

Coronopus didymus (wormseed): an evidence-based review for primary health care

Coronopus didymus (mastruço): uma revisão baseada em evidências para a Atenção Primária à Saúde

Coronopus didymus (mástil): una revisión basada en evidencias para la Atención Primaria a la Salud

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Abstract

Introduction: The use of medicinal plants is a widespread traditional practice, especially in Brazil, with significance in primary health care (PHC). *Coronopus didymus* (mastro) is commonly used in folk medicine because of its potential anti-inflammatory and antioxidant properties. Despite this, scientific evidence supporting its therapeutic use remains limited, requiring a critical analysis to integrate these practices into the Unified Health System (SUS). **Objective:** To evaluate the scientific studies on *C. didymus* between 2003 and 2023, investigating evidence of its therapeutic properties and its applicability in the context of PHC in Brazil. **Methods:** A systematic review was conducted in the PubMed, Embase, and Virtual Health Library (VHL) databases. After searching for the term “*Coronopus didymus*” and applying inclusion and exclusion criteria, 42 articles were analyzed. Duplicate studies, those focused on non-medicinal applications, or involving other plants were excluded. The publications analyzed *in vitro* data, animal models, and population interviews. **Results:** Of the 42 articles analyzed, 14 met the final criteria. The biological activities identified include antioxidant (41.6%), anti-inflammatory (16.6%), anti-arthritis (16.6%), antifungal (8.3%), antipyretic (8.3%), and antiviral (8.3%) properties. The most frequent bioactive compounds were flavonoids, polyphenols, alkaloids, and tannins. Some preclinical studies highlighted promising effects, such as hepatoprotective action, reduction of blood glucose, and wound healing. However, no clinical trials validating these effects in humans were found. **Conclusions:** Although *C. didymus* is widely used in traditional medicine, the lack of robust clinical studies prevents its formal recommendation in PHC. Available evidence is limited to preclinical studies suggesting therapeutic potential in antioxidant and anti-inflammatory properties. There is an urgent need for research to assess its safety, efficacy, and toxicity in humans. Thus, *mastro* still lacks sufficient scientific support to be integrated into SUS as a therapeutic alternative.

Keywords: *Coronopus didymus*; Medicinal plants; Phytotherapy; Primary health care.

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Resumo

Introdução: O uso de plantas medicinais é uma prática tradicional amplamente difundida, especialmente no Brasil, com relevância na Atenção Primária à Saúde (APS). O *Coronopus didymus* é amplamente utilizado na medicina popular devido às suas potenciais propriedades anti-inflamatórias e antioxidantes. Apesar disso, a evidência científica que respalda seu uso terapêutico permanece limitada, exigindo uma análise crítica para integrar essas práticas ao Sistema Único de Saúde (SUS). **Objetivo:** Avaliar a produção científica sobre *Coronopus didymus* (mastruço) entre 2003 e 2023, investigando evidências sobre suas propriedades terapêuticas e sua aplicabilidade no contexto da APS no Brasil. **Métodos:** Foi realizada uma revisão sistemática baseada em evidências nas bases PubMed, Embase e Biblioteca Virtual em Saúde (BVS). Após a busca pelo termo “*Coronopus didymus*” e a aplicação de critérios de inclusão e exclusão, 42 artigos foram analisados. Estudos repetidos, focados em aplicações não medicinais ou com outras plantas foram excluídos. As publicações analisaram dados *in vitro*, em modelos animais e em entrevistas populacionais. **Resultados:** Dos 42 artigos analisados, 14 preencheram os critérios finais. As atividades biológicas identificadas incluem propriedades antioxidantes (41,6%), anti-inflamatórias (16,6%), antiartríticas (16,6%), antifúngicas (8,3%), antipiréticas (8,3%), e antivirais (8,3%). Os compostos bioativos mais frequentes foram flavonoides, polifenóis, alcaloides e taninos. Alguns estudos pré-clínicos destacaram efeitos promissores, como ação hepatoprotetora, redução da glicose sanguínea e cicatrização de feridas. No entanto, não foram encontrados ensaios clínicos que avaliassem esses efeitos em humanos. **Conclusões:** Embora o *Coronopus didymus* seja amplamente utilizado na medicina tradicional, a falta de estudos clínicos robustos impede sua recomendação formal na APS. As evidências disponíveis são limitadas a estudos pré-clínicos, que sugerem potencial terapêutico em propriedades antioxidantes e anti-inflamatórias. Há uma necessidade urgente de pesquisas que avaliem sua segurança, eficácia e toxicidade em humanos. Assim, o mastruço ainda carece de suporte científico suficiente para ser integrado ao SUS como alternativa terapêutica.

Palavras-chave: *Coronopus didymus*; Plantas medicinais; Fitoterapia; Atenção Primária à Saúde.

Resumen

Introducción: El uso de plantas medicinales es una práctica tradicional ampliamente difundida, especialmente en Brasil, con relevancia en la Atención Primaria a la Salud (APS). *Coronopus didymus* (mastuerzo) se utiliza comúnmente en la medicina popular debido a sus potenciales propiedades antiinflamatorias y antioxidantes. A pesar de esto, la evidencia científica que respalde su uso terapéutico sigue siendo limitada, lo que requiere un análisis crítico para integrar estas prácticas al Sistema Único de Salud (SUS). **Objetivo:** Evaluar la producción científica sobre *Coronopus didymus* entre 2003 y 2023, investigando evidencia sobre sus propiedades terapéuticas y su aplicabilidad en el contexto de la APS en Brasil. **Métodos:** Se realizó una revisión sistemática basada en evidencia en las bases de datos PubMed, Embase y la Biblioteca Virtual en Salud (BVS). Después de buscar el término “*Coronopus didymus*” y aplicar los criterios de inclusión y exclusión, se analizaron 42 artículos. Se excluyeron los estudios repetidos, aquellos centrados en aplicaciones no medicinales o con otras plantas. Las publicaciones analizaron datos *in vitro*, en modelos animales y entrevistas poblacionales. **Resultados:** De los 42 artículos analizados, 14 cumplieron con los criterios finales. Las actividades biológicas identificadas incluyen propiedades antioxidantes (41,6%), antiinflamatorias (16,6%), antiartríticas (16,6%), antifúngicas (8,3%), antipiréticas (8,3%) y antivirales (8,3%). Los compuestos bioactivos más frecuentes fueron flavonoides, polifenoles, alcaloides y taninos. Algunos estudios preclínicos destacaron efectos prometedores, como la acción hepatoprotectora, reducción de glucosa en sangre y cicatrización de heridas. Sin embargo, no se encontraron ensayos clínicos que validaran estos efectos en humanos. **Conclusiones:** Aunque *Coronopus didymus* se utiliza ampliamente en la medicina tradicional, la falta de estudios clínicos robustos impide su recomendación formal en la APS. Las evidencias disponibles se limitan a estudios preclínicos que sugieren un potencial terapéutico en propiedades antioxidantes y antiinflamatorias. Existe una necesidad urgente de investigaciones que evalúen su seguridad, eficacia y toxicidad en humanos. Por lo tanto, el mastruerzo aún carece de apoyo científico suficiente para ser integrado al SUS como una alternativa terapéutica.

Palabras clave: *Coronopus didymus*; Mastuerzo; Plantas medicinales; Fitoterapia; Atención Primaria de Salud.

INTRODUCTION

The use of medicinal plants is ancient, both in Brazil and around the world. Their use has been extremely relevant to human evolution and the history of medicine, with plants being used to produce, from specific parts, herbal products and homemade preparations such as infusions, poultices, and decoctions that act on the body. These preparations are used in different stages of the health-disease process, such as in the relief of symptoms, in the treatment of defined ailments, as well as in the promotion of health and the prevention of diseases.

The use of medicinal plants has reached such an extensive magnitude that 81% of the world's population uses them,¹ demonstrating the breadth of the practice and its evident ease of access, an important point highlighted by the World Health Organization (WHO) in the Alma-Ata Declaration in 1978.²

Approximately 40% of the medicines available in current therapy were developed from natural sources: 25% from plants, 13% from microorganisms and 3% from animals.³ Despite this, studies are still needed to investigate and validate the efficacy and safety of numerous plants for specific applications.

In primary health care (PHC), the use of medicinal plants can offer several benefits, such as expanding therapeutic options, reducing costs, valuing popular knowledge and stimulating the local economy. In the context of the Brazilian Unified Health System (SUS), this practice is especially encouraged through Integrative and Complementary Health Practices (PICS).⁴

The incorporation of medicinal plants into SUS follows guidelines from the National Policy on Medicinal Plants and Phytotherapeutic Products, established in 2006 by the Ministry of Health, the federal body responsible for formulating public health policies. To this end, scientific evidence of efficacy and safety, quality control, health registration, and feasibility of production and distribution in the public health system are required.^{5,6}

The implementation of this policy involves the joint action of bodies such as the Secretariat of Science, Technology and Innovation and the Economic-Industrial Complex of Health (SECTICS), the National Health Surveillance Agency (Anvisa), the Oswaldo Cruz Foundation (Fiocruz), the Ministry of Agriculture and Livestock (MAPA), and the Brazilian Institute of Environment and Renewable Natural Resources (IBAMA), especially when it comes to native species.^{5,7}

The aim of this study was to evaluate, both quantitatively and qualitatively, the scientific production on *Coronopus didymus* (L) Sm., popularly known as mastruço or mastruz, mentruz, mentrasto, mastruz-miúdo, and mastruço-rasteiro, among others. This plant belongs to the family Brassicaceae, is an annual or biennial herbaceous plant with a creeping habit and branched stems that spread across the ground. Its leaves are deeply lobed, with serrated margins and a characteristic strong odor when crushed. The flowers are small, greenish and whitish, with reduced or absent petals, gathered in terminal inflorescences. The fruit is a flattened silique, divided into two rounded lobes. The species is widely distributed in temperate and subtropical regions, being found in disturbed environments such as sidewalks, crops, and vacant lots. It is often considered a weed, but it has a history of use in traditional medicine and is widely used in various regions of the world due to beliefs about its medicinal properties, being traditionally used in the treatment of inflammation, pain, and digestive problems.⁸ Furthermore, in popular opinion surveys conducted in various locations, such as São Luiz Gonzaga, Tamil Nadu, and São Paulo, the plant is frequently considered effective in relieving pain and inflammation.⁹⁻¹¹

Mastruço is one of the most widely used plants in traditional medicine in Rio Grande do Sul, as indicated by SES/RS Ordinance 588/2017, which recognizes its therapeutic potential. However, despite this official recommendation, the scientific literature does not provide sufficient evidence to support its use for medicinal purposes. Studies indicate that the effectiveness of mastruço still lacks rigorous scientific proof, leading to the need for more research to validate its properties and ensure its safety for health. This discrepancy between traditional practice and scientific evidence highlights the importance of robust scientific support for the use of medicinal plants.

The analysis in this review seeks to deepen the understanding of the widespread use of this plant in traditional medicine, especially since it is commonly used in the treatment of frequent symptoms in PHC complaints, as it is a widely known and popularly used plant. These aspects justify the importance of investigating its properties and applications, considering the relevance of integrating traditional knowledge into health practices. Although the relationship with the principle of comprehensiveness of SUS is not direct, the recognition and appreciation of traditional use can contribute to broader and more contextualized care, aligned with the reality of users.

The National Policy on Medicinal Plants and Herbal Medicines, from 2006, in one of its resolutions, aims to promote and value popular practices associated with the use of medicinal plants and homemade preparations.¹² Thus, the present work aimed to discuss and analyze the use of the plant *C. didymus* in the context of family and community medicine.

This review is part of a series of actions and projects related to the Intersectoral Policy on Medicinal Plants and Herbal Medicines of the municipality of Nova Petrópolis (RS), which has been using medicinal plants in basic health units (UBSs) since 2005. In the current phase, new species with potential for local production and inclusion in UBSs are being considered, and the scientific literature is being reviewed to assist in decision-making.

The aim of this study was to conduct a critical and detailed analysis of the existing scientific production regarding the medicinal use of *C. didymus*, focusing on the available evidence on its therapeutic properties. This research seeks to investigate and understand both the biological effects observed in experimental studies and the implications of this use in traditional medicine, especially in the context of PHC in Brazil, with an emphasis on family and community medicine practices. Furthermore, this work aims to improve scientific knowledge about the plant's therapeutic potential, particularly in the areas of anti-inflammatory, antioxidant, analgesic, and other applications mentioned in previous studies, contributing to the strengthening of integrative and complementary practices within SUS and promoting a more solid foundation for the use of medicinal plants in public health, highlighting the available evidence regarding their therapeutic properties.

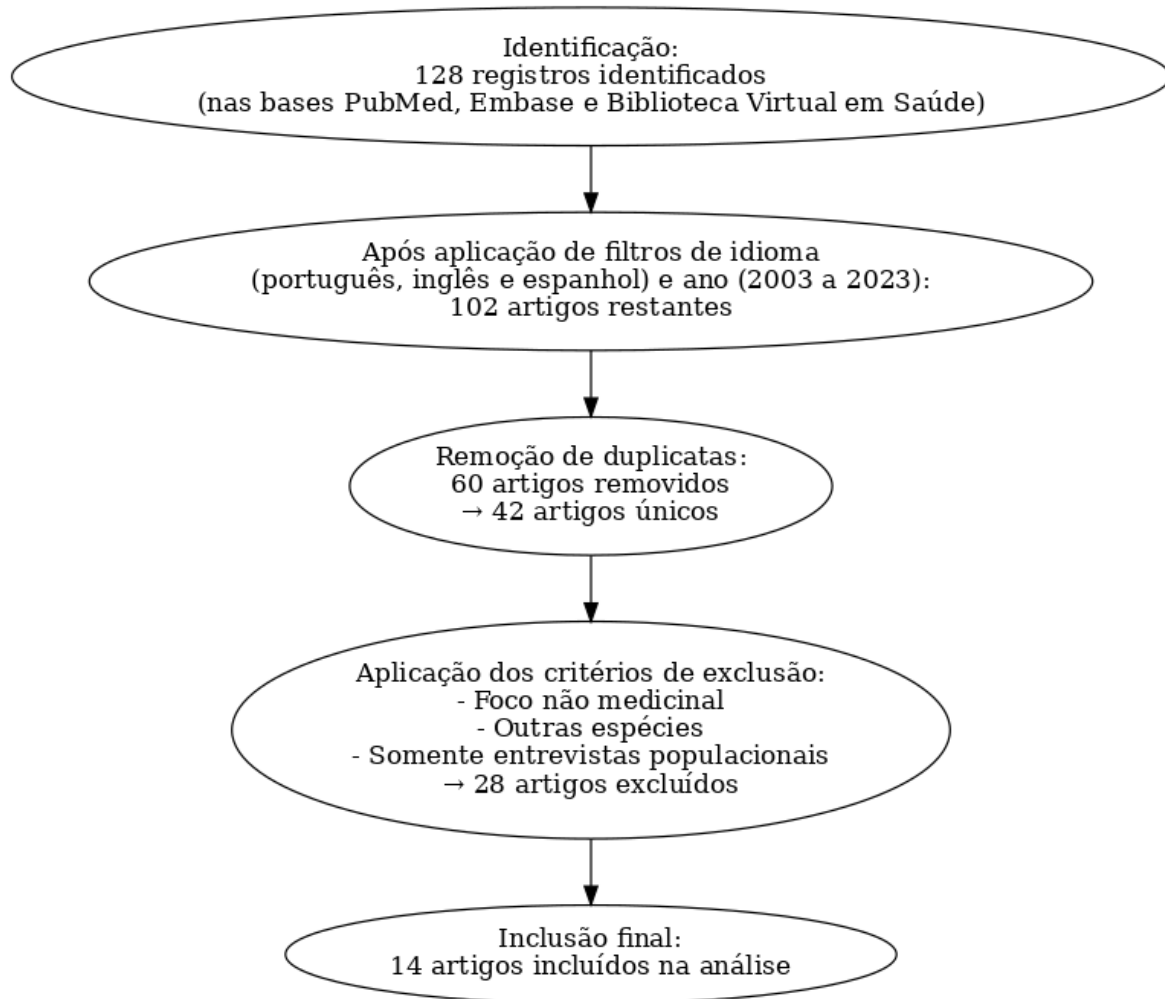
METHODS

A systematic review based on evidence was conducted on the species *C. didymus*, with an emphasis on its medicinal applications in the context of PHC. The review was conducted between November 2023 and January 2024, and included scientific publications indexed in the PubMed (MEDLINE), Embase, and Virtual Health Library (VHL) databases. The search term used was exclusively "*Coronopus didymus*," as it is the official scientific name of the plant studied and is directly related to the cultivation of the species at the Nova Petrópolis Training Center (CETANP).

The choice of a systematic review is justified by the exploratory nature of the study, which aimed to collect, organize, and critically discuss the available scientific knowledge on the therapeutic properties of the plant, encompassing different types of evidence—*in vitro*, *in vivo*, and observational. The guiding question that guided this review was: "What scientific evidence is available on the therapeutic effects of the plant *Coronopus didymus* and its possible applicability in primary health care in Brazil?"

Inclusion and exclusion criteria for the studies were defined beforehand. Scientific publications that met the following criteria were included: studies published between 2003 and 2023, written in Portuguese, English, or Spanish, and that directly addressed the medicinal effects of the plant *C. didymus*. Articles using any type of experimental model were considered eligible, including *in vitro*, *in vivo* (in animal models), or observational studies that presented experimental analysis of the plant's therapeutic properties. The selection focused on research that evaluated the plant's pharmacological properties. Duplicate studies across databases, studies focused on non-medicinal purposes (such as soil remediation), studies with other plant species or that mentioned the plant only incidentally, and articles based exclusively on population interviews or without experimental evaluation of therapeutic properties were excluded.

The initial search resulted in 128 publications. After applying the language and publication year filters, 102 articles remained. After excluding duplicates across databases, 42 distinct articles were selected. The aforementioned exclusion criteria were then applied, leaving 14 articles considered eligible for the final analysis (Figure 1).



Source: Own work.

Figure 1. Flowchart of the process for identifying, screening, excluding, and including articles used in the review.

The study evaluation process was carried out in two review stages. First, two groups of independent reviewers evaluated the selected articles in the three databases. Then, a second round of peer review was conducted between the groups, aiming to ensure greater rigor in the selection and classification of articles. This double process was implemented to reduce bias and increase consistency in the analysis.

Data extraction from eligible articles was done using the Zotero program, used to manage and archive references, and Microsoft Excel, which served to tabulate and systematize the following variables: study type, outcomes investigated, presence of exclusion criteria, active ingredients identified, part of the plant used, preparation method, and level of evidence of the articles.

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RESULTS

The study described initially yielded 128 publications. After applying filters, this was reduced to 102 articles. Subsequently, an evaluation was conducted to find duplicate articles across the databases, resulting in a final number of 42 articles to be evaluated. Of these, 12 were tested *in vitro* and 8 in animals, and 6 publications presented results from interviews with the population of specific regions, evaluating its popular use. After applying the exclusion criteria, only 14 articles remained, which were used as the basis for the review. No scientific studies were found investigating the medicinal use of *C. didymus* in humans, highlighting the need for further research to evaluate its potential therapeutic properties. A brief description of the included studies is provided in Table 1.^{5,13-23}

Table 1. Summary of key findings and methodological designs.

Authors	Method	Part of plant used	Plant derivative used	Phytochemical compound	Outcome
Muzammi et al. ¹³	<i>In vitro</i>	Leaves	Alcoholic extract	Polyphenols	Antioxidants, antiproliferatives and alpha-glucosidase activity
Saleem et al. ¹⁴	Animals	Whole plant	Aqueous and ethanolic and aqueous extracts	Flavonoids	Antiarthritic and anti-inflammatory Chrysoeriol showed better protective effect than the glycoside,
Shakoor et al. ¹⁵	<i>In vitro</i>	Not specified	Aqueous solution	Flavonoids	inhibited superoxide anion produced enzymatically by the xanthine/xanthine oxidase system
Mantena et al. ¹⁶	<i>In vitro</i>	Not specified	Crude methanolic extract	Flavonoids	<i>C. didymus</i> inhibited <i>A. fumigatus</i> by up to 27.3% and <i>A. niger</i> by 48%.
Noreen et al. ²³	Animals	Whole plant	Aqueous extract	Flavonoids	Antiallergic, antipyretic, hypoglycemic, and hepatoprotective.
Saleem et al. ¹⁷	<i>In vitro</i>	Aerial parts	Ethanoic extract	5,7,4'-trihydroxy-3'-methoxyflavone-4'-O-β-D-glucoside, 5,7,4'-trihydroxy-3'-methoxyflavone-4'-O-(6"-acetyl)-β-D-glucoside and 5,7,4'-trihydroxy-3'-methoxyflavone	Anticancerous.
Busnardo et al. ¹⁸	Animals	Whole plant	Aqueous extract	Delphinidin-3-glucoside, diosmetin, 3-feruloyl-4,5-dicaffeoylquinic acid and gallic acid	Antiarthritic and safe for long-term use.
Prabhakar et al. ¹⁹	Animals	Leaves	Hydroalcoholic extract	Not specified	Anti-inflammatory

Continue...

Table 1. Continuation.

Authors	Method	Part of plant used	Plant derivative used	Phytochemical compound	Outcome
Prabhakar et al. ²⁰	Animals	Not specified	Aqueous extract	Not specified	Radioprotective and oxidative stress reducer
Ruffa et al. ²²	Animals	Not specified	Aqueous extract	Not specified	Reduces oxidative stress
Nitz et al. ²¹	<i>In vitro</i>	Not specified	Active extract	Flavonoids	HIV-1 antiviral
Ministério da Saúde ⁵	Animals	Not specified	Aqueous extract	Not specified	Aids in wound healing and significantly increases the number of fibroblasts

Source: Own work.

Of these remaining articles, the main effects reported in clinical trials with *C. didymus* were: antioxidant: 41.6%;^{13-16,24} anti-arthritic: 16.6%;^{14,17} anti-inflammatory: 16.6%;^{14,18} and free radical scavenging: 16.6%.^{16,19} All effects are described in detail in Table 2.

Table 2. Results of the biological activities evidenced.

Biological effect	Number of studies	Percentage (%)
Antioxidant	5	41.6
Antifúngal	1	8.3
Anti-inflammatory	2	16.6
Antiarthritic	2	16.6
Antiallergic	1	8.3
Hepatoprotective	1	8.3
Free radical scavenger	2	16.6
Radioprotective	1	8.3
Anticancer activity	1	8.3
Hypoglycemic	1	8.3
Antiviral	1	8.3
Wound healing	1	8.3
Antiproliferative	1	8.3

Source: Own work.

Based on the results obtained, it was observed that, of the 18 valid articles, 12 (66.6%) specified the presence of chemical compounds in the analyzed samples, while 6 (33.3%) did not present this information. Among the 12 articles that mentioned compounds, it was possible to identify a diversity of chemical substances, which reinforces the multifactorial nature of herbal medicines, whose action is generally not due to a single isolated active ingredient, but rather to the combination of various constituents with synergistic effects.

Among the compounds reported, flavonoids were the most frequent, cited in 50% of the articles that specified compounds. Polyphenols, ethyl acetate (an organic solvent used in the extraction of chemical compounds from the plant), chlorogenic acid, alkaloids, tannins, and glucosinolates were mentioned in only one article each, corresponding to 8.3% (1/12) of the articles valid for this analysis. It is worth highlighting that, in some cases, these compounds acted as chemical markers — used for quality control

and standardization of samples — rather than as directly responsible for a particular pharmacological action. This variety of compounds found points to the complexity of the chemical composition of the plants used and may be fundamental to guiding future research, especially with regard to the characterization and standardization of extracts with specific therapeutic purposes.

One of the animal studies¹⁶ showed that the aqueous extract of *C. didymus* presented significant antiallergic effects, evidenced by the reduction of allergic reactions in experimental models. In addition, the extract demonstrated a remarkable antipyretic effect, leading to a decrease in fever in treated animals. Regarding the control of blood glucose levels, the extract resulted in a significant reduction, suggesting benefits for the management of diabetes. Finally, it was observed that the extract provided substantial hepatoprotective action, helping to prevent liver damage and maintain its health.

Saleem et al.¹⁷ investigated the anti-arthritic potential of the aqueous extract of *C. didymus* in Wistar rats, demonstrating that the treatment significantly reduced inflammation and pain in the joints in arthritis models. In addition, safety tests showed that the extract did not cause toxicity in the vital organs of the animals. The authors concluded that *C. didymus* presents promising therapeutic efficacy for arthritis, with a favorable safety profile, recommending further studies on its mechanisms of action.

A study by Busnardo et al.¹⁸ sought to evaluate the anti-inflammatory effect of the hydroalcoholic extract of *C. didymus* leaves, using models of pleurisy and paw edema in mice. The authors concluded that this plant has remarkable anti-inflammatory properties, possibly due to the inhibition of inflammatory mediators and enzymes associated with the inflammatory process. Prabhakar et al.²⁰ evaluated and optimized the radioprotective capacity of the most potent fraction of an aqueous extract of *C. didymus* in Swiss albino mice exposed to whole-body γ radiation; they assessed the antioxidant status and lipid peroxidation in the livers of surviving mice. The study results showed that the CDF1 fraction of the *C. didymus* extract offered up to 70% radioprotection in treated mice. In addition, in surviving mice, CDF1 restored normal levels of antioxidant enzymes and reduced lipid peroxidation, suggesting a reduction in oxidative stress caused by radiation.

Nitz et al.²¹ investigated the impact of the medicinal plants *C. didymus* and *Calendula officinalis* on tissue regeneration and healing speed. Histological and morphometric analyses were performed to evaluate the effectiveness of the treatments. The results indicated that both plant extracts produced a significant improvement in the healing process compared to the control group, with *Calendula officinalis* showing a more pronounced effect in reducing healing time and improving the quality of regenerated tissue.

According to *in vitro* studies, it was possible to conclude that *C. didymus* leaf extracts contain a rich composition of polyphenols that contribute to their antioxidant, antiproliferative and antidiabetic properties.¹⁰ Flavonoids isolated from the aerial parts of *C. didymus* possess significant cytotoxic activity against tumor cells.¹⁴ O-glycosylation of chrysoeriol from *C. didymus* improves its antioxidant properties and reactivity with free radicals. *C. didymus* appears to be an herb with antiviral potential against a range of RNA and DNA viruses.²² This plant has antioxidant, antidiabetic, anti-inflammatory, and antiproliferative activity.¹⁵ Flavonoid compounds isolated from *Coronopus* have shown significant cytotoxic activity against cancer cell lines.²³ Certain fractions of the plant contain bioactive compounds that may protect against oxidative stress, suggesting the plant's potential as a source of antioxidant agents.¹⁹

CONCLUSION

This review showed that the available scientific evidence on *C. didymus* is mostly concentrated in preclinical studies, conducted *in vitro* or with animal models. These studies suggest therapeutic properties,

such as antioxidant, anti-inflammatory, hepatoprotective, hypoglycemic, and wound-healing actions. However, no controlled clinical trials in humans were found, which substantially limits the direct applicability of this evidence in the clinical practice of PHC in Brazil.

Although Anvisa allows the simplified registration of medicinal plants with proven traditional use for at least 30 years, provided there are no reports of significant toxicity, the studies included in this review do not document this continuous history of safe and traditional use with this exposure time. In addition, population interviews were excluded, precisely because of the purpose of this review, which aims to evaluate experimental and pharmacological evidence with greater methodological rigor. Therefore, there is not enough basis, neither scientific (clinical trials) nor traditional (documented use ≥ 30 years), to justify at this time the therapeutic incorporation of *C. didymus* into SUS, whether through conventional means or through simplified registration.

Given this scenario, the study highlights a significant gap in the scientific literature and underscores the need for new studies with greater methodological rigor. Thus, it is recommended that *C. didymus* be included in clinical research agendas, preferably by public educational institutions and through calls for proposals to encourage research on medicinal plants. Such a direction would bring a proactive dimension to the debate, expanding the scientific value of the discussion and strengthening the species' potential as a possible member of the group of medicinal plants and phytotherapeutic products officially recognized within the scope of SUS.

CONFLICT OF INTERESTS

Nothing to declare. mastrução

AUTHORS' CONTRIBUTIONS

JGT: Project management, Formal analysis, Conceptualization, Data curation, Writing – first draft, Writing – review & editing, Investigation, Methodology, Funding acquisition, Resources, Software, Supervision, Validation, Visualization. FJP: Project management, Formal analysis, Conceptualization, Data curation, Writing – original draft, Writing – review & editing, Investigation, Methodology, Funding acquisition, Resources, Software, Supervision, Validation, Visualization. LVT: Project management, Formal analysis, Conceptualization, Data curation, Writing – original draft, Writing – review & editing, Investigation, Methodology, Funding acquisition, Resources, Software, Supervision, Validation, Visualization. MV: Project management, Formal analysis, Conceptualization, Data curation, Writing – original draft, Writing – review & editing, Investigation, Methodology, Funding acquisition, Resources, Software, Supervision, Validation, Visualization. GCA: Project management, Formal analysis, Conceptualization, Data curation, Writing – original draft, Writing – review & editing, Investigation, Methodology, Funding acquisition, Resources, Software, Supervision, Validation, Visualization.

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