

Wound-healing properties of *Stryphnodendron adstringens* (barbatimão) in skin and mucosa injuries: a scoping review protocol

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ABSTRACT

Objective: This review will map the literature on the types of research and methods used to investigate the wound-healing properties of *Stryphnodendron adstringens* (barbatimão) in skin and mucosa injuries.

Introduction: *Barbatimão* is a Brazilian native plant and its wound-healing properties have been described in literature since the colonial period. It is one of the 71 plants included in the Brazilian health system's national list of medicinal plants of interest. However, existing literature reviews on the subject are limited, not comprehensive, lack a search strategy, and lack peer review.

Inclusion criteria: This scoping review will include all types of published and unpublished sources that investigate the wound-healing properties of *barbatimão* to treat any type of skin or mucosa injury in humans, animals, or in vitro, in any context.

Methods: A scoping review will be conducted following JBI methodology. The main databases to be searched will include Embase (EBSCOhost), CINAHL (EBSCOhost), Scopus, PubMed (EBSCOhost), ScienceDirect, Lilacs, SciELO, CUIDEN, MOSAICO, Web of Science, Epistemonikos, and Google Scholar. Unpublished studies will also be considered. Two independent reviewers will examine titles and abstracts and select and read full-text sources for possible inclusion. Subsequently, the reviewers will extract and synthesize the data, which will be presented as a map, diagram, or table, according to the review objectives.

Review registration: Open Science Framework osf.io/w57m4

Keywords: barbatimão; *stryphnodendron adstringens*; *stryphnodendron barbatiman*; wound healing

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Introduction

Stryphnodendron adstringens, commonly known as *barbatimão*, is a tannin-rich Brazilian native plant found in the Cerrado and Caatinga phytogeographic areas, mainly in the midwest and southwest regions of the country. It is taxonomically classified in the *Fabaceae* family, genus *Stryphnodendron* Mart., and its scientific name is *Stryphnodendron adstringens* (Mart.) Coville.¹ Its wound-healing

properties have been described by several European naturalists since the Brazilian colonial period. In 1803, the Portuguese physician, Bernardino Antonio Gomes, highlighted the wound-healing properties of *barbatimão* when applied topically.² The naturalist Johann Emanuel Pohl and the botanist Frei Velozzo both extolled its virtues as an astringent curative treatment.^{2–4} It is important to note that native plants were used for medicinal purposes by Indigenous peoples long before the Portuguese arrived in Brazil, and that this popular knowledge was passed down from generation to generation through unwritten traditions. The arrival of the Portuguese and other European peoples in Brazil only served to

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document this traditional use in written format. A recent literature review revealed that there have been 81 traditional uses of the plant's bark, mainly as an astringent agent and in the treatment of injuries and wound-healing, over the last 500 years of Brazilian history.³

Although its prevalence is not known, it is widely used in folk medicine in Brazil, especially by economically vulnerable groups and minorities, such as puerperal women undergoing perineal repair, adults without access to conventional health care, indigenous communities, and peoples of African descent.^{5,6} *Barbatimão* is mainly used in topical preparations made from the bark of the stem in infusions, macerations, and decoctions. It is also sold in public markets and local fairs in some regions of the country, where it has an established market. In summary, its use is associated with groups that value folk and traditional medicine.^{6–9}

The importance of the plant in traditional medicine has been recognized not only nationally, but also globally. To provide guidelines for its purpose and use, *barbatimão* has been included in the Brazilian Pharmacopoeia and the National List of Medicinal Plants of Interest to the Unified Health System (*Sistema Único de Saúde*). This list designates plants with potential therapeutic value that are considered important for public health and welfare. It is one of the 71 plant species traditionally used in the country, with high potential to guide scientific research studies and provide raw materials for phytotherapeutic medications. Recognizing the importance of ensuring safety, the Brazilian Ministry of Health and the World Health Organization (WHO) have established policies to ensure safe access and appropriate use of medicinal plants.¹⁰

A preliminary search was conducted, which identified a large body of experimental literature. The studies demonstrate the wound-healing properties of *barbatimão* in vitro and in vivo, especially in the rodent population. For example, in one study conducted on Wistar rats, the group treated with *barbatimão* showed complete epithelialization 14 days after the start of treatment, while the control group, treated only with physiological solution, showed incomplete epithelialization over the same 14-day period ($P < 0.001$).¹¹ In another in vivo study carried out on diabetic rats, the animals were divided into 4 groups corresponding to 4, 7, 10, and 14 days of use

of *barbatimão*. The treatment proved successful in wound healing ($P < 0.05$), even in the presence of comorbidities associated with the clinical condition.¹² Unfortunately, human studies are limited, with few case reports. Only one clinical study showed promising results in the treatment of decubitus pressure ulcers, with 70% of the injuries healed within 2 months and 100% of the injuries healed at the end of 6 months.^{13–16} There is a notable absence of clinical trials.^{5,17} Because *barbatimão* continues to be widely used by economically disadvantaged and minority groups, reflecting its association with folk and traditional medicine, and because few studies on the efficacy of this treatment have been conducted, a scoping review of the wound-healing properties of *barbatimão* is appropriate to identify research gaps, guide future investigations, and determine key policy points that will advance research agendas and develop safety aspects of *barbatimão*.^{5–9}

In order to identify the types of literature reviews produced on the topic, a second, more refined preliminary search was conducted in PROSPERO, MEDLINE, the Cochrane Database of Systematic Reviews, Open Science Framework, Campbell Collaboration, Carpha database, Epistemonikos, and *JB* Evidence Synthesis, and no current or in-progress scoping or systematic reviews on the topic were identified. However, there were non-peer-reviewed studies reporting on historical records of traditional uses of the plant. These reviews did not specify a search strategy, nor did they include unpublished studies.¹⁸ This review will differ from those studies because of its specific emphasis on *Stryphnodendron adstringens* and its relevance to human applications. The main objective is to encompass a broad spectrum of published and unpublished literature, setting it apart from prior reviews characterized by a lack of comprehensive search strategies and peer-review mechanisms.¹⁶

In summary, this scoping review aims to map the entire literature on *barbatimão*'s wound-healing properties in skin and mucosal injuries, encompassing research conducted on humans, animals, in vitro, and across various contexts. Its justification lies in the need for a comprehensive understanding of the research methodologies employed and the types of evidence available. This review will be useful for patients and health professionals, and will be in line with the WHO and Brazil's government agencies, such as the Ministry of Health and the Unified Health System.

Review questions

What is the current extent of scientific research on the wound-healing properties of *Stryphnodendron adstringens* (*barbatimão*) on skin and mucosa injuries in humans, animals, and in vitro, considering various contexts?

- i) What types of studies have been conducted on the wound-healing properties of *Stryphnodendron adstringens* (*barbatimão*) in skin and mucosa injuries in humans, animals, and in vitro?
- ii) What dosage and formulation of *Stryphnodendron adstringens* (*barbatimão*) were used in the studies?
- iii) What are the characteristics of the participants and contexts?

Inclusion criteria

Participants

This review will consider studies that include any animal models, in vitro, along with research involving humans with any type of skin or mucosal lesion, with the use of *Stryphnodendron adstringens* (*barbatimão*). There will be no limits on comorbidities, age, skin color, race, or gender. It was decided to extend the review to include non-human participants due to the scarcity of human participant research on the topic. Broadening the inclusion criteria beyond humans will allow for a comprehensive analysis of the available evidence, identifying the types of studies, methodologies, and potential gaps that will serve as the basis for future research.

Concept

This review will consider sources that assess the wound-healing properties of *Stryphnodendron adstringens* in skin or mucosa injuries, used topically, in any dosage, duration, and formulation modality of the plant (including extracts, dyes, solutions, ointment, cooked bark, or any part of the plant). We will also consider sources that present the geographical locations where approaches using *barbatimão* have been developed, as well as the characteristics of the service/community that has used the plant for wound healing. We will also consider participant attributes, such as sex, age, gender, race, species, sample size, comorbidities, and the results observed in these groups.

Context

This review will consider studies carried out in any context (hospital, laboratory, or community), culture, and geographical location.

Types of sources

This review will consider published and unpublished studies with experimental and quasi-experimental designs, including randomized controlled studies, non-randomized controlled studies, before-and-after studies, and interrupted time series studies. In addition, in vivo and in vitro studies will be considered. This review will also consider analytical observational studies, including prospective and retrospective cohort studies, case-control studies, and analytical cross-sectional studies. Descriptive observational study designs, such as case series, individual case reports, and cross-sectional descriptive studies, or other relevant study designs will be considered. Systematic reviews, ethnobotanical, qualitative studies, theses, dissertations, and clinical trial reports that meet the inclusion criteria will also be considered.

Methods

The review will be carried out according to the JBI methodology for scoping reviews¹⁹ and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR).²⁰ The review protocol was registered in Open Science Framework (osf.io/w57m4).

Search strategy

The objective of the search strategy will be to locate published and unpublished literature. A limited initial search of PubMed (EBSCOhost), CINAHL (EBSCOhost), and Scopus was carried out to identify articles on the topic. The keywords contained in the titles and abstracts of the relevant articles and the indexing terms used to describe the articles were used to develop a complete search strategy for PubMed (EBSCOhost; see Appendix I). The search strategy, including all the keywords and indexing terms identified, will be adapted for each database and/or information source. The reference lists of all included evidence sources will be searched for additional documents. There will be no date or language limitations on the articles. Regarding translations, some of the reviewers are native speakers of Portuguese and

English; sources written in other languages will be translated using DeepL (DeepL, Cologne, Germany).

The databases to be searched will include Embase (EBSCOhost), CINAHL (EBSCOhost), Scopus, PubMed (EBSCOhost), ScienceDirect, LILACS, SciELO, CUIDEN, MOSAICO, Web of Science, Epistemonikos, and Google Scholar. The sources of unpublished literature to be researched will include clinical trial records such as ClinicalTrials.gov, International Clinical Trials Registry Platform (ICTRP), Brazilian Registry of Clinical Trials (*Registro Brasileiro de Ensaios Clínicos*, REBEC), as well as theses and dissertations (Brazilian Digital Library of Theses and Dissertations and CAPES Catalog of Theses and Dissertations). Congress annals will also be included. If a source cannot be retrieved, we will attempt to contact the authors of the article via email up to 2 times.

Study selection

After the search, all the identified records will be grouped and loaded to Mendeley Reference Manager v2.67.0 (Mendeley Ltd., Elsevier, Netherlands) and duplicates will be removed. Following a pilot test, 2 independent reviewers will assess the titles and abstracts against the inclusion criteria. Potentially relevant sources will be retrieved in full and their citation details imported into the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI; JBI, Adelaide, Australia).²¹ The full text of selected citations will be assessed in detail against the inclusion criteria by 2 independent reviewers. Reasons for exclusion of full-text papers that do not meet the inclusion criteria will be recorded and reported in the scoping review. Any disagreements that arise between the reviewers at each stage of the selection process will be resolved through discussion or with a third reviewer. The results of the search and inclusion process corresponding to the sources will be reported in full in the final scoping review and presented in a PRISMA flow diagram.²²

Data extraction

Data will be extracted from papers by 2 independent reviewers using a data extraction tool developed by the reviewers (see Appendix II). The extracted data will include specific details about the participants, concept, context, study characteristics, and main findings relevant to the review question, for example, species examined (eg, humans, mice, rabbits);

injury site; intervention frequency or duration; dosage; *barbatimão* formulation method used; comparison groups; and gaps identified by the study. The data extraction tool will be tested by 2 independent reviewers on 3 randomly selected studies. The tool may be modified and revised as necessary during data extraction. Any modifications will be detailed in the final scoping review. Any disagreements between the reviewers will be resolved through discussion or with a third reviewer. If appropriate, the authors of the articles will be contacted twice to request missing or additional data.

Data analysis and presentation

The data will be presented as a map in diagrammatic or tabular format. A narrative summary will accompany the tabulated results and/or graphs. This narrative will serve as a critical component of the analysis, elucidating how the findings and patterns identified in the data align with the overarching review objective and research questions. It will also facilitate a deeper understanding of the context and implications of the data, thus contributing to broader comprehension of the field.

The results will be categorized and stratified by several relevant criteria. These categorizations will include, but not be limited to, study design, year of publication, context, species examined, specific injury site, frequency or duration of intervention, dosage, formulation modalities of the plant, comparison groups, and any additional conceptual categories that may arise during data extraction. This meticulous categorization will not only facilitate a structured and comprehensive synthesis, but will also make it possible to identify trends, gaps, and potential areas for future research.

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Author contributions

RTSCD conceived the project, performed the literature search, wrote the final version of the manuscript, approved the final version to be published, and agreed to be responsible for all aspects of the work. ACB, MLGR, and VHAM contributed to the

design of the project, drafted the manuscript, critically reviewed the final version of the manuscript for intellectual content, approved the final version to be published, and agreed that RTSCD would be responsible for all aspects of the work. JMN contributed to the technical review of the reviewers' suggestions and improvement of the language, especially with regard to the English language.

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Appendix I: Search strategy

PubMed (EBSCOhost)
Search conducted: September 11, 2023

Search	Query	Records retrieved
#1	("fabaceae"[MeSH Terms] OR "fabaceae"[All Fields] OR "barbatimão"[All Fields] OR "stryphnodendron"[All Fields]) AND "adstringens"[All Fields]	60
#2	"Wound-healing"[MeSH Terms] OR "Wound-healing"[All Fields] OR "healing"[All Fields] OR "Wounds and Injuries"[Mesh] OR "Skin"[Mesh] OR "Mucous Membrane"[Mesh] OR "Skin wounds"[All Fields] OR "skin lesions"[All Fields] OR "mucosa"[All Fields]	1,793,739
#3	#1 AND #2	14

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Appendix II: Draft data extraction tool

Date:	
Reviewer: <input type="checkbox"/> 1 <input type="checkbox"/> 2	
Full title of source:	
Domain	Extracted information
Study characteristics	Author(s): Source: <input type="checkbox"/> Published <input type="checkbox"/> Unpublished Year of publication: Country: Language: <input type="checkbox"/> English <input type="checkbox"/> Portuguese <input type="checkbox"/> Spanish <input type="checkbox"/> Other: _____ Type of literature: <input type="checkbox"/> Thesis <input type="checkbox"/> Dissertation <input type="checkbox"/> Article <input type="checkbox"/> Book <input type="checkbox"/> Other: _____ Type of study (methodology): Aim/purpose: In case of literature reviews: Databases consulted (quantity/names of databases) Number and types of studies included
Population and sample size	Species examined: <input type="checkbox"/> Humans <input type="checkbox"/> Animals <input type="checkbox"/> In vitro Number of participants: Comorbidities: Comparison groups:
Concept characteristics	Injury site: Origin of the injury (eg, induced, spontaneous): <i>Barbatimão</i> formulation method used: Dosage: Intervention frequency/duration: Wound characteristics:
Context characteristics	<input type="checkbox"/> Hospital <input type="checkbox"/> Laboratory <input type="checkbox"/> Community Other relevant information:
Gaps identified by the study	
Additional notes	