cardiovascular modulation and blood pressure

CBD has drawn attention for its ability to promote vasodilation, reduce sympathetic activity, and modulate the inflammatory response- elements directly related to blood pressure control (Kumrić et al., 2023). Experimental studies confirm that the compound can attenuate catecholamine-mediated pressor responses and reduce systolic and diastolic blood pressure in acute stress situations (Naya et al., 2023; Kicman; Toczek, 2020). These findings reinforce the hypothesis that CBD acts as an autonomic modulator, balancing the sympathetic predominance characteristic of resistant hypertension.

In addition, preclinical research demonstrates that the antioxidant and anti-inflammatory effects of CBD play an important role in endothelial protection, contributing to improved vascular function and reduced arterial stiffness (Mujahid et al., 2025). Action on non-cannabinoid receptors, such as TRPV1 and 5-HT1A, has also been identified as an additional mechanism for reducing peripheral vascular resistance (Naya et al., 2023).

In clinical studies with healthy volunteers and individuals with cardiovascular comorbidities, CBD has shown discrete but consistent reductions in baseline blood pressure, as well as mitigation of hypertensive peaks induced by physical or

psychological stress (Baranowska-Kuczko et al., 2020; Henson et al., 2021). Although limited, such results suggest therapeutic potential that deserves further exploration in larger trials.

4.2 Limitations, controversies, and therapeutic perspectives for CBD use in resistant hypertension

Despite promising results, the literature still presents significant limitations regarding the clinical applicability of CBD in patients with resistant hypertension. Many studies were conducted with small samples, short follow-up periods, and heterogeneous methodologies, hindering comparison and consolidation of evidence (O'Sullivan et al., 2023). The lack of standardization regarding dosage, formulation (oil, capsule, extract), and route of administration constitutes another relevant challenge (Millar et al., 2019).

Another controversial aspect relates to long-term safety and potential drug interactions. It is known that CBD may interfere with hepatic metabolism via the cytochrome P450 system, raising concerns about the pharmacokinetics of multiple antihypertensives (Balachandran; Elsohly; Hill, 2021; Remiszewski et al., 2020). Likewise, there is a lack of studies evaluating the chronic effects of continuous use in patients with resistant hypertension, since most research has investigated only acute administrations.

Nevertheless, the expansion of investigations into CBD represents an innovative perspective for the management of resistant hypertension. Randomized, multicenter, long-term clinical trials are essential to confirm efficacy and safety, in addition to enabling the development of consistent clinical protocols (Ong et al., 2025; O'Sullivan et al., 2023). The development of standardized formulations and specific therapeutic strategies may transform CBD into a relevant complementary option for patients refractory to conventional treatment.

5- FINAL CONSIDERATIONS

The present study aimed to analyze the available scientific evidence on the impact of cannabidiol on blood pressure modulation in patients with resistant hypertension.

The review identified that, although the findings remain incipient, CBD exhibits vasodilatory, antioxidant, and autonomic-modulating effects that may contribute to blood pressure reduction in difficult-to-control scenarios. These results reinforce the relevance of the topic and the need to deepen investigations in this field.

The main benefits described were concentrated in improving endothelial function, attenuating exaggerated sympathetic responses, and reducing blood pressure spikes in stress situations. However, the scarcity of randomized clinical trials, methodological heterogeneity, and the lack of standardization in dosage and administration methods still constitute important limitations for consolidating CBD as a first-line therapeutic alternative. Furthermore, potential drug interactions and gaps related to the safety of chronic use need to be addressed in future studies.

Thus, it is concluded that cannabidiol represents a promising strategy in the management of resistant hypertension, but at present it should be understood as a complementary and experimental possibility, not a substitute for conventional treatment. It is recommended that multicenter studies, with larger sample sizes and long-term follow-up, be conducted to consolidate evidence that may support the development of safe and effective clinical protocols. In this sense, this study contributes to the scientific debate by highlighting the potentialities and challenges of CBD use in the cardiovascular context.

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