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Topically Applied Anti-Inflammatory Properties of Medicinal Plants: A Systematic Review

Propriedades anti-inflamatórias de plantas medicinais aplicadas topicamente: Uma revisão sistemática

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RESUMO

Nesta pesquisa sobre plantas medicinais brasileiras aplicadas topicamente para a inflamação, buscou-se explorar suas propriedades anti-inflamatórias, preenchendo lacunas científicas e ampliando estratégias terapêuticas naturais. O estudo, conduzido em abril e maio de 2023, seguiu o protocolo PRISMA, selecionando artigos na *ScienceDirect* e armazenando dados no *software StArt*. Foram analisados estudos que destacaram a diversidade taxonômica e a aplicação tópica de plantas, especialmente em folhas. Óleos essenciais (OE) foram frequentemente examinados, revelando potencial anti-inflamatório. O edema inflamatório induzido foi comum para avaliar extratos, mostrando efeitos moduladores de citocinas como IL-10, TNF-α e MPO, além de mediadores como PGE2 e LTB4. O estudo reconheceu limitações metodológicas e contextuais, enriquecendo a discussão. Conclui-se que extratos e OE apresentam promissoras propriedades anti-inflamatórias, oferecendo opções naturais de tratamento e potencial para reduzir o uso de produtos químicos agressivos. A pesquisa destaca a biodiversidade brasileira como fonte medicinal e ressalta a importância da preservação ambiental.

Palavras-chave: Inflamação cutânea. Compostos bioativos. Farmacologia vegetal. Atividade anti-inflamatória. Extratos vegetais.

ABSTRACT

In this investigation of topically applied Brazilian medicinal plants for inflammation, the aim was to explore their anti-inflammatory properties, bridging scientific gaps and expanding natural therapeutic strategies. The study, conducted in April and May 2023, adhered to the PRISMA protocol, selecting articles from ScienceDirect and storing data in the StArt software. Analyzed studies highlighted taxonomic diversity and the topical application of plants, particularly leaves. Essential oils (EO) were frequently examined, revealing anti-inflammatory potential. Induced inflammatory edema was common for evaluating extracts, demonstrating modulatory effects on cytokines such as IL-10, TNF-α, and MPO, along with mediators like PGE2 and LTB4. The study acknowledged methodological and contextual limitations, enriching the discussion. It is concluded that extracts and EO exhibit promising anti-inflammatory properties, offering natural treatment options and potential for reducing the use of aggressive chemicals. The research underscores Brazilian biodiversity as a medicinal source and emphasizes the importance of environmental preservation.

Keywords: Cutaneous inflammation. Bioactive compounds. Plant pharmacology. Anti-inflammatory activity. Plant extracts.

INTRODUCTION

In the realm of medicinal research, plants emerge as a treasure trove of chemical resources, offering both organic and inorganic compounds with a vast array of exploratory potentials. Over the years, plants have frequently been employed as complementary therapies, influenced by age-old practices and guidance passed down from generation to generation.[1]

A particularly intriguing focus has been the topical application of medicinal plants in the treatment of inflammation. Inflammation, a fundamental immune response, constitutes the body's first line of defense, aiming to safeguard tissues against damage and invasive agents.[2] Understanding this intricate and regulated dynamic of the inflammatory response not only elucidates its protective role but also provides opportunities for innovative therapeutic interventions. The anti-inflammatory properties found in certain medicinal plants can play a crucial role in modulating this intricate molecular cascade, promoting a successful resolution of inflammation and the restoration of tissue homeostasis.[3,4]

In this context, exploring the potential of topically applied medicinal plants opens promising perspectives for safer and more natural therapeutic strategies in managing inflammatory conditions. The study of the anti-inflammatory properties of medicinal plants assumes significance for society and public health. As one of the mega-diverse nations, Brazil hosts an exceptional botanical wealth, manifested through its unique and extensive biodiversity.[5] Within this context, a knowledge gap exists that calls for more comprehensive research, particularly within the Brazilian setting. While the potential of plant compounds has been explored in modern therapy and complex molecule synthesis, it is important to emphasize that approximately 30% of available therapeutic medications derive from natural sources, including plants.[5]

Despite this potential, the topical application of medicinal plants in the treatment of inflammation remains an underexplored area and lacks deeper investigations. While the use of medicinal plants is frequent as an alternative or complement to conventional therapies, millions of individuals dealing with pain and inflammation seek more innovative methods due to the limitations of traditional approaches. Understanding the inflammatory response, with its intricate molecular cascade, is central to this advancement, as a controlled inflammatory response is crucial for eliminating harmful stimuli and restoring tissue homeostasis.[2,4] Therefore, exploring the anti-inflammatory properties of medicinal plants, with a focus on

topical application, not only fills a research gap but also offers an innovative perspective for effective and accessible therapeutic approaches, enriching the spectrum of options for population health. In light of this, the study's objective is to investigate and assess the anti-inflammatory effects of topically applied Brazilian medicinal plants through a systematic review conducted in accordance with the PRISMA statement.

2. MATERIALS AND METHODS

This study was conducted following the PRISMA protocol.[6] During the months of April and May 2023, an electronic search was conducted in the *ScienceDirect* database to select articles on the anti-inflammatory properties of Brazilian medicinal plants. For the database search across title, abstract, and keyword fields, both Portuguese terms ("*plantas medicinais*," "*efeitos anti-inflamatórios*," "*uso tópico*," and "*tratamento farmacológico*") and English terms ("medicinal plants," "anti-inflammatory effects," "topical use," "pharmacological treatment," and "Brazilian") were used, combined with Boolean operators.

The variables assessed in this systematic review included the plant part tested, type of extract, evaluated biological activity, method of assessing biological activity (in vivo or in vitro tests), and outcomes. Publications from January 2013 to April 2023 were included. Articles not written in English, reviews, articles published in conference proceedings, theses, editorials, and any other non-original reports were excluded from this systematic review. The data were imported and stored in the StArt software, a free tool developed at LaPES (Laboratório de Pesquisa em Engenharia de Software) at UFSCAR (Universidade Federal de São Carlos), available at http://lapes.dc.ufscar.br/ferramentas/start-tool.

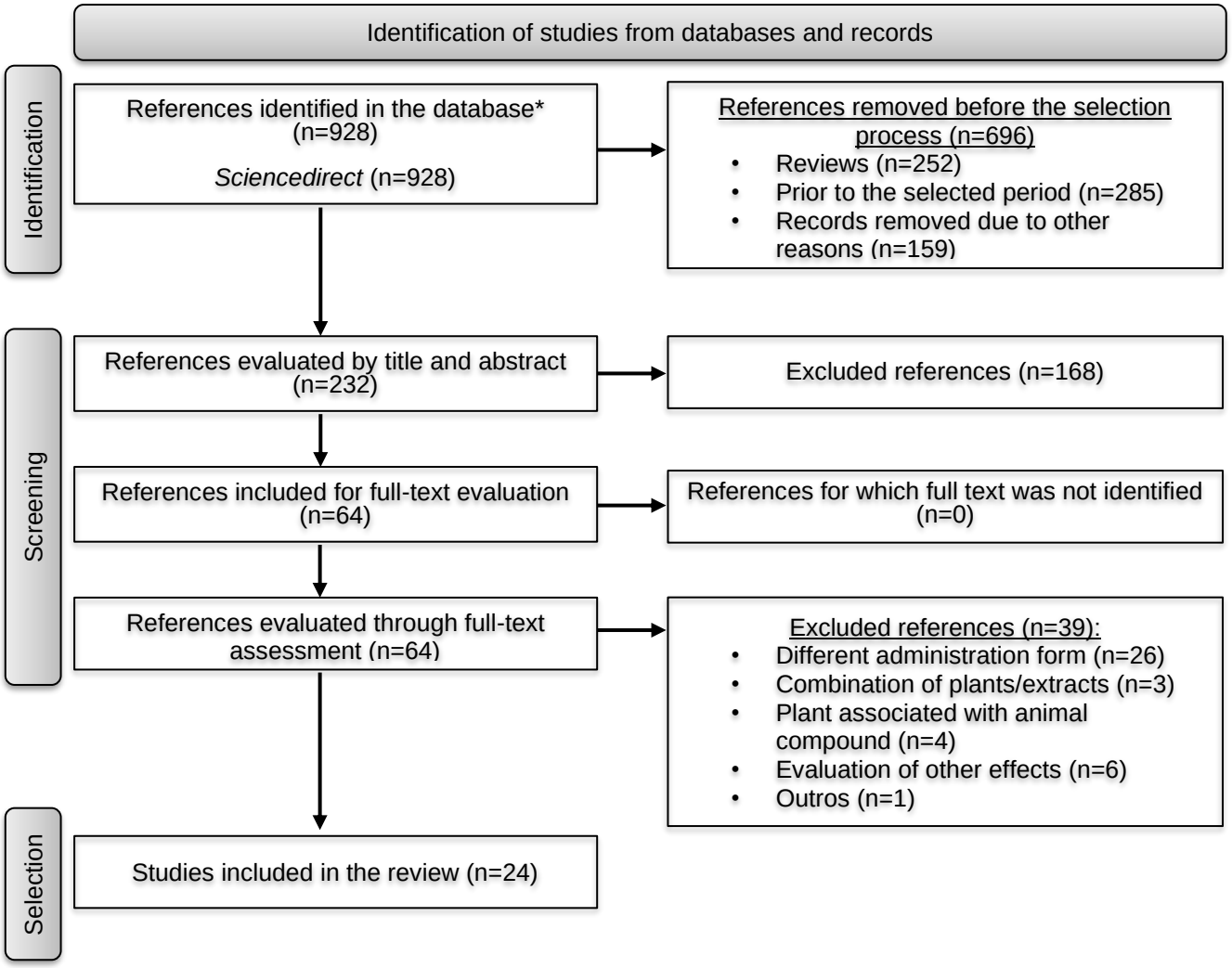
Duplicate references were excluded, and article titles and abstracts were examined, as well as full texts, to extract relevant data. A flowchart illustrating these steps can be viewed in Figure 1. Summarized data were presented in tables and figures.

3. RESULTS

Initially, 928 articles were identified in Sciencedirect. After removing duplicates and selecting relevant titles and abstracts, 64 articles underwent materials and methods analysis. Among these, 24 articles met the established inclusion and exclusion criteria. The progression of the selection process, as well as the number of articles at each stage, is visually depicted in Figure 1 of the Flowchart. An overall understanding of the 24 articles incorporated in this study is provided in Table 1. This careful compilation offers a

comprehensive view of the characteristics of the conducted studies and serves as a valuable resource for comprehending the techniques used in investigating the anti-inflammatory properties of medicinal plants that are popular in Brazil.

Figura 1 - O diagrama de fluxo do PRISMA representa os processos de seleção e revisão.



Source: Compiled by the author (2023).

Table 1 - Variables and Parameters of Brazilian Studies on Topically Applied Anti-Inflammatory Properties of Medicinal Plants.

Year	Author	Plant name	Collection / acquisition location	Part of the plant used	Extract type	Bioassay Model	Outcomes
2013	Horino-uchi et al.[7]	*Combretum leprosum*	Viçosa, Ceará, Brazil	Flowers	Ethanol-based	Extract tested topically on the skin using the method of mouse ear edema induced by TPA and croton oil*.	Reversal of the inflammatory and hyperproliferative process of the skin
2013	Trivella-tograssi et al.[8]	*Chenopodium ambrosioides (Amarantaceae)*	Cáceres, Mato Grosso, Brazil	Leaves and stems	Ethanol-based	Cream with EE (1%, 3%, and 5%) applied to edema on the inner side of the right ear induced by different inflammatory agents.	Inhibition of mediators (BK, NO, SP, PGE2, and TNF-α) and enzymes (MPO and ADA) involved in inflammatory and painful processes.
2013	Prudente et al.[9]	*Malva sylvestris*	AC, São Paulo, SP, Brazil	Leaves	Hydroalcoholic	Extract (1.0 mg/ear) tested in chronic inflammatory process induced by multiple applications of TPA.	Reduced edema from the first day of application. Prevented the increase of MPO and NAG enzymatic activity. Reduced epidermal hyperproliferation.
2014	Oliveira et al.[10]	*Lippia sidoides*	PADETEC, UFCE, Ceará, Brazil	NE	OE	Essential oil (100%, 50%, 25%, and 12%) tested on skin irritation lesion induced by a scalpel blade irritation test.	Reduced the wound area. The 12% essential oil (EO) showed that the expression of the mediators COX-2 and VEGF in inflammatory and epidermal cells was absent on the 7th day.
2015	Hoepers et al.[11]	*Aleurites moluccana (Euphorbiaceae)*	AC, São Paulo, SP, Brazil	Leaves	Hydroalcoholic	Semi-solid (20% colloidal SiO2) containing extract (10mg/g) tested topically on mouse ear edema induced by croton oil* using the ear edema method.	Reduction of edema, CXCL1/KC levels, IL-1β, and TNF, resulting in a decrease in neutrophil migration.
2015	Peters et al.[12]	*Wilbrandia ebracteata*	Grão-Pará, Santa Catarina, Brazil	Roots	Ethyl acetate	Extract tested (0.2, 0.4, or 0.8 mg in acetone solution) on mice in an ear edema model induced by Croton oil*.	Anti-edematogenic activity that may be related to the activity of PLA2A2, COX, and LOX enzymes, as well as NO inhibition. It was not active in the chronic edema model.
2016	Mendes et al.[13]	*Sapium glandulatum*	Antonina, Paraná, Brazil	Leaves	Hydroalcoholic	Extract (0.1, 0.3, or 1.0 mg) was tested on mice in ear edema induced by TPA* or AA*.	Inhibited edema formation and leukocyte migration, as well as the expression of pro-inflammatory cytokines IL-1β, IL-6, and TNF-α in the tissue.

2016	Brum et al.[14]	*Poikilacanthus glandulosus (Nees) Ariza*	Santiago, Rio Grande do Sul, Brazil	Leaves	Aqueous	Extract tested (0.01–1000 µg/ear) on mice using the mouse ear edema method induced by croton oil*.	Reduced ear edema and cell migration. Inhibited MPO activity.
2017	Martins et al.[15]	*Croton rhamnifolioides*	Aiuaba, Ceará, Brazil	Leaves	OE	Essential oil (EO) tested (2.5, 5, 10, and 20 mg/mL/ear) in acute inflammation in the right ear (inner and outer sides) of mice induced by croton oil*.	Antiedematogenic effect promoting the inhibition of IL-1β and TNF-α production.
2018	Xavier-Santos et al.[16]	*Jatropha gossypiifolia*	Santa Cruz, Rio Grande do Norte, Brazil	Leaves	Aqueous	Gels (1.0, 2.5, or 5.0%) of lyophilized extract tested topically using the mouse ear edema method induced by croton oil*.	Reduced edema, nitrite levels, and MPO enzyme activity. In chronic inflammation (1.0% gel), it reduced edema, lipid peroxidation, and glutathione depletion.
2018	Oliveira-Tintino et al.[17]	*Croton campestris*	Chapada do Araripe, Ceará, Brazil	Leaves	OE	Essential oil (EO) tested (25, 50, 100, and 200 mg/kg) in acute inflammation in the left ear of mice induced by croton oil*.	Reduced edema (both chronic and acute). However, when evaluating the ear mass at the end of the experiment, no edema-reducing action was observed for the oil at higher doses. At high concentrations, it may exhibit edematogenic effects.
2019	Ascari et al.[18]	*Baccharis punctulata (Asteraceae)*	Santa Helena, Paraná, Brazil,	Leaves	OE	Essential oil (EO) tested (0.1, 0.3, and 1.0 mg/ear) in acute inflammation in the right ear induced by TPA administration.	Reduced edema formation. Inhibited the increase in MPO enzyme activity. Decreased cellular infiltration.
2019	Campo-nogara et al.[19]	*Nasturtium officinale*	AC, Santa Maria, Rio Grande do Sul, Brazil	Stems and Leaves	Ethanol-based	Extract (1 mg/ear) and gel formulations (3%; 15 mg/ear) were tested on mice in an ear edema model induced by Croton oil*.	Inhibited acute edema. Reduced MPO activity, infiltration of inflammatory cells, and chronic inflammatory parameters. Decreased cytokine levels (MIP-2 and IL-1β). Increased expression of IkB-α protein.
2020	Salem et al.[20]	*Cissus gongylodes*	Alfenas, Minas Gerais, Brazil	Leaves	Decoction	Product from decoction (0.05, 0.5, and 3 mg) tested topically on the left ear of mice using the mouse ear edema method induced by Croton oil*.	Reduced edema, resulting in anti-edematogenic action. Inhibition of mediators (PGE2 and LTB4). Decreased TNF-α cytokine level.
2020	Bran-demburg o et al.[21]	*Baccharis dracunculifolia (Asteraceae)*	Santa Helena, Paraná, Brazil	Leaves	OE	Essential oil (EO) tested in a model of cutaneous dermatitis induced on the right ear of mice by TPA* (2.5 µg/ear) or AA*.	Reduced edema formation. Lower cellular influx in inflamed tissue and decreased keratinocyte hyperproliferation.

2020	Campo-nogara et al.[22]	*Casearia decandra*	Capão da Canoa, Rio Grande do Sul, Brazil	Leaves	Ethanol-based	Extract tested (0.001, 0.01, 0.1, and 1 mg/ear) topically on the skin using the mouse ear edema method induced by croton oil*.	Inhibited edema formation. Decreased MPO activity. Reduced infiltration of inflammatory cells through suppression of pro-inflammatory cytokine production, consequently inhibiting reactive oxygen and nitrogen species (ROS/RNS) production.
2020	Rocha et al.[23]	*Cyperus rotundus. (Cyperaceae)*	AC, Bangalore, Índia	Comme rcial powder	Ethanol-based	Extract (0.1, 0.3, or 1.0 mg) was tested on mice in ear edema induced by TPA* or AA*.	Reduced edema, cellular migration, keratinocyte proliferation rate, induced MPO tissue activity. Inhibited TPA-induced epidermal hyperplasia.
2020	Cretella et al.[24]	*Moringa oleifera*	AC, Assunção, Paraguai,	Seeds	Oil	Oil (1, 3, 10 µL/ear diluted in acetone and 20 µL/ear) tested in a dermatitis model induced by topical application of TPA, phenol, or AA on the ear of mice.	Reduced edema formation and MPO enzyme activity. Inhibited cellular infiltration and the increase in epidermal thickness.
2020	Horino-uchi et al.[25]	*Vochysia bifalcata Warm*	Antonina, Paraná, Brazil.	Leaves	Hydroethanolic	Extract (0.03–1.0 mg/ear) tested in a model of cutaneous dermatitis induced by croton oil (0.4 mg/ear) or TPA (2.5 µg/ear) on the right ear of mice.	Reduced edema formation, cellular infiltration, and levels of IL-6 and TNF-α. In the chronic model, it reduced edema formation and cellular infiltration. It inhibited epidermal hyperproliferation and the expression of PCNA.
2021	Santos et al.[26]	*Licania rigida Benth.*	Missão Velha, Ceará, Brazil	Leaves	Hydroalcoholic	Extract tested (5, 25, 50, 100, 200, 400, and 500 mg/Kg) topically on the right ear edema of mice induced by croton oil*.	The extract possibly acts by inhibiting the production of eicosanoids.
2021	Corrêa et al.[27]	*Miconia albicans (Sw.) Triana*	Tibagi, Paraná, Brazil	Fruits	Methanolic	Extract tested (20 µL of solution containing 2.5 mg per ear in 70% acetone solution) on mice in an ear edema model induced by Croton oil*.	Inhibited edema and leukocyte recruitment through indirect quantification of MPO enzyme activity. Reduced the carrageenan-induced inflammatory response and decreased the concentration of pro-inflammatory mediators (TNF-α and IL-1β).
2021	Veras et al.[28]	*Verbesina macrophylla*	Camocim de São Félix, Pernam-buco, Brazil	Leaves	OE	Extract tested (0.2, 0.4, or 0.8 mg in acetone solution) on Swiss albino mice in an ear edema model	Reduced acute edema. Inhibited the pro-inflammatory cytokines IL-1β and TNF-α.

						induced by Croton oil*.	
2022	Xavier-Santos et al.[29]	*Ipomoea pes-capre (Convolvulaceae)*	Natal, Rio Grande do Norte, Brazil	Leaves	Hydroethanolic	GIPC (100mg) tested (1, 24, 48, and 72 h) through TIC where filter papers (2 cm2) were impregnated with GIPC on the dorsal part of the animals, which were then visually examined for inflammatory signs and adverse effects. GIPC (5%) tested on Swiss mice in an ear edema model induced by Croton oil*.	In the TIC, no changes were observed in the skin. In the ear edema (acute phase), treatment with GIPC did not inhibit edema and did not lead to a decrease in MPO levels. In the chronic phase, it significantly reduced ear mass, and MPO enzyme activity was decreased.
2023	Lima et al.[30]	*Hyptis crenata*	Salvaterra, Pará, Brazil	Leaves	OE	Essential oil (EO) was tested on mice using an ear edema model induced by xylene at doses of 30, 100, and 300 mg/kg.	Significantly inhibited ear edema.

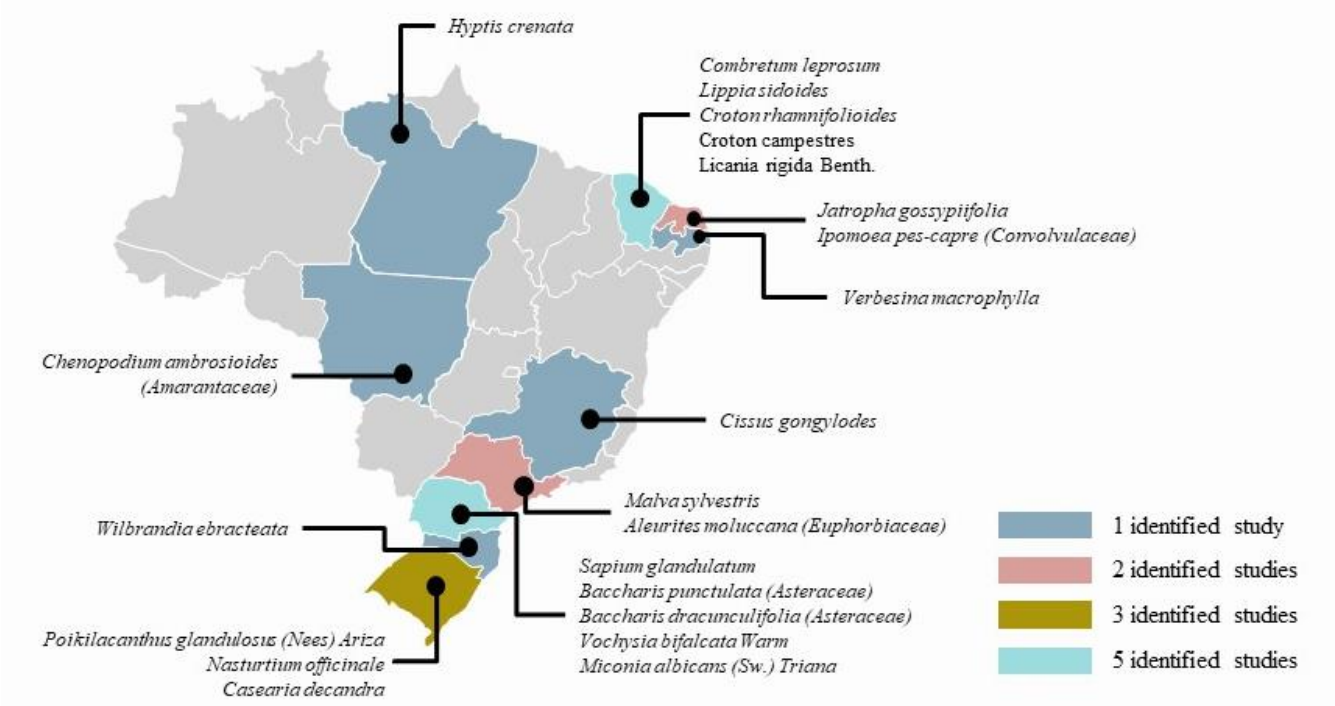
Source: Compiled by the author (2023).

*Irritating agent

Legend: AA: Arachidonic Acid; AC: Commercially Acquired; ADA: Adenosine Deaminase; BK: Bradykinin; cm2: Square centimeters; COX: Cyclooxygenase; COX-2: Cyclooxygenase-2; CXCL1: Chemokine (C-X-C motif) ligand 1; EHMS: Hydroalcoholic extract of M. sylvestris; ROS/RNS: Reactive Oxygen Species/Reactive Nitrogen Species; GIPC: Ipomoea pes-capre gel; II: Induced Inflammation; IkB-α: Inhibitor of kappa B alpha; IL-1β: Interleukin-1β; IL-6: Interleukin-6; Kg: Kilograms; LOX: Lipoxygenase; LTB4: Leukotriene B4; mg: Milligrams; MIP-2: Macrophage Inflammatory Protein-2; MPO: Myeloperoxidase; NAG: N-Acetylglucosaminidase; NE: Not specified; NO: Nitric Oxide; OE: Essential Oil; PADETEC: Technological Development Center; PCNA: Proliferating Cell Nuclear Antigen; PGE2: Prostaglandin E2; PLA2A2: Phospholipase A2 type IIA; SiO2: Silicon Dioxide; SP: Substance P; TIC: Topical Irritation Test; TNF-α: Tumor Necrosis Factor alpha; TPA: 12-O-tetradecanoylphorbol-13-acetate; VEGF: Vascular Endothelial Growth Factor; vt: total volume; µg: Micrograms; µL: Microliters.

A distribution of publications across different locations reveals interesting insights in the context of this scientific research. The cartographic representation of states in Brazil shows a notable variation in the quantity of research concentrated on the anti-inflammatory properties of topically applied medicinal plants (Figure 2). The state of Ceará stands out with the highest number of publications in this theme, with 5 articles published. The state of Paraná is also notable with five publications, while Rio Grande do Sul has 3 publications. These results demonstrate a diverse regional distribution, highlighting the scientific focus in different regions of Brazil. This geographical analysis not only helps define research patterns but also provides an enlightening overview of areas that have been focused on investigating the therapeutic properties of medicinal plants in the anti-inflammatory context.

Figure 2 - National Scenario: Spatial Visualization of Studies on Anti-Inflammatory Medicinal Plants by State.



Source: Compiled by the author (2023).

It is of paramount importance to highlight that the present article aims to describe the anti-inflammatory properties of medicinal plants studied when applied topically, focusing on the analysis of studies conducted within the national territory. Figure 2 illustrates the geographical distribution of the collection/acquisition locations of the plants used as the object of study. It is relevant to point out that, despite the studies by Rocha et al.[23] and Cretella et al.[24] originating in Brazil, the utilized inputs were commercially acquired from Bangalore (India) and Asunción (Paraguay), respectively, in the form of powder and seeds. This study contributes to a comprehensive understanding of the therapeutic applications of Brazilian medicinal plants and their potential anti-inflammatory properties, while also highlighting the significance of global relationships within the realm of scientific research.

4. DISCUSSION

There is significant evidence of taxonomic diversity among plant organisms that are being studied for their anti-inflammatory potential and anti-edematogenic properties. The analysis conducted on a compilation of 24 scientific contributions outlines the absence of a systematic and recurring pattern in terms of the investigated plant entities, featuring 24

taxonomically distinct species. This analysis points to a significant confirmation of the growing national interest in plant-based pharmaceutical agents that can be safely and rationally employed.[1] Brazil finds itself among the nations hosting megadiversity, characterized by an exceptional wealth of botanical entities.[5] The intrinsic heterogeneity within the spectrum of investigations on Brazilian soil is manifested through the distinctive biodiversity permeating its territory. The country holds the privilege of being part of the select group of nations recognized for their "megadiversity" status.[31]

Within the scope of this study, a notable trend was observed in exploring anti-inflammatory properties through the evaluation of different anatomical parts of plants. Remarkably, leaves emerged as the most prevalent focus,[7–9,11,13–20,22,26,28–30] corroborating concurrent findings previously established by.[32] The prominence of this approach can be attributed to easy accessibility, active metabolism, and the diversity of compounds found in leaves and roots, which generally contain a wide variety of substances, including flavonoids, terpenoids, and polyphenols, known for their anti-inflammatory activities.[33]

Among the presentations of plant entities, essential oil (EO) showed a prominent prevalence in the studies (n=8), followed by ethanolic extracts (n=5) and hydroalcoholic extracts (n=5). In the literature,[10,15,17,18,21,28,30,34] reports regarding the use of EO in inflammatory processes and wound healing promotion are recorded, suggesting the existence of multiple intrinsic mechanisms through which these compounds exert such beneficial effects. Research indicates that EO, exemplified by lavender oil, demonstrated the ability to modulate TGF-b and type I collagen levels.[34] Furthermore, EO exhibit advantageous attributes as promising agents in infection prevention,[35,36] and their high content of mono- and sesquiterpenes grants them anti-inflammatory applications.[15]

In multiple studies[11,12,14,15,17,19,20,22,25–29,37], the inflammatory lesion was provoked using the ear edema induction approach with an inflammatory agent. Notably, croton oil was chosen as the agent to induce the inflammatory process due to its recognized applicability, given its capacity to promote inflammatory reactions. This model has been employed in investigating anti-inflammatory substances, as it provides an illustrative scenario of anti-edematogenic activity within an acute inflammatory context.[38]

Croton oil triggers an acute inflammatory response, characterized by the generation of prostaglandins (PGs) and leukotrienes (LTs), increased vascular permeability, edema, and neutrophil infiltration. Edema formation is instigated by vasodilation mechanisms and increased vascular permeability, promoting the extravasation of proteins and water and

establishing local oncotic pressure.[39,40] Notably, the prevalence of pro-inflammatory activities associated with croton oil is attributed to arachidonic acid formation. Consequently, inhibitors of the enzyme phospholipase A2 (PLA2), as well as those targeting the cyclooxygenase and lipoxygenase pathways, have shown efficacy in attenuating edema.[39]

Through the enlightening scenario triggered by croton oil and/or other inflammatory agents like TPA,[7,9,13,18,21,23–25] which share analogous mechanisms, there is an opportunity to deepen the understanding of inflammation. This phenomenon, as an evolutionarily preserved safeguard process, represents a critical mechanism for survival.[41] The inflammatory response, a complex cascade of physiological events, provides protection to the body's tissues and organs. In this context, cytokines act as mediators playing a vital role in orchestrating the inflammatory response. However, the excessive triggering of pro-inflammatory cytokines due to injury can lead to systemic manifestations, characterized by hemodynamic instability and metabolic disturbances.[42,43]

Among the studies analyzed in this review, Combretum leprosum [7] demonstrated the ability to reverse the inflammatory and hyperproliferative skin process. Among the signs of inflammation, inflammatory edema is the hallmark of acute inflammation and is associated with increased hydrostatic pressure secondary to vasodilation, resulting in significant fluid loss and accumulation in the interstitial tissue. Plant species such as *Malva sylvestris*[9], *Aleurites moluccana (Euphorbiaceae)*[11], *Sapium glandulatum*[15], *Poikilacanthus glandulosus (Nees) Ariza*[14], *Jatropha gossypiifolia*[16], *Croton campestres*[17], *Baccharis punctulata (Asteraceae)*[18], *Nasturtium officinale*[19], *Cissus gongylodes*[20], *Baccharis dracunculifolia (Asteraceae)*[21], *Casearia decandra*[22], *Cyperus rotundus. (Cyperaceae)*[23], *Moringa oleífera*[24], *Vochysia bifalcata Warm*[25], *Miconia albicans (Sw.) Triana*[27], *Verbesina macrophylla*[28] and Hyptis *crenata*[30] were capable of reducing acute inflammatory edema, as pronounced edema can lead to complications and slow down the recovery process.

In the context of the inflammatory process, beyond edema formation, an intricate array of mediators plays a significant role in its regulation. Notable among these mediators are proteins known as cytokines and enzymes. The importance of cytokines lies in their ability to act as cell messengers, transmitting vital information between different immune system cells. However, the classification of cytokines based on cell origin and biological function remains challenging. A categorizing approach recognizes division into groups such as interleukins (IL) (IL-1 to IL-35), tumor necrosis factors (TNF-α), chemokines (chemotactic cytokines), interferons (IFN), and mesenchymal growth factors. This categorization reflects

the functional diversity and varied origin of cytokines, which play essential roles in the orchestration and modulation of complex inflammatory mechanisms.[32]

However, in the studies, the application of extracts inhibited/reduced interleukins IL-1β[11,13,15,27,28,44] and IL-6[13,25]. The studies[7–10,12,14,16–18,20,22–24,26] did not provide a description of which interleukin(s) displayed alterations.

Another key indicator in the context of the inflammatory process is TNF-α, produced by cells such as macrophages and lymphocytes. Its binding to receptors triggers an immune and inflammatory response, activating cells and recruiting neutrophils and monocytes. Furthermore, its biological effects may include the induction of apoptosis. An analysis of the studies[7,8,11,13,15,20,27,28] showed a correlation with TNF-α levels, enhancing the understanding of this inflammatory marker.

The relevance of the enzyme MPO in the inflammatory process, especially in the acute phase, is crucial. However, this enzyme exhibits an inherent duality to inflammation, as it can harm tissues by generating reactive oxygen species, harmful to healthy cells. Inhibition, therefore, proves essential. In the studies,[8,9,14,16,18,22–24,27,29,44] the used extracts demonstrated a remarkable ability to inhibit or reduce MPO levels, suggesting promising potential in controlling the inflammatory response.

The studies also addressed the effect of extracts on mediators PGE2 (prostaglandin E2)[8,20] and LTB4 (leukotriene B4).[20] Specifically, in vivo research on the decoction extract of Cissus gongylodes[20] highlighted its ability to inhibit PGE2 and LTB4 mediators, playing a significant role in controlling the inflammatory process. These mediators stem from arachidonic acid, released in response to inflammation, and play an essential role in amplifying and sustaining the inflammatory response.

It is crucial to note that investigating species from a taxonomic perspective is not limited solely to evaluating their anti-inflammatory effects. It has become imperative to address the systemic impacts resulting from such applications to ensure a comprehensive view of underlying therapeutic safety. For example, Croton campestres[17], included in this investigation, demonstrated edema-reducing properties in both chronic and acute scenarios. However, when evaluated through its hydroalcoholic extract in Drosophila melanogaster, it revealed adverse consequences, including compromised locomotor activity, induction of mortality, and increased cellular stress-related markers.[45]

The analyses of these studies provided a comprehensive and enlightening understanding of the topical anti-inflammatory properties of these plants. The findings

suggested that several Brazilian plant extracts were effective in reducing edema caused by inflammatory agents, indicating potential anti-inflammatory effects. They also revealed mechanisms of action, such as the modulation of inflammatory mediators like prostaglandins, leukotrienes, and cytokines. The influence of geographical and contextual factors was observed, demonstrating the richness of the Brazilian flora as a potential source of anti-inflammatory agents. The discoveries provided a scientific field for the development of specialized plant-based therapies and pointed the way for future research aimed at optimizing these therapies and obtaining a deeper understanding of the underlying mechanisms of their anti-inflammatory properties.

It is essential to note that this study, aimed at examining the anti-inflammatory effects of medicinal plants, is not exempt from inherent limitations. These limitations require a cautious approach in both the delimitation and interpretation of the study. Some potential limitations include the inherent heterogeneity of primary studies, the methodological quality of these studies, editorial oversight that may affect result publication, data access restrictions, contextual and geographical influences, the possibility of bias in the selection of botanical samples, and variations in the utilized methodologies. These considerations enrich the analytical perspective and facilitate a more solid scientific discussion.

5. CONCLUSION

The rich variety of species in the country has piqued researchers' interest in discovering the medicinal benefits of these plants. The results revealed that various Brazilian plant extracts showed remarkable anti-inflammatory properties, and the essential oils extracted from some plants hold promise for reducing edema and the inflammatory response. These conclusions are particularly relevant in the context of skin treatments. The topical application of plant extracts with anti-inflammatory properties can offer a natural and effective approach to treating these conditions. Furthermore, this approach can reduce the need for aggressive chemicals sometimes used in conventional treatments. The study emphasizes the importance of Brazil's biodiversity as a potential source of medicinal compounds. In this context, valuing and preserving the wide variety of medicinal plants found in Brazilian territory can not only lead to additional therapeutic discoveries but also help preserve the environment.

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