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# **CURRENT OVERVIEW OF CLINICAL RESEARCH WITH HERBAL TOOTHPASTES IN BRAZIL: A SCOPING REVIEW<sup>1</sup>**

## **PANORAMA ATUAL DE PESQUISAS CLÍNICAS COM DENTIFRÍCIOS HERBAIS NO BRASIL: UMA REVISÃO DE ESCOPO**

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### **ABSTRACT**

Toothpastes are multipurpose cosmetic products that play an important role in daily oral hygiene, and natural formulations have attracted scientific and industrial interest worldwide. Despite Brazil's favorable biodiversity, knowledge gaps remain regarding the state of the art of plant-derived products in this field. This study aimed to map current clinical research on herbal toothpastes in Brazil. A scoping review was conducted by searching the ReBEC platform for the period from 2011 to 2025, using the descriptor *dentifrício* ('toothpaste') and including trials conducted in humans. The extracted data were synthesized narratively. The final sample consisted of ten studies on herbal toothpastes, corresponding to 22.7% of clinical studies on toothpastes. A greater temporal concentration was observed from 2020 onward. The population profile consisted mainly of adults with good general and oral health, with marked sample heterogeneity, ranging from dozens to hundreds of volunteers, and follow-up periods ranging from one week to one year. The toothpastes were predominantly uniherbal formulations, with green tea and peppermint derivatives being the most prominent. Plant-based compounds were used as therapeutic or flavoring agents. Only 40% of the herbal toothpastes contained fluoride, which may limit their anticaries

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effect and suggests that these formulations should be used with caution. Despite the limitations of this exploratory study, the findings indicate a low number of phase I clinical trials on herbal toothpastes in Brazil, highlighting the need for further validation of their safety and efficacy, as well as for biotechnological innovation in new national products.

**Keywords:** Toothpastes. Dentifrices. Biological products. Phytotherapy.

## RESUMO

Dentifrícios são cosméticos multifuncionais importantes para a higiene bucal diária, e suas formulações naturais têm despertado interesse científico e industrial no cenário global. Apesar da biodiversidade brasileira favorável, ainda há lacunas de conhecimento sobre o estado da arte dos produtos derivados de plantas nessa temática. Este estudo objetivou mapear a produção atual de pesquisas clínicas com dentifrícios herbais no Brasil. Foi realizada uma revisão de escopo, com busca na plataforma ReBEC no período de 2011 a 2025, utilizando o descritor *dentifrício* e incluindo ensaios conduzidos em seres humanos. Os dados extraídos foram sintetizados de forma narrativa. A amostra final foi composta por dez estudos com dentifrícios herbais, correspondendo a 22,7% dos estudos clínicos com dentifrícios. Observou-se maior concentração temporal a partir de 2020. O perfil populacional foi composto principalmente por adultos com boa saúde geral e bucal, com acentuada heterogeneidade amostral, variando de dezenas a centenas de voluntários, e períodos de acompanhamento de uma semana a um ano. Os dentifrícios apresentaram predominantemente formulações uniherbais, com maior destaque para derivados de chá verde e hortelã-pimenta. Os compostos vegetais foram utilizados como agentes terapêuticos ou flavorizantes. Apenas 40% dos dentifrícios herbais continham flúor, o que pode limitar seu efeito anticárie e sugere que essas formulações devem ser utilizadas com cautela. Apesar das limitações deste estudo exploratório, os achados indicam baixa casuística de ensaios clínicos de fase I no Brasil sobre dentifrícios herbais, evidenciando a necessidade de maior validação de sua segurança e eficácia, bem como de inovação biotecnológica em novos produtos nacionais.

**Palavras-chave:** Cremes dentais. Dentifrícios. Produtos biológicos. Fitoterapia.

## INTRODUCTION

Toothbrushing with toothpaste is considered the most widespread oral hygiene practice worldwide and is widely recommended by health professionals (Lisbôa;

Abegg, 2006). This practice combines the mechanical action of toothbrush bristles with the abrasive and therapeutic agents present in toothpaste formulations, enhancing dental biofilm removal and contributing to the prevention of oral diseases, such as dental caries, gingivitis, and halitosis (Claydon, 2008; Lisboa; Abegg, 2006). Its ease of use, low cost, and proven effectiveness make this strategy accessible and effective for maintaining population oral health (Claydon, 2008).

In recent decades, interest among the population and industry in natural products as alternatives to the synthetic compounds traditionally used in various health-related fields has grown significantly (Brasil, 2015). This movement is driven by greater concern regarding the toxicity of chemical substances, the search for greater pharmacological activity and more biocompatible products, as well as the need for more affordable options for the population (Francisco, 2009). In the context of oral health, this trend has encouraged the investigation of plant-based compounds with antimicrobial, anti-inflammatory, antioxidant, and healing properties, which may act as adjuvants in the prevention and control of oral diseases when incorporated into toothpastes (Amanpour *et al*, 2023).

Brazil has extensive biodiversity, comprising both native and introduced species and representing around 20% of the world's flora (Cherobin *et al*, 2022). This biological heritage makes the country strategically important for the development of health-related natural products and represents a vast field for the bioprospecting of bioactive substances with therapeutic potential (Cherobin *et al*, 2022; Domingues *et al*, 2021). In Dentistry, this plant diversity offers opportunities for the formulation of herbal toothpastes, including powders, extracts, essential oils, and other derivatives with antiseptic, anti-inflammatory, and healing properties, while also contributing to the development of more sustainable and affordable products (Domingues *et al*, 2021).

Despite this promising outlook, there remains a gap in the national scientific literature regarding clinical trials that evaluate the efficacy and safety of toothpastes containing herbal agents. Under Brazilian legislation, toothpastes are classified as personal hygiene cosmetics and do not require clinical studies for validation before commercialization (Brasil, 2022). However, within the pyramid of scientific evidence, long-term studies are needed to reduce the risk of adverse reactions, such as contact allergies affecting the lips and oral mucosa (Groot, 2017).

Therefore, it is essential to map existing scientific efforts and identify which active ingredients have been most frequently investigated in clinical research. This study aimed to assess the current landscape of clinical trials registered in Brazil that investigate herbal toothpastes.

## MATERIAL AND METHODS

### Study Design

A quantitative, bibliometric, cross-sectional study based on online document analysis was conducted and structured as a scoping review. Scoping studies, or scoping reviews, aim to map the main concepts underlying a given field of knowledge, examine the extent, scope, and nature of the available research, summarize and disseminate research findings, and identify existing knowledge gaps (Mak; Thomas, 2022).

To accurately identify the best available information, the PVO framework was used as an exploratory search strategy, in which 'P' refers to the problem, 'V' to the variables or limits, and 'O' to the outcomes (Menezes *et al*, 2015). Based on this framework, the search considered toothpastes as the 'P', a two-decade time frame as the 'V', and categorical variables related to the study population and herbal toothpastes investigated in clinical studies as the 'O'.

Raw data were collected from self-reported public research records available in the Brazilian Registry of Clinical Trials or ReBEC (Brasil, 2025a), an electronic database of clinical studies conducted in Brazil. Data collection was carried out between April and June 2025.

### Eligibility Criteria

The search strategy used the term *dentifrício* ('toothpaste') applied to the intervention field. After the initial retrieval, records were screened for eligibility according to the following criteria: clinical studies conducted in humans, dentifrices containing plant-based compounds, and minimum availability of information for analysis.

All clinical trial records registered between 2011 and 2025 that involved the use of toothpastes containing natural plant-based agents, used alone or in combination, and administered to humans were included. Studies that exclusively evaluated other dental products, such as mouthwashes, varnishes, or cariostatic agents, as well as those containing only mineral or synthetic compounds, were excluded. All information available on the online platform was read in full, including titles and detailed descriptions of study interventions, eligibility criteria, and outcomes. Sample stratification was based on the PRISMA 2020 flow diagram (Page *et al*, 2021).

The categorical variables considered in the review were study design, year of registration on the platform, number of participants, follow-up period, plant species

used in the dentifrice, function of the herbal component, and presence of fluoride in the formulation. The extracted data were synthesized in narrative and tabular form.

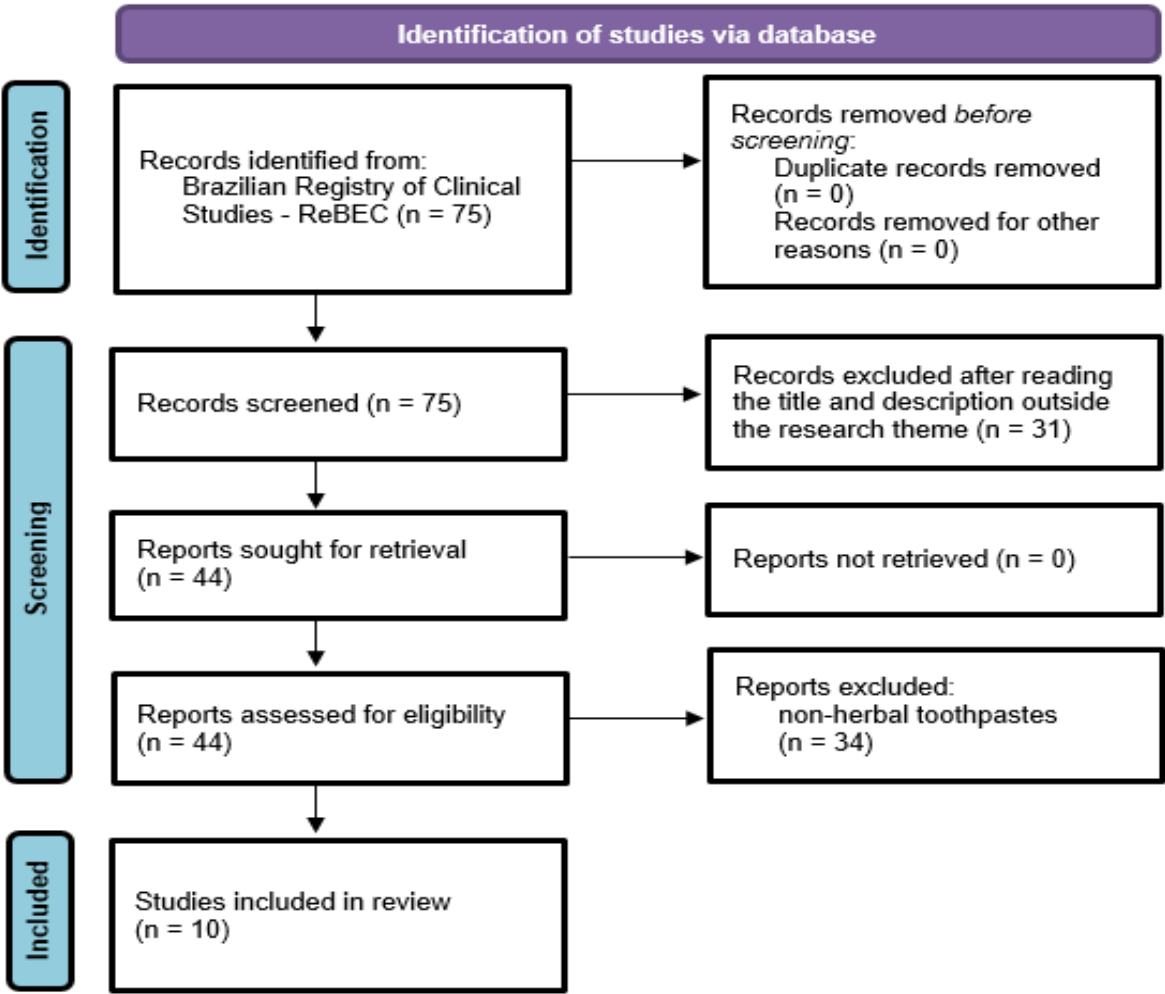
Ethical Aspects

This study was conducted in accordance with the bioethical principles currently applicable in Brazil to research using publicly accessible secondary data, as established by National Health Council Resolution No. 510/2016.

RESULTS

The search on the ReBEC platform identified 75 records related to dental products. Of these, 31 were excluded because they did not refer to toothpastes, as they evaluated mouthwashes, varnishes, or cariostatic agents. Therefore, 44 studies on toothpastes remained. Among them, 10 studies (22.7%) met the inclusion criteria for herbal toothpastes (Figure 1).

Figure 1: Flow diagram for scope review.



Source: Research Data.

The records were distributed throughout the analyzed period, with a higher concentration between 2020 and 2024. This pattern may indicate a recent increase in interest in herbal toothpastes in Brazil, as well as greater awareness and use of the national clinical trials registry platform (Table 1).

**Table 1:** Studies with herbal toothpastes based on the year of registration.

| ReBEC code  | Year |
|-------------|------|
| RBR-4x9pk3m | 2024 |
| RBR-7dz5y9x | 2024 |
| RBR-7scgp3h | 2021 |
| RBR-6kr745  | 2019 |
| RBR-25b7xh  | 2021 |
| RBR-5t258m  | 2021 |
| RBR-3424pzq | 2021 |
| RBR-55g6cm  | 2020 |
| RBR-34r4dz  | 2020 |
| RBR-9f3ctb  | 2018 |

**Source:** Research Data.

Sample heterogeneity was observed among the records analyzed, with the number of recruited volunteers ranging from 19 to 200 participants. Most studies were conducted with healthy adults, although some included specific groups, such as older adults, patients with periodontal disease, or individuals with implant-supported dentures. Herbal toothpastes were associated with different outcome measures, including plaque control, gingivitis, dentin hypersensitivity, halitosis, and denture stomatitis (Table 2).

**Table 2:** Studies with herbal toothpastes based on research design.

| ReBEC code  | Sample number and health condition                                                                                                                                                                            |
|-------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| RBR-4x9pk3m | 60 young adult patients with healthy body systems and good oral health                                                                                                                                        |
| RBR-7dz5y9x | 200 healthy adults with at least 15 uncrowned permanent natural teeth, excluding third molars, with a mean baseline gingival index $\geq 1.5$ , and generalized periodontitis stages II or III, grades A or B |
| RBR-7scgp3h | 60 patients systemically healthy between 18 and 60 years old, with partial dentures supported by definitive implants installed for more than 6 months                                                         |
| RBR-6kr745  | 100 individuals with healthy body systems, of any age, both genders, completely edentulous, users of upper complete dentures for over one year and with the presence of denture stomatitis in the upper arch  |
| RBR-25b7xh  | 19 adults with healthy body systems and good oral health                                                                                                                                                      |
| RBR-5t258m  | 80 elderly people, over 65 years old, healthy, with gingivitis                                                                                                                                                |
| RBR-3424pzq | 80 adults $\geq 18$ years old, with a tooth with dentin hypersensitivity greater than or equal to 4                                                                                                           |
| RBR-55g6cm  | 90 adults, with healthy body systems and at least 20 uncrowned natural permanent teeth, excluding third molars, 6 teeth with a bleeding site on probing and an average gingival index $\geq 1.5$              |
| RBR-34r4dz  | 100 volunteers of both genders, $\geq 18$ years old, with at least 20 natural teeth and 6 incisors and upper canines without caries, restorations or prostheses                                               |
| RBR-9f3ctb  | 100 volunteers without systemic diseases and with healthy oral conditions, both genders, between 18 and 45 years old, with at least 20 healthy teeth                                                          |

**Source:** Research Data.

Clinical studies on herbal toothpastes showed highly heterogeneous follow-up periods, ranging from one week to one year. Follow-up periods of 30 days or four weeks were the most frequent, accounting for 40% of the sample. Thirty percent of the registered studies did not report the duration of clinical monitoring (Table 3).

**Table 3:** Studies with herbal toothpastes with clinical monitoring.

| ReBEC code  | Clinical follow-up |
|-------------|--------------------|
| RBR-4x9pk3m | 4 weeks            |
| RBR-7dz5y9x | 12 months          |
| RBR-7scgp3h | Not informed       |
| RBR-6kr745  | 1 week             |
| RBR-25b7xh  | Not informed       |
| RBR-5t258m  | 4 weeks            |
| RBR-3424pzb | 6 months           |
| RBR-55g6cm  | Not informed       |
| RBR-34r4dz  | 30 days            |
| RBR-9f3ctb  | 30 days            |

**Source:** Research Data.

Sixteen different plant species were identified. Most studies evaluated toothpastes containing a single plant species (seven studies; 70%), whereas multiherbal formulations included three to four species (three studies; 30%). The most frequently reported individual species were green tea (*Camellia sinensis*) and peppermint (*Mentha piperita*) (Table 4).

**Table 4:** Studies with herbal toothpastes based on plant origin.

| ReBEC code  | Plant species                                                                                                                                                                              |
|-------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| RBR-4x9pk3m | Dragon's Blood ( <i>Croton lechleri</i> )                                                                                                                                                  |
| RBR-7dz5y9x | Cramberry ( <i>Vaccinium macrocarpon</i> ), Aloe ( <i>Aloe vera</i> ), Calendula ( <i>Calendula officinalis</i> ), Green tea ( <i>Camellia sinensis</i> )                                  |
| RBR-7scgp3h | Green tea ( <i>Camellia sinensis</i> )                                                                                                                                                     |
| RBR-6kr745  | Melaleuca ( <i>Melaleuca alternifolia</i> ), White pine ( <i>Pinus strobus</i> ), Black sucupira ( <i>Bowdichia virgilioides Kunth</i> )                                                   |
| RBR-25b7xh  | Peppermint ( <i>Mentha piperita</i> )                                                                                                                                                      |
| RBR-5t258m  | Echinacea tincture ( <i>Echinacea purpurea</i> ), Myrrh (tree <i>Commiphora myrrha</i> ), Ratania tincture ( <i>Krameria lappacea</i> ), Chamomile tincture ( <i>Matricaria recutita</i> ) |
| RBR-3424pzb | Orange ( <i>Citrus sinensis</i> )                                                                                                                                                          |
| RBR-55g6cm  | Clove ( <i>Syzygium aromaticum</i> )                                                                                                                                                       |
| RBR-34r4dz  | Peppermint ( <i>Mentha piperita</i> )                                                                                                                                                      |
| RBR-9f3ctb  | Rosemary ( <i>Rosmarinus officinalis Linn.</i> )                                                                                                                                           |

**Source:** Research Data.

The compounds were used both as therapeutic agents, with antiseptic, anti-inflammatory, antiplaque, or healing purposes, and as flavoring agents. Of the ten studies, five used the compounds exclusively as therapeutic agents, whereas five used them as flavoring agents, including one case in which synergism with a therapeutic agent was reported as a possible secondary benefit (Table 5).

**Table 5:** Studies with herbal toothpastes based on the function of the herbal component.

| ReBEC code  | Function of the herbal component |
|-------------|----------------------------------|
| RBR-4x9pk3m | Therapeutic agent                |
| RBR-7dz5y9x | Flavoring and Therapeutic agent  |
| RBR-7scgp3h | Therapeutic agent                |
| RBR-6kr745  | Therapeutic agent                |
| RBR-25b7xh  | Flavoring                        |
| RBR-5t258m  | Therapeutic agent                |
| RBR-3424pzq | Flavoring                        |
| RBR-55g6cm  | Flavoring                        |
| RBR-34r4dz  | Flavoring                        |
| RBR-9f3ctb  | Therapeutic agent                |

**Source:** Research Data.

It was observed that four of the ten studies (40%) presented formulations containing fluoride, while the others were free of this anticaries agent (Table 6).

**Table 6:** Studies with herbal toothpastes based on fluoride content.

| ReBEC code  | Presence of fluoride |
|-------------|----------------------|
| RBR-4x9pk3m | No                   |
| RBR-7dz5y9x | No                   |
| RBR-7scgp3h | No                   |
| RBR-6kr745  | No                   |
| RBR-25b7xh  | Yes                  |
| RBR-5t258m  | No                   |
| RBR-3424pzq | Yes                  |
| RBR-55g6cm  | Yes                  |
| RBR-34r4dz  | Yes                  |
| RBR-9f3ctb  | No                   |

**Source:** Research Data.

## DISCUSSION

The results of this scoping review show that the number of clinical trials registered in Brazil involving dentifrices with plant-based compounds remains very low. Although Brazil has one of the greatest biodiversities on the planet, with substantial potential for the bioprospecting of bioactive compounds, scientific exploration aimed at developing dental products, especially herbal dentifrices, is still limited (Cherobin *et al*, 2022).

Fluctuations in research on specific dental products have been reported in the literature and are influenced by scientific and technological advances, as well as by consumer market trends, as observed for biomaterials (Castro-Silva *et al*, 2021). However, the small number of studies on herbal toothpastes limited further interpretation because the records were widely distributed across the years analyzed. During and after the COVID-19 pandemic, digital marketing intensified and public interest in self-care increased in Brazil, which ranked second worldwide in Google searches related to toothpastes (Di Profio *et al*, 2023). This context may partially explain the higher number of studies on herbal toothpastes registered in the last five years.

Studies involving young, healthy adults and relatively small samples are consistent with the typical characteristics of phase I clinical trials. However, the validation of these products remains limited in more vulnerable populations, such as older adults, immunosuppressed individuals, and patients with systemic diseases, who are more commonly addressed in phase II trials. Short follow-up periods were also frequent, as reported in a review of herbal toothpastes, in which clinical studies generally lasted up to four weeks, with only a few extending to six months for more detailed assessment of antibiofilm and antigingivitis effects (Pessotti; Pannuti; Raitz, 2006).

The identification of native plant species is highly important, as it subjects researchers to Law No. 13,123/2015 and to regulation by the National System for the Management of Genetic Heritage and Associated Traditional Knowledge (SisGen), within the legal certainty and sustainable principles that govern the economic use of Brazilian biodiversity (Brasil, 2025b).

*Aloe vera*, *Citrus sinensis*, *Echinacea purpurea*, *Matricaria recutita*, *Pinus strobus*, *Rosmarinus officinalis* L., and *Syzygium aromaticum* are considered introduced or exotic species in Brazilian biodiversity by the Ministry of Agriculture and Livestock (Brasil, 2025b). The Brazilian Biodiversity Information System also classifies

*Bowdichia virgilioides* Kunth and *Croton lechleri* as native species; *Calendula officinalis*, *Camellia sinensis*, and *Mentha piperita* as introduced species; and *Commiphora myrrha*, *Krameria lappacea*, *Melaleuca alternifolia*, and *Vaccinium macrocarpon* as exotic species absent from Brazilian wild flora (Brasil, 2025c).

The herbal toothpastes identified in this review included several plant species with distinct biological properties and potential roles in preventing and managing oral diseases.

*Camellia sinensis* is rich in polysaccharides, caffeine, polyphenols, amino acids, antioxidants, and micro- and macronutrients. It has pharmacological properties, including antimicrobial, antidiabetic, and anti-inflammatory activities, in addition to benefits for oral health, particularly in relation to dental caries and periodontal diseases (Valadas *et al*, 2021). Green tea has also been reported to help protect against several oral conditions, including caries, gingivitis, periodontitis, halitosis, and oral malignancies. Moreover, it may prevent oxidative stress, reduce inflammation caused by cigarette smoke, and decrease dentin erosion and abrasion (Khurshid *et al*, 2016).

*Mentha piperita* is an aromatic plant with antibacterial, antiviral, antifungal, and anti-inflammatory properties. Its oils and extracts have shown activity against cariogenic bacteria, such as *Streptococcus mutans*, and may contribute to caries prevention, plaque control, halitosis reduction, and the management of oral inflammation, supporting its use as an ingredient in oral hygiene products (Fayed, 2019).

Dragon's blood is a reddish resinous oil extracted from the *Croton lechleri* tree and has been used by Indigenous populations in traditional Amazonian medicine because of its ethnopharmacological properties. Its extract exhibits anti-inflammatory, wound-healing, antidiarrheal, anticancer, antirheumatic, antiseptic, and antioxidant activities (Peres *et al*, 2023).

*Calendula officinalis*, commonly known as calendula, is a flowering plant with antifungal, anti-inflammatory, and antibacterial properties (Lopes; Soares, 2022). Toothpaste containing alcoholic extract of calendula flowers may serve as a useful adjunct for reducing gingival bleeding (Amoian *et al*, 2010).

Orange essential oil can be extracted from fruit-processing residues, and its main component is limonene. This compound may be used as a solvent and flavoring agent and has potential applications in the health field because of its antioxidant and antimicrobial activities, as well as its possible role as an active ingredient in products aimed at cholesterol control (Orso *et al*, 2022).

*Aloe vera*, commonly known as aloe, is a medicinal plant with anti-inflammatory and antioxidant properties. It has been reported to be effective as an adjunct to periodontal treatment because of its clinically demonstrated antibacterial and anti-inflammatory effects (Silva *et al*, 2021).

Although the herbal compounds discussed individually show potential benefits for oral health, most trials do not provide details on extract concentration, standardization, or the stability of the active ingredients in toothpaste formulations. This limitation hinders the extrapolation of these findings to clinical practice (Mehta *et al*, 2024).

A major limitation affecting the acceptability of most herbal toothpastes is the absence of fluoride as a primary therapeutic agent for caries prevention and control. Herbal products alone do not provide the same combined antimicrobial, demineralization-inhibiting, and enamel-remineralizing effects promoted by fluoride (Cury; Tenuta, 2014).

## CONCLUSION

Clinical trials on herbal toothpastes registered in Brazil remain scarce, despite the potential of the country's biodiversity. The identified plant species show relevant biological properties, such as antimicrobial, anti-inflammatory, and healing effects, particularly related to biofilm and gingivitis control. However, the absence of fluoride in most formulations and the heterogeneity among studies indicate the need for more robust and standardized research.

Despite its limitations, this scoping review provides a current overview of the use of plant-based compounds in clinical studies on toothpastes in Brazil and may serve as a basis for future investigations. This study highlights both existing gaps and opportunities, reinforcing the importance of investing in innovation and scientific validation of herbal toothpastes in the country.

## AUTHOR'S CONTRIBUTIONS

**Conception and design:** Lopes AGP and Castro-Silva II; **Acquisition of data:** Lopes AGP and Freire EVDC; **Analysis and interpretation of data:** Lopes AGP, Freire EVDC and Castro-Silva II; **Manuscript preparation:** Lopes AGP, Freire EVDC and Castro-Silva II; **Critical revision:** Lopes AGP and Castro-Silva II; **Final approval of the version to be published:** Castro-Silva II.

## **CONFLICT OF INTEREST**

The authors declare that there are no conflicts of interest related to this study.

## **FUNDING**

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## **DECLARATION OF USE OF ARTIFICIAL INTELLIGENCE TOOLS**

No artificial intelligence-assisted technologies were used in the preparation of this work.

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