



Technological Prospecction and Scientific Evidence of the Antimicrobial Activity of *Bixa orellana*: An Integrative Review

Brenda de S. Moreno¹ · Ludmilla P. G. C. Abreu¹ · Gabriella de O. Silva¹ · Lucas M. Syllos¹ · Jhenyfer B. dos Santos¹ · Ronaldo G. Abreu¹ · Patrícia O. de Andrade¹ · Graziella A. Joanitti¹ · Marcella L. B. Carneiro¹

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Abstract

Bixa orellana L., Bixaceae, is a plant native to tropical America, traditionally used in folk medicine. Its bioactive compounds exhibit therapeutic potential, particularly in terms of antimicrobial properties. This study aimed to conduct an integrative review to explore the current knowledge and technological applications of annatto-derived compounds in the health field, highlighting their antimicrobial potential, particularly in the context of wound healing and associated anti-inflammatory processes, as well as possible innovations based on these properties. An integrative review was conducted using the PICo framework. Searches were performed in eight scientific databases and three patent repositories using structured search strings with descriptors in Portuguese and English. Studies from the last 5 years and relevant patents were included. Eleven scientific articles and 17 patents were selected. The main compounds derived from annatto demonstrated antimicrobial activity against 25 microbial strains. Technological analysis revealed an increase in patent filings related to the therapeutic use of annatto, especially in Brazil, with an emphasis on polymeric films and nanofibers aimed at antimicrobial activity in a wound healing context. The findings highlight *B. orellana* as a promising source for developing innovative herbal medicines with significant antimicrobial potential. Nonetheless, methodological standardization and further clinical studies are necessary to validate experimental evidence.

Keywords Annatto · Technological prospecction · Antimicrobial activity · Bioprospecting · Natural compounds · Innovation

Introduction

Biodiversity is fundamental to life on the planet, and Brazil is home to one of the richest biodiversities in the world, distributed across six biomes: the Amazon, Cerrado, Atlantic Forest, Caatinga, Pampas, and Pantanal. Many economists regard biodiversity as a new paradigm for national development (Ministério da Saúde 2012). With advances in scientific and technological knowledge, resources once considered mere raw materials have become strategic assets,

especially when their applications, such as cosmetics and therapeutics, are fully realized. The therapeutic use of nature is as ancient as human civilization. Historically, medicinal plants have played a critical role in both phytotherapy and drug discovery. Moreover, the prophylactic, curative, palliative, or diagnostic use of phytotherapeutics was officially recognized by the WHO in 1978, which recommended the widespread dissemination of knowledge required for their use, considering medicinal plants essential tools for pharmaceutical care (Ministério da Saúde 2006).

In this context, *Bixa orellana* L., Bixaceae, is a plant native to tropical areas of the Americas, rich in carotenoid derivatives, terpenoids, tocotrienols, and flavonoids (Shahid-ul-Islam et al. 2016). Its seeds contain a total of eight pigments classified as carotenoids, which give the plant its distinctive red color (Pacheco et al. 2019). Among these, bixin is the primary pigment, with over 24 compounds isolated from the seeds and more than 100 volatile substances identified in aqueous extracts. Notable derivatives include

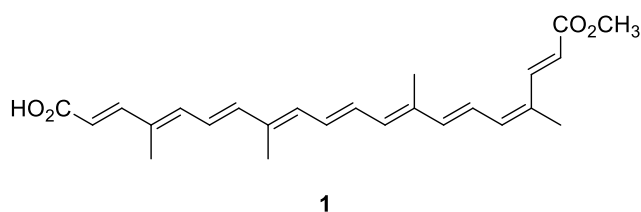
Brenda de S. Moreno and Ludmilla P. G. C. Abreu contributed equally to this work.

✉ Marcella L. B. Carneiro
marbretas@unb.br

¹ Laboratório de Compostos Bioativos e Nanobiotecnologia, Universidade de Brasília, Campus Darcy Ribeiro, Brasília, DF, Brazil

norbixin, a demethylated compound with common commercial applications. Additional components include gerynolgeraniol, alpha- and beta-carotene, orellin, flavonoids, lutein, salicylic acid, phenylalanine, and tryptophan (Vilar et al. 2014). This phytochemical diversity endows the plant with significant pharmacological potential and diverse therapeutic applications (Lima et al. 2001). The plant's longstanding use by traditional communities further underscores its therapeutic value (Mercadante et al. 1996).

Bixin (**1**) is a liposoluble carotenoid and is one of the most effective natural quenchers of singlet oxygen (1O_2) and scavengers of free radicals (Rivera-Madrid et al. 2016). As the predominant pigment in the seed, comprising up to 80% of the total pigment, it was the first *cis*-carotenoid isolated from natural sources (Mercadante et al. 1996; Ajaghaku et al. 2020). Both bixin and norbixin have been extensively studied for their medicinal properties and constituents such as carotenoids, tocotrienols, and tocopherols (Louro and Santiago 2016). These compounds exhibit anti-inflammatory (Pacheco et al. 2019), antimicrobial (Nathan et al. 2019), antioxidant (Osorio et al. 2021), cytotoxic, and antiproliferative activities against cancer cell lines *in vitro* (Silva et al. 2024) and have demonstrated efficacy against fungi, as well as Gram-positive and Gram-negative.



Given the growing global concern over antimicrobial resistance, the investigation of natural compounds as alternative therapeutic agents has gained increasing relevance. Bioactive substances derived from plants, such as those found in *B. orellana*, offer promising potential in combating pathogenic microorganisms, especially those associated with serious public health challenges. The exploration of these natural resources not only contributes to the development of safer and more affordable treatments but also fosters innovation in health care through a biodiversity-based approach (Silva et al. 2024).

The therapeutic applications of *B. orellana* are diverse, whether through the direct use of its active compounds or through their synergistic incorporation into biomaterials or in combination with other compounds to enhance bioavailability and stability, thereby maximizing therapeutic potential (Pires et al. 2015; Yang et al. 2021).

Technological prospecting studies are critical for reducing uncertainties in strategic decision-making (Paranhos and Ribeiro 2018). According to Coelho et al. (2005), prospecting is necessary to identify the most critical pressing opportunities and research and development needs. As

such, technological foresight provides decision-makers with a foundation for crafting innovative strategies. These studies also help map scientific and technological advancements, identify market trends, and recognize potential competitors.

As supply and demand for new products and services grow, innovators increasingly seek ways to protect, promote, and commercialize their inventions. In this context, patents emerge as a key form of intellectual property, safeguarding technological products and processes. Access to technological information serves as a competitive advantage, enabling companies to evaluate external threats and opportunities, evaluate internal capabilities, and identify strategic strengths (Tigre 2006).

To maintain competitiveness, companies must innovate, and competitive intelligence is essential for monitoring competitor actions, acquisitions, and investments, and other data crucial for anticipating emerging innovations (Ribeiro 2018). Given the relevance of annatto, this study aimed to conduct an integrative review using the PICo framework and structured search strings to examine the current scientific knowledge and technological applications of annatto-derived compounds in the context of health, with particular emphasis on their antimicrobial properties.

Given the relevance of *B. orellana*, this study aimed to conduct an integrative review using the PICo framework and structured search strategies to examine the current scientific evidence and technological applications of its bioactive compounds in the health field, highlighting their antimicrobial potential and exploring their relevance in associated anti-inflammatory and wound healing processes.

Material and Methods

This integrative review was conducted by the Methodological Guidelines for Systematic Reviews (Page et al. 2021) and structured using the PICo acronym for non-clinical studies (Araújo 2020), where P (Problem) refers to the synthesis of evidence, I (Interest) to the use of *B. orellana*, and Co (Context) to antimicrobial applications.

The integrative review enables the synthesis of broader findings and allows the inclusion of both primary and secondary studies, making it a comprehensive research approach (Ercole et al. 2014). It serves as a tool to consolidate heterogeneous studies, offering a holistic perspective on a specific subject and strengthening scientific evidence for more informed decision-making (Weise et al. 2020).

In addition to bibliographic searches in article databases, a technological prospecting analysis was performed using patentometric, a metric-based approach for studying patent indicators to identify innovation trends and technologies based on the technical content of patent documents (Adelaide et al. 2019). To support this study with scientific and technological elements,

patent analysis was conducted to assess the technological maturity of the antimicrobial applications of *B. orellana*.

The following sections outline the methodologies adopted for prospecting studies in scientific and patent databases.

Eligibility Criteria

Inclusion Criteria

The inclusion criteria for selecting publications were (i) studies available in full-text and published within the last 5 years to ensure up-to-date information on the subject; (ii) publications in English, Portuguese, or Spanish; and (iii) coherence with the proposed PICO framework (scientific evidence of *B. orellana* as an antimicrobial agent). For patents, inclusion criteria included (i) patents addressing the topic, specifically *B. orellana* in an antimicrobial context, and (ii) patents in either English or Portuguese. It is important to note that the 5-year publication window was applied exclusively to the systematic search that defined the analytical corpus of this integrative review.

Exclusion Criteria

Publications were excluded if they were (i) duplicate entries; (ii) unavailable in full text; (iii) dissertations, conference proceedings, and abstracts; (iv) published in languages other than Portuguese, English, or Spanish; and (v) studies not addressing the proposed topic.

For patents, exclusions included (i) patents retrieved from multiple databases and (ii) patents unrelated to the review's antimicrobial focus.

Information Sources and Search Strategies

A general search string was structured for the eight databases consulted, using DeCS/MeSH descriptors combined with the Boolean operators “AND” and “OR.” The general search string employed was as follows: ((*Bixaceae* OR “*Bixa orellana*” OR *Bixa* OR “*Bixa acuminata*” OR *Bixaceas* OR *Cochlospermum* OR *Kondagogu* OR *Urucu* OR *Urucueiro* OR *Urucum* OR “*Urucum-da-Mata*” OR *Urucuzeiro*) AND (“Anti-Infective Agents” OR (Agent AND Anti-Infective) OR (Agent AND Anti-Microbial) OR (Agent AND Anti-microbial) OR (Agents AND Anti-Infective) OR (Agents AND Anti-Microbial) OR (Agents AND Antiinfective) OR (Agents AND Antimicrobial) OR “Anti Infective Agent” OR “Anti Infective Agents” OR “AntiMicrobial Agent” OR “Anti-Microbial Agents” OR “Anti-Infective Agent”

OR “Anti-Microbial Agent” OR “Anti-Microbial Agents” OR “Antiinfective Agents” OR “Antimicrobial Agent” OR “Antimicrobial Agents” OR Microbicide OR Microbicides OR (“Anti-Infective Agents” AND Local))).

The bibliographic databases consulted were PubMed/MEDLINE, IEEE Xplore, Web of Science - Core Collection (Clarivate Analytics), Scopus (Elsevier), BVS (Bireme), ScienceDirect (Elsevier), CINAHL (EBSCOhost), and Cochrane Library. Searches were conducted on May 9, 2024, and publications were organized in Rayyan — Intelligent Systematic Review (Ouzzani et al. 2016), which was also used to eliminate duplicate references. Specific search strings tailored to the requirements of each database are detailed in Table S1.

Patent searches were performed in INPI, Espacenet, and Patentscope, using broad descriptors like “Urucum,” “*Bixa orellana*,” or “Annatto” to select all studies involving this plant. An overview of the main classifications of the studies identified was also performed.

Study Selection and Data Extraction

The selection of eligible publications was conducted in two phases by authors LPGCA and GOS independently, using the Rayyan software. All screening decisions were performed independently by human reviewers, and Rayyan was used solely as a support tool for organizing and managing references. The process was carried out in two phases: (i) initial screening based on title and abstract, and (ii) full-text assessment of the studies selected in phase 1. In cases of disagreement between authors at any stage, discrepancies were resolved through discussion with a third reviewer (MLBC). The number of eligible publications in each phase was documented using the PRISMA 2020 Flow diagram (Page et al. 2021).

Data extraction from eligible studies was carried out by the same authors from phases 1 and 2. There were no disagreements in this step. A standardized table was developed by the authors and validated using six randomly selected eligible studies (after phase 2) related to the topic. Extracted information included (i) author, year, and country of study; (ii) study design and sample used; (iii) objectives; (iv) biological activity identified (antimicrobial); (v) technology and plant organ used; and (vi) study limitations. The primary outcome analyzed was scientific evidence of antimicrobial activity of *B. orellana*.

For patents, author BSM selected findings containing the terms “Urucum,” “*Bixa orellana*,” or “Annatto” in titles and/or abstracts. Duplicate patents across databases were excluded. Data extraction involves reading each selected patent application and tabulating information on the following: (i) database; (ii) study title; (iii) patent application number; and (iv) year of publication.

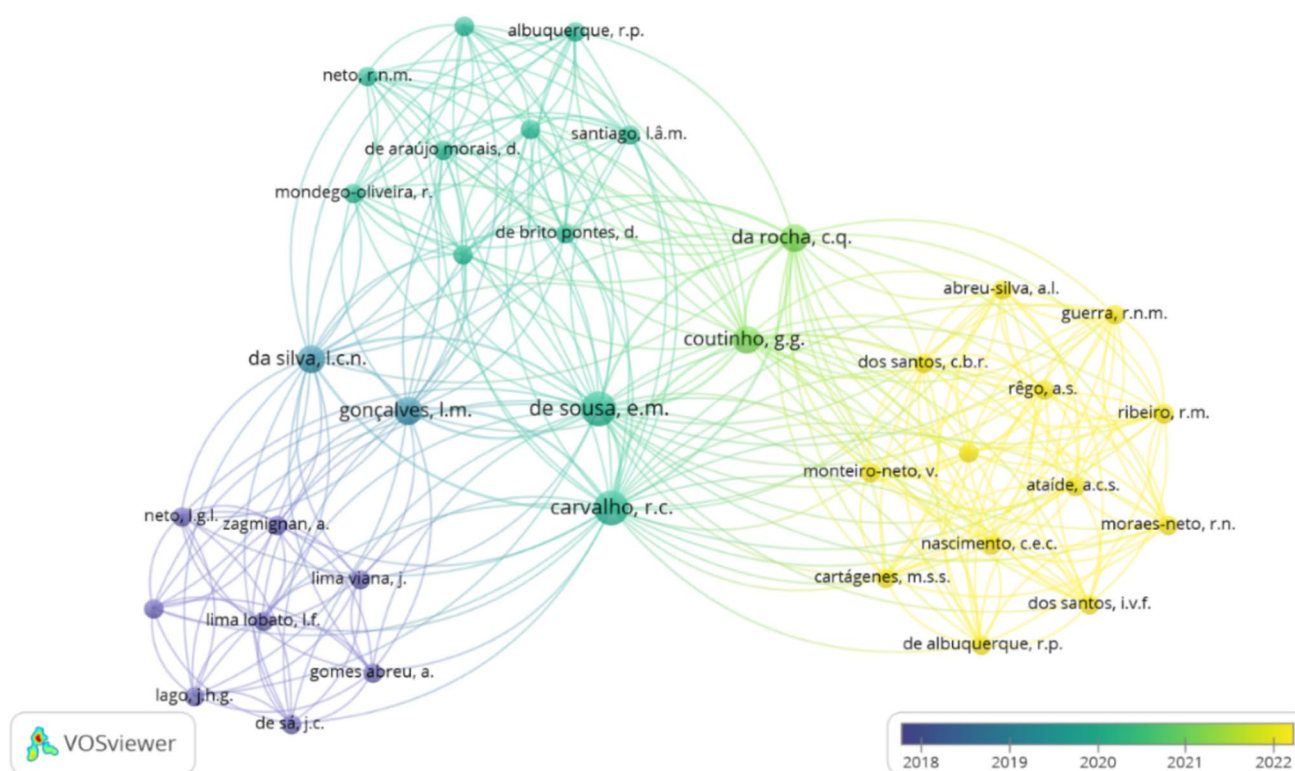


Fig. 1 Network map with overlay of the publication year of eligible studies regarding authors and their coauthorships. Created by the authors in VOSviewer 1.6.18 (CWTS 2023)

Results

Bibliometric Analysis

The VOSviewer 1.6.18 software (27) was used for the bibliometric analysis of eligible studies. Initially, the number of publications per author used in this review, and their co-authorships between the studies were analyzed. The software gave higher visual weight to more recent publications, assigning them as yellow and green clusters. In contrast, older studies were represented in bluish clusters. For interpretation and better visualization, the network format was chosen with an overlay of the publication year, as shown in Fig. 1.

In the bibliometric analysis, it was also possible to examine the frequency of keyword occurrences in scientific literature as well as the relationships and strength among them. The software used to generate the figures applies to the cited sources extracted from reference strings as the unit of analysis. Therefore, interrelationships among terms were represented by connecting lines and color-cued clusters. The size of the circle corresponds to the frequency of term occurrence in the analyzed publications; the larger the circle, the more frequently the term appears. A minimum occurrence threshold of 2 was set in the software, as illustrated in Fig. 2.

Bibliometric analysis is important for ensuring the technical and scientific reliability of the proposed study and in providing a quantitative mapping of the research field. It made it possible to observe author collaboration patterns and the breadth of scientific references on this topic, helping identify emerging research trends. The most cited terms indicate consolidated areas of interest within the scientific community. In this regard, it is inferred that studies involving the antimicrobial application of *B. orellana* are significantly prominent, reinforcing its relevance as a therapeutic agent.

This antimicrobial application is consistently associated with *B. orellana* through terms related to photodynamic therapies in the following clusters: “antimicrobial photodynamic therapy,” “dental caries,” and “photosensitizing agents.” These findings suggest scientific interest in the use of this species as an agent with potential antimicrobial activity, particularly in photoactivated contexts, as these terms are linked to microbial control. Furthermore, this inference is supported by literature, which highlights its action against Gram-positive and Gram-negative bacteria and its inhibition of biofilms. However, as this is a bibliometric analysis, this inference should be interpreted as indicative of a research trend and requires validation through experimental and clinical studies.

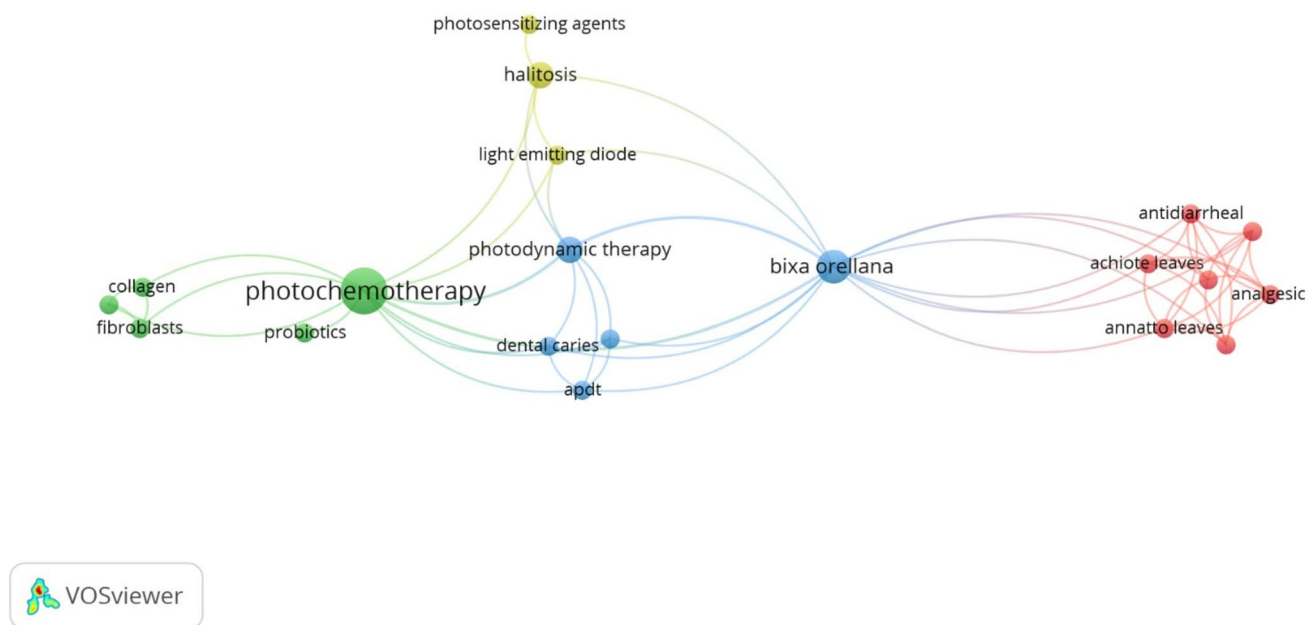


Fig. 2 Network of co-occurring terms related to *Bixa orellana*, antimicrobial activity, wound healing, and technological applications, derived from keywords of eligible studies. Map generated by the

authors in VOSviewer 1.6.18 (CWTS 2023). Node size represents term frequency; cluster colors indicate thematic groupings

Study Selection

Figure S1 illustrates the flowchart of the search and selection of articles from databases. The initial search returned 111 articles, 28 of which were duplicates. Thus, 83 articles underwent title and abstract screening. Of these, 20 were excluded for being published more than 5 years ago, one lacked full-text availability, and 48 did not meet the eligibility criteria. Consequently, 14 articles were selected for full-text assessment, of which three were excluded for not addressing the research question, resulting in a final sample of 11 eligible articles, as shown in Figure S1.

Additionally, based on the literature review, 250 patents were initially identified in the research databases, and 41 were removed for being duplicates. The remaining 209 patents records were based on their titles, abstracts, and descriptions to determine whether they addressed the antimicrobial activity of annatto/*B. orellana*. After this evaluation, 192 patents were excluded for irrelevance, leaving 17 eligible patents, as illustrated in Figure S1.

Characteristics of the Included Studies

The characteristics of the 11 eligible articles are detailed in Table S2. Among them, three were reviews (one narrative and two systematic), and eight were experimental studies, including one randomized clinical trial, six *in vitro* studies, and two *in vivo* studies, one of which also included *in silico* analysis. Most of the articles originated from Brazil

($n = 7$, 63.6%), followed by Colombia ($n = 2$), India ($n = 1$), and Indonesia ($n = 1$). The highest number of publications occurred in 2020 ($n = 4$), with an increase in 2022 ($n = 3$) and further outputs in 2022 and 2023 (two each).

The antimicrobial evaluation showed *B. orellana* was tested against various strains. The narrative review reported 13 bacterial strains, while the systematic reviews cited four and eight, respectively. Among experimental studies, the highest number of tested strains was six in *in vitro* studies, while the *in vivo* studies included four. Key microorganisms included Gram-positive bacteria such as *Staphylococcus aureus* ($n = 6$) and Gram-negative bacteria such as *Escherichia coli* ($n = 5$), as well as fungi such as *Candida albicans* ($n = 2$).

Various plant parts were used, including seeds, leaves, fruits, or a combination of these parts. Crude extract was the most tested. Only one study incorporated a dry extract into an experimental dual-cure cement, and another encapsulated dry seed extract in a protein gel. Some works investigated isolated compounds such as bixin, geranylgeraniol, tocopherols, and tocotrienols (Quiroz et al. 2020).

Notably, the leaves contained most of the active antimicrobial compounds: procyanidin B2 (bacteriostatic effect on *Porphyromonas gingivalis* and antiviral action against influenza virus) and B3 (action against *S. aureus*), lutein (*Listeria monocytogenes*, *Aspergillus niger*, *Trichophyton mentagrophytes*, *C. albicans*, and activity against hepatitis B), elagitanin isomer (*E. coli*), deoxyhexose of ellagic acid (*E. coli*, *S. aureus*, *Pseudomonas aeruginosa*), and cryptoxanthin (*S.*

Table 1 Comparative antimicrobial activity of annatto (*Bixa orellana*) extracts and derived compounds reported in the literature

Microorganisms	MIC	Extract type	Concentration range	Type of effect	Study
<i>S. aureus</i> , <i>E. coli</i>	250–1000 µg/ml	Plant extracts	100–2000 µg/ml	Bacteriostatic	Nascimento et al. 2000
Gram-positive bacteria	64–256 µg/ml	Flavonoids (natural compounds)	10–500 µg/ml	Bacteriostatic	Cushnie and Lamb 2011
Gram+/Gram– bacteria	100–500 µg/ml	Volatile oils	Variable	Bacteriostatic	Burt 2004
<i>Streptococcus mutans</i> , <i>Lactobacillus</i> spp., <i>Candida albicans</i>	9.375–37.5 µg/ml	Natural compounds (mixed plant-derived substances)	~ 10–1000 µg/ml	Bacteriostatic/anti-fungal	Dabur 2007
Gram-positive and Gram-negative bacteria	0.8 mg/ml to 3.2 mg/ml	Plant extract or isolated compounds	42.36 and 32.85 µg/ml	Bacteriostatic and bactericidal	Zhong 2022

aureus, *S. epidermidis*, *Salmonella typhimurium*, *Proteus vulgaris*). Geraniol, found in both leaves and seeds, inhibited *Mycobacterium tuberculosis* and *Leishmania amazonensis* (Neto et al. 2020). In total, *B. orellana* demonstrated antimicrobial activity against 25 strains.

Table 1 summarizes representative antimicrobial activity ranges reported in the literature for plant-derived compounds, including extracts, flavonoids, and volatile oils. The data are presented for contextual comparison and are not restricted to the studies included in the present review. Variations in methodology, microbial strains, and experimental conditions should be considered when interpreting these values.

Characteristics of the Included Patents

Following the data collection process presented in Figure S1, the 17 patents included were analyzed and organized in Table S3.

It is well established that natural products contribute substantially to modern drug development. Thus, research on safe, stable, and effective natural-based pharmaceuticals can inform the synthesis of new molecules. Accordingly, there has been a growing number of studies focused on this class of raw materials, aiming at the subsequent development of products, processes or technologies with potential for broad application. This process, referred to as the translational stage, involves converting scientific knowledge into practical applications. Ultimately, it culminates in the generation of innovations intended for commercial or clinical use, at which point there is a clear need to ensure intellectual property protection through patenting (Woolf 2008).

In this context, *B. orellana* has been extensively studied for its microbicidal and antimicrobial properties. Technological prospecting of the species has grown, with a significant rise in patent applications since 2014 (Fig. 3) likely due to increased use of the patent system to protect plant-based innovations.

It is important to highlight that patents can be classified into three primary statuses: filed (pending), granted, and expired. The status of a filed patent refers to an application that has been submitted to the competent authority, such as the Brazilian National Institute of Industrial Property (INPI), and is therefore still under examination. At this stage, the applicant holds only an expectation of rights, and the examination process may take several years until a final decision is issued (MCTI 2022).

In contrast, a patent classified as granted indicates that the competent authority has approved the application, thereby conferring upon the holder the exclusive right to exploit the invention. Consequently, third parties are prohibited from producing, using, selling, or importing the protected product or process without prior authorization. Finally, a patent is considered expiring when its term of protection has lapsed. In such cases, the invention enters the public domain, allowing unrestricted use and commercialization by any part without the need for authorization (MCTI 2022).

Based on the analysis, it was observed that the countries with the highest number of patent filings were Brazil, leading in all three searched databases, followed by China in second place, and India in third. Most deposits were found in Patentscope (Fig. 4).

To better reflect technological maturity, the 17 included patent records were classified by legal status and by available evidence of translational stage. Patent legal status was verified in the original databases (INPI, Espacenet, Patentscope) and categorized as “filed/pending,” “granted,” or “expired.” Where available, patent documents and associated public records were screened for indications of translational progress (e.g., prototype description, preclinical data, regulatory filings, or commercial products). This classification shows that a majority of applications remain at the filing or pending stage, with only a minority granted and an even smaller subset showing evidence of downstream translational activity (prototype or preclinical data). Therefore, the number of

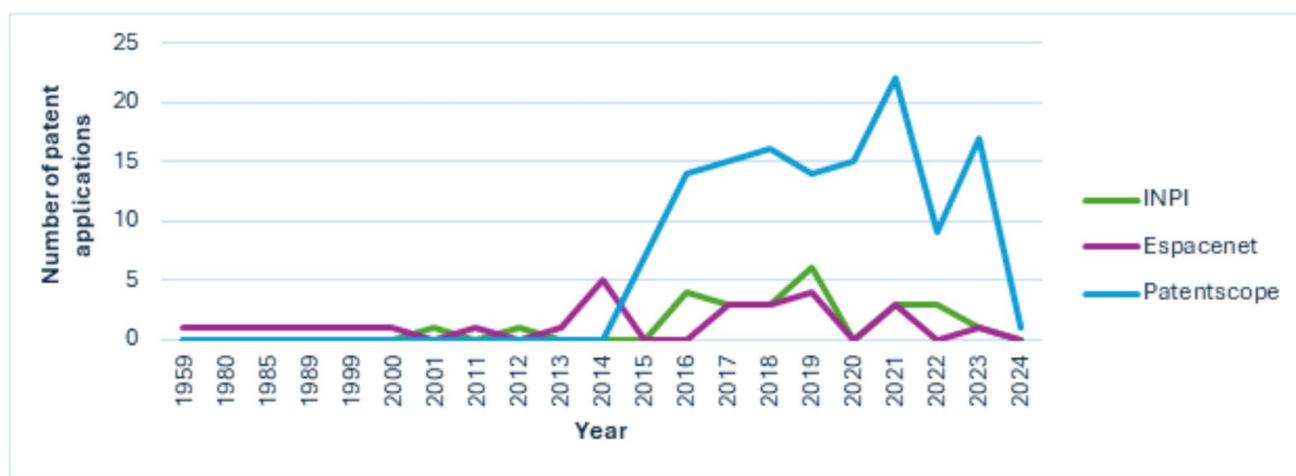


Fig. 3 Temporal distribution of patent applications

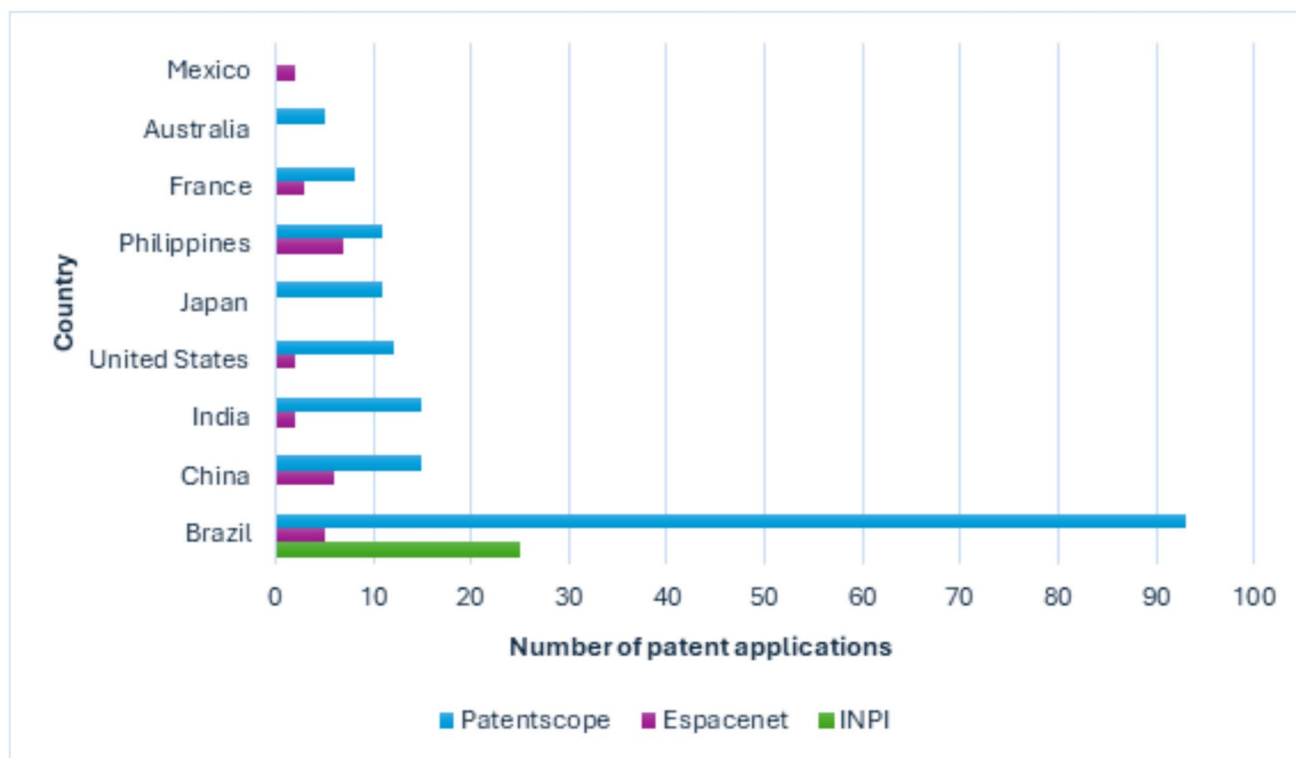


Fig. 4 Patent applications by country

patent filings should not be interpreted as direct evidence of clinical or commercial maturity.

Between 2020 and 2023, 37.5% more patents than articles were identified, as seen in Fig. 5. Over these 5 years, patent filings consistently outnumbered scientific publications every year, although no regular publication pattern was observed. Patent databases use the International Patent Classification (IPC) system, a hierarchical code system that

organizes patents by technical fields across all languages. The IPC is used for indexing and retrieving patent documents (INPI 2021).

The system organizes patent documents using a combination of letters and numbers that correspond to specific areas. Each application is assigned to a section, representing a broad field, which is further subdivided into classes, subclasses, groups, and subgroups (INPI 2021). In this study,

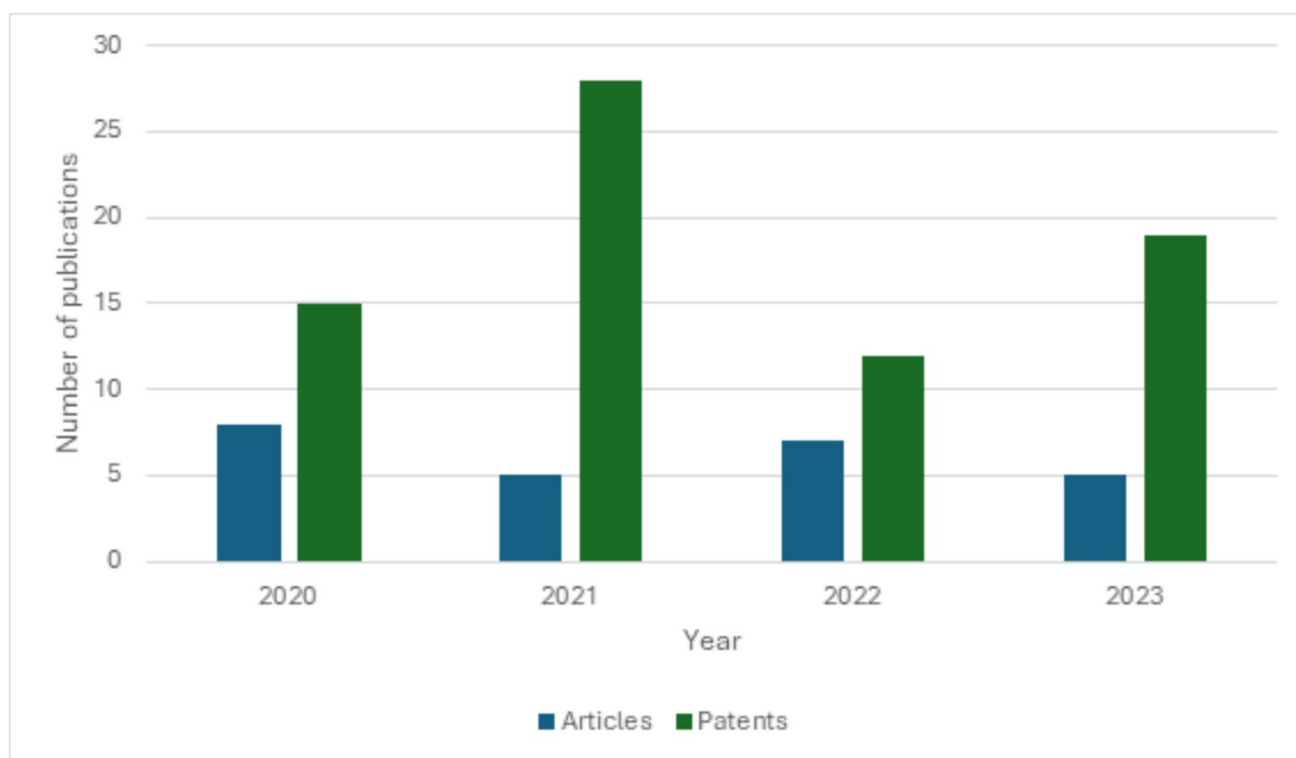


Fig. 5 Patent versus scientific articles relationship from 2020 to 2023

most patents were classified under section “A” (Human Necessities), particularly class “23” (food and food products) and class “61” (medical, veterinary, and hygiene sciences), the latter being the most directly relevant to the study’s scope. Within class “61,” the main subclasses were “K” (medical, dental, or personal hygiene preparations); “P” (therapeutic activity of compounds or preparations); and “Q” (cosmetics or hygiene use of products).

It is important to emphasize that patent filings alone do not equate to clinical or commercial readiness. Many patent applications remain at an early, pre-translational stage, and do not progress to preclinical validation or clinical trials; therefore, patent counts should be interpreted cautiously when inferring technological maturity or therapeutic potential (Munos 2009; Dimasi et al. 2016).

On relevant patent BR1020160201900 A2 describes a phytotherapeutic antimicrobial formulation derived from *B. orellana* leaves, including forms such as capsules and ointments. It demonstrated bacterial and fungal activity and bio-film degradation using a hydroalcoholic extract obtained via cold maceration from fresh plants (Figueiredo et al. 2018). Invention BR1020180697005 A2 describes a complex formulation primarily characterized by its antibacterial activity, based on *B. orellana* extract and *Triticum aestivum* L., Poaceae, for veterinary applications. In addition to its antimicrobial properties, the formulation also exhibits wound

healing effects beneficial for the treatment of open lesions, as well as insect and ectoparasite repellent activity. This formulation can be developed into various pharmaceutical forms to meet the specific needs of different pathologies (Nobre et al. 2020).

Finally, inventions IN4621/MUM/2015 and IN4622/MUM/2015 describe a method for extracting an organic compound from medicinal plants, including *B. orellana*, with antibacterial activity aiding in the treatment of multi-drug-resistant urinary tract infections (ITU-MDR) (Sahare and Moon 2016a, b). Patents focusing exclusively on wound healing were excluded, as the study focused on antimicrobial applications.

Potential Bias Risks

Bias risk analysis specifically involves a critical evaluation of the methods used in each study and the identification of potential sources of systematic error that could distort the effect estimate. In this sense, it measures only internal validity, assessing whether the study is reliable and whether it demonstrates methodological rigor. Thus, bias risk analysis does not allow for the externalization or extrapolation of findings, nor does it support clinical recommendations (Hartling et al. 2009; Viswanathan et al. 2017; Nguyen et al. 2021; Sargeant et al. 2022).

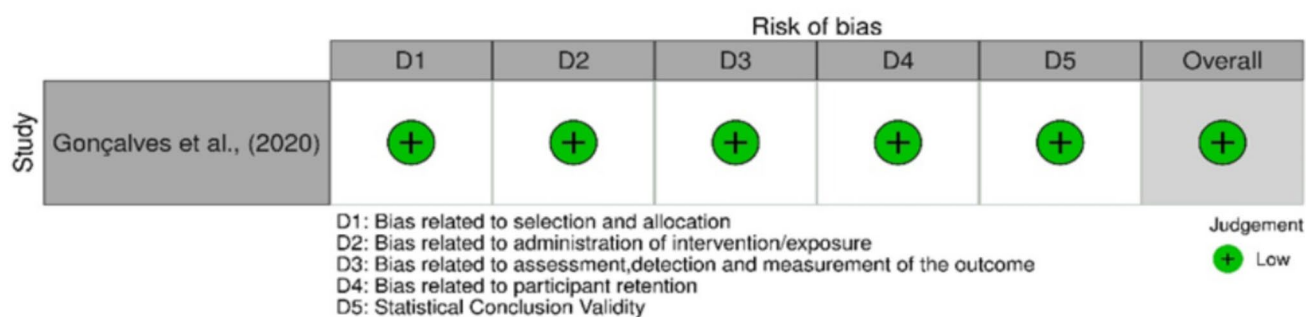


Fig. 6 RoB 2 for RCT risk of bias analysis

This study employs an integrative review methodology, which includes different designs to synthesize knowledge comprehensively, prioritizing critical methodological analysis and narrative synthesis (Whittemore and Knafl 2005; da Silva et al. 2020; Kutcher and LeBaron 2022; Fain 2024).

To analyze the risk of bias and methodological quality of the included studies, the RoB 2 tool for randomized controlled trials (RCT), the Science in Risk Assessment and Policy (SciRAP) tool for the *in vitro* and *in vivo* studies, and the Joanna Briggs Institute (JBI) Critical Appraisal Tools were applied to remaining study types (SCIRAP.ORG 2018; McArthur et al. 2020). Thus, it was observed that nine (81.8%) of the studies included in this review had a low risk of bias, meaning that the probability of systematic errors or methodological limitations influencing the results of each study is low. Therefore, they are of good methodological quality, which can be seen in Figs. 6 and 7 and Table S4.

Discussion

General Aspects

Bixa orellana is a plant native to the tropical regions of the Americas, rich in carotenoid derivatives, terpenoids, tocotrienols, and flavonoids (Shahid-ul-Islam et al. 2016). Among its main bioactive compounds, bixin and norbixin stand out, both of which are associated with antimicrobial and wound healing properties. As a result, *B. orellana* has garnered growing scientific interest, particularly in the health field, where numerous studies have explored its pharmacological potential (Lima et al. 2001; Vilar et al. 2014). This review gathers findings from the literature regarding therapeutic products derived from the plant that underwent patentability processes or technological registration, with results reinforcing the antimicrobial activity of *B. orellana*, which demonstrated activity against 25 microbial strains, corroborating previously

reported therapeutic effects. Although the primary focus of this article is the antimicrobial effects of *B. orellana*, the included studies also reported significant anti-inflammatory and wound healing properties. Therefore, these additional pharmacological activities will also be addressed in the following sections.

Antimicrobial Activity

The widespread use of *B. orellana* is well known, ranging from its use in culinary applications as a natural dye to its application in folk medicine, particularly for its notable wound healing, antimicrobial, and antioxidant properties. Studies such as that by Irobi (1996) highlight the antimicrobial activity of the organic extract from urucum leaves, particularly against Gram-positive bacteria such as *S. aureus*, *Streptococcus faecalis*, and *Bacillus subtilis* (Irobi et al. 1996). Regarding the study by Gonçalves et al. (2005), it was demonstrated that the hydroalcoholic extract of *B. orellana* showed antimicrobial activity against *S. pyogenes*, *S. aureus*, and *Proteus mirabilis*.

The methanolic extract from the leaves and seeds in the study by Medina-Flores et al. (2016) exhibited antimicrobial activity against *S. mutans* and *S. sanguinis*. Another study demonstrating the antimicrobial activity of *B. orellana* was conducted by Majolo (2009), where different extractions of annatto were performed, including hydroethanolic extraction, decoction, and infusion. The various extracts were tested to evaluate their antimicrobial activity against five bacteria: *S. aureus*, *Enterococcus faecalis*, *L. monocytogenes*, *S. enteritidis*, and *E. coli*. The results from the hydroethanolic extraction showed superior activity regardless of the bacteria tested. This result may be due to the higher temperatures used in the other methods, which could lead to the loss of essential components. Among the bacteria tested, the most sensitive to the antibacterial activity of the extracts, regardless of the extraction method, were *Enterococcus faecalis* and *L. monocytogenes*, while *E. coli* showed the least sensitivity.

In the study by Pierpaoli et al. (2017), it was demonstrated that treatment with daptomycin combined with tocotrienols derived from *B. orellana* was significantly more effective against methicillin-resistant *S. aureus* compared to treatment with the drug alone. Rojas et al. (2006) compared various extraction methods (ethanol, water, hexane) and reported that the ethanol extract exhibited the greatest antimicrobial activity, with measurable action against *S. aureus*, *E. coli*, and particularly *Bacillus cereus*. Although the authors observed lower MIC values for the annatto ethanolic extract than for gentamicin sulfate against *B. cereus*, this comparison should be interpreted with considerable caution. Differences in microbial inocula, growth media, MIC determination protocols, solvent residues, and the chemical complexity of multi-compound plant extracts versus single-molecule antibiotics preclude direct equivalence claims, particularly in the absence of internationally standardized reporting (e.g., CLSI or EUCAST guidelines). Furthermore, the unit of measurement is not directly comparable, while gentamicin MICs reflect a defined molecular concentration, plant-extract MICs reflect the dry mass of a heterogeneous mixture in which the proportion of bioactive constituents is rarely quantified. Such head-to-head comparisons are therefore best understood as preliminary indicators of antimicrobial potential rather than evidence of therapeutic substitutability or clinical equivalence. The work by Fleischer et al. (2003) confirmed the action of the ethanolic extract of *B. orellana* leaves and seeds against bacterial colony growth, demonstrating significant activity against both Gram-positive and Gram-negative bacteria, including *Streptococcus aureus*, *S. pyogenes*, *P. aeruginosa*, *E. coli*, *Bacillus subtilis*, and *S. typhi*. Furthermore, it was noted that the leaf extract exhibited more pronounced activity than the seed extract.

The phytochemical compounds from the seed and leaf extracts of *B. orellana* that exhibit antimicrobial activity are listed in Table S5. The antimicrobial activity of *B. orellana*

is particularly relevant in wound healing because microbial colonization and biofilm formation sustain inflammation and impair tissue regeneration (Shen et al. 2025; Versey et al. 2021). In this context, annatto-derived compounds may exert a multifunctional therapeutic effect by simultaneously reducing microbial load and modulating inflammatory responses, thereby facilitating progression through the proliferative and remodeling phases of repair (Trinh et al. et al. 2022). This infection–repair interplay positions *B. orellana* as both an antimicrobial and a supportive regenerative agent; and it therefore constitutes a central interpretative axis of this review.

The following paragraph expands experimental factors that modulate reported antimicrobial findings and explains why results vary across studies. Overall, the antimicrobial activity of *B. orellana* extracts shows considerable variability, depending on experimental conditions. A recurrent trend across studies is higher efficacy against Gram-positive bacteria, such as *S. aureus*, compared with Gram-negative species like *E. coli*, which may be attributed to differences in cell-wall structure and permeability barriers. In addition, extraction methods significantly influence bioactivity, with hydroalcoholic and methanolic extracts generally exhibiting greater antimicrobial potential, likely because they recover higher amounts of phenolic compounds and flavonoids.

However, methodological heterogeneity remains a major limitation, as studies employ different assays (e.g., agar diffusion vs broth microdilution), concentration ranges, and reporting standards, often without adequate phytochemical characterization. Furthermore, although still limited, emerging evidence suggests that some *B. orellana* compounds may interfere with microbial adhesion and biofilm formation, which is particularly relevant in chronic wound environments. These factors highlight the need for standardized protocols and more robust experimental designs to enable meaningful comparisons and translational advancement (Santos et al. 2022; Trinh et al. 2022).

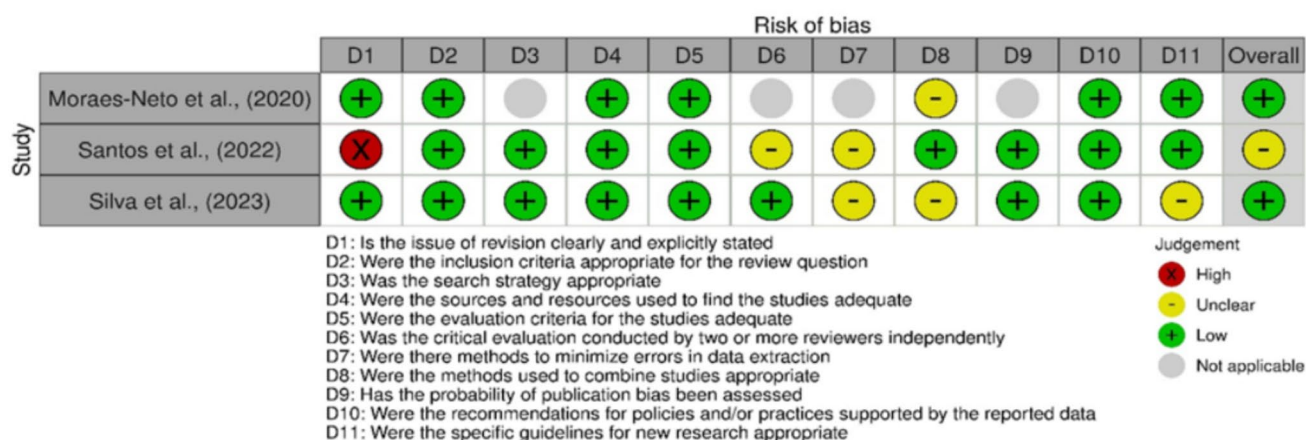


Fig. 7 JBI Critical Appraisal Tools for analyzing the risk of bias in narrative and systematic reviews

A structured comparison of antimicrobial outcomes across the included studies (see Table S2A) further highlights the variability in reported efficacy. Minimum inhibitory concentration (MIC) values ranged widely depending on the type of extract, microorganism tested, and experimental methodology. In general, hydroalcoholic and methanolic extracts demonstrated greater antimicrobial potency, particularly against Gram-positive bacteria such as *S. aureus*, whereas Gram-negative organisms such as *E. coli* tended to show lower susceptibility. Additionally, studies employing broth microdilution methods reported more precise and comparable MIC values, while agar diffusion assays often yielded qualitative or semi-quantitative results. These findings reinforce that differences in extraction methods, tested concentrations, and assay protocols significantly influence antimicrobial outcomes and limit direct comparability across studies. These limitations prevented the performance of quantitative synthesis or meta-analysis.

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These limitations are further examined in the section “Potential Bias Risks,” where issues related to the lack of methodological standardization, heterogeneity of experimental assays and reporting practices, and other sources of variability are critically evaluated, as they hinder direct comparability and limit the translational relevance of the antimicrobial findings (see Figs. 5 and 6 and Table S4).

Anti-inflammatory Activity

In terms of anti-inflammatory activity, compounds such as β -cryptoxanthin and lutein reduced inflammatory mediators, while bixin increased Nrf2 levels, promoting antioxidant protection. Additionally, other bioactive constituents of *B. orellana* have demonstrated modulatory effects on key inflammatory pathways. Procyanidin B2 and geranylgeraniol reduced nuclear factor kappa B (NF- κ B) expression, while geranylgeraniol and lutein inhibited the cyclooxygenase-2 (COX-2) enzyme. Ethyl acetate and ellagic acid extracts from the leaves also suppressed COX-2 activity, contributing to the attenuation of the inflammatory response (Neto et al. 2020).

Bixin, in particular, not only increased nuclear factor erythroid 2-related factor 2 (Nrf2) levels but also decreased reactive oxygen species and elevated glutathione concentrations, thereby offering cellular protection against oxidative DNA damage. These combined effects reflect the compound's antioxidant and cytoprotective potential. These anti-inflammatory and antioxidant actions also correlate with the phytocomplex's regenerative capacity, as evidenced by increased tissue reepithelialization, fibrin deposition, fibroblast proliferation, and collagen density, along with a reduction in neutrophil infiltration in wound sites (Neto et al. 2020).

Despite these promising pharmacological findings, current literature remains limited by the predominance of *in vitro* and preclinical studies, highlighting the need for more robust, randomized clinical trials. In this regard, more randomized clinical trials and technological appropriation are suggested, given the low-cost potential of *B. orellana* and its proven wound healing (Capella et al. 2016) and antimicrobial (Nathan et al. 2019) activity, highlighting its great potential as a phytotherapeutic agent for the health sector, especially in scenarios where microbial infection compromises the healing process.

The growing body of research in drugs derived from natural sources not only contributes to contemporary medicine but also serves as a model for developing synthetic molecules (Aguar 2019). Technological prospecting related to urucum has shown a significant increase since 2014, reflecting a growing trend in the use of patents as a protection mechanism for plant-based innovations. The data indicate that Brazil is the leading country in patent filings involving urucum, with most of the applications registered in the Patentscope database, where the International Patent Classification is used to organize and facilitate the search for innovations. Within class “61,” the most frequent subclasses include those dealing with medical and therapeutic preparations, underscoring the relevance of urucum in medicine. However, it is important to recognize the limitations associated with these studies. Patent protection, although essential, may present challenges, such as difficulty in meeting patentability criteria and the need to demonstrate the efficacy and safety of the products (Jochem et al. 2011).

In summary, *B. orellana* represents a promising source for the development of new drugs, with a notable increase in the number of patents involving its antimicrobial and wound healing effects, which act synergistically in therapeutic applications (Santos et al. 2022). The growth in patent usage reflects an increased appreciation for research on natural products and the search for effective therapeutic alternatives. The continuation of this trend may not only foster innovation in phytotherapy but also support the preservation of traditional knowledge and the appreciation of biodiversity.

Wound Healing Activity

Wound healing is a complex response involving several interconnected stages in a signaling cascade that ensures tissue homeostasis after injury. Importantly, this process is strongly influenced by the presence of microbial infection, which can prolong inflammation and delay tissue repair. In this context, the antimicrobial activity of *B. orellana* becomes particularly relevant, as it contributes to infection control while simultaneously supporting regenerative mechanisms. The stages are categorized as follows: the inflammatory phase, the proliferative phase, and the maturation phase. Initially, the inflammatory phase is characterized by vasodilation and the migration of inflammatory cells to the injury site, resulting in clot formation and the release of chemical mediators. The proliferative phase follows, where fibroblasts and keratinocytes proliferate, promoting new tissue formation and reepithelialization. The final maturation phase involves scar tissue remodeling, where collagen is reorganized, and vascularization decreases, resulting in a more resilient scar (Rousselle et al. 2019).

In this regard, evidence supports the therapeutic potential of *B. orellana* in the processes of tissue regeneration and wound healing, with synergistic and additive effects in combating microorganisms at the wound site (Piva et al. 2014; Vilar et al. 2014). This potential is attributed to carotenoids such as bixin, geranylgeraniol, and tocopherols, which have been extensively investigated as alternative treatments for chronic wounds. Bixin, a carotenoid found in the seeds, has demonstrated effects in reducing pain and inflammation, thereby supporting the progression of the healing process. Additionally, the presence of secondary metabolites in *B. orellana* suggests a synergistic effect that enhances wound healing, making it a promising candidate for topical treatment. These findings have led to the plant becoming a target for studies, with results from both *in vitro* and *in vivo* experimental models reinforcing the efficacy of *B. orellana* extract in healing or enhancing the healing process (Pacheco et al. 2019; Santos et al. 2022).

In *in vivo* studies with Wistar rats, the application of ointments containing annatto extract led to a significant reduction in wound area and an increase in reepithelialization compared to control groups. Histological and clinical evaluations revealed a greater fibrin presence and reduced exudate in animals treated with bixin-based compounds, suggesting a more efficient healing response compared to conventional treatments. In a specific experiment, reductions of 13.8 and 25% in wound size were observed after 4 and 7 days of treatment, respectively, and an increase of 2.26% in the reepithelialization surface after 4 days of therapy (Capella et al. 2016). These results further support the effectiveness of *B. orellana* extract in promoting healing and restoring epithelial tissue.

Wound healing is a multifactorial process influenced not only by cellular and molecular mechanisms but also by the presence of bacterial infection, which can delay regeneration by triggering excessive inflammation. Bacterial contamination—particularly when microbial load exceeds 10^5 CFU/g—can result in purulent exudation, edema, pain, and tissue necrosis, significantly impairing the healing process (Quege et al. 2008; Tazima et al. 2008). In this context, the antimicrobial and anti-inflammatory actions of bixin are especially relevant, as they support key stages such as inflammation modulation, wound contraction, and collagen maturation, as highlighted in preclinical studies (Piva et al. 2014; Capella et al. 2016).

The topical use of bixin-containing formulations, whether as ointments, disinfectants, or integrated into delivery systems, enhances its therapeutic potential. Several technological innovations have emerged from this approach, aiming to enhance the efficacy and delivery of *B. orellana*-derived compounds. For example, Garcia et al. (2018) and Millan et al. (2018) described polycaprolactone nanofiber systems loaded with bixin that promote effective healing of chronic and ulcerative wounds, including in diabetic patients. In a similar vein, Figueiredo et al. (2019) developed biodegradable films based on cassava or rice starch containing lyophilized *B. orellana* extract, also aiming to accelerate epithelial repair in both diabetic and non-diabetic individuals.

Advances also include chitosan-based and starch-melamine polymeric matrices (BR 1020200146858 A2; BR 1020190040327 A2), as well as ceramic and polymeric scaffolds designed for tissue engineering applications (BR 1020170180808 A2), all of which incorporate *B. orellana* extract as a bioactive agent to stimulate both *in vivo* and *in vitro* regeneration (Ferreira et al. 2019; Junior and Rodrigues 2020; Viana et al. 2022). Additional patents describe the use of annatto oil extracts for topical and oral applications, supporting epithelial and mucosal healing (BR PI 10000390 A2) (Magalhães 2011). This potential is further supported by patent BR PI 0921269 A2, which describes a composition combining an oxidizing agent and a photoactivator, suggesting its use in phototherapy involving *B. orellana* to accelerate wound healing (Piergallini et al. 2018).

Among the eligible patent applications, relatively few focus exclusively on standalone antimicrobial formulations, while a substantially larger proportion targets wound healing technologies that incorporate antimicrobial functionality (for example, polymeric films, foams, and nanofibers). This pattern suggests that technological translation of *B. orellana* research has favored multifunctional biomaterials that combine infection control with regenerative support rather than isolated antimicrobial products. Only a small number of filings explicitly claim

antimicrobial-only uses (*e.g.*, two in Brazil; two in India), whereas most wound-oriented patents describe composite systems in which annatto extracts are embedded in polymeric matrices to accelerate healing and reduce microbial contamination. Together, these observations indicate a clear translational trend: although scientific evidence supports the antimicrobial activity of *B. orellana*, developers have prioritized integrated wound management solutions, leaving targeted preclinical and clinical validation of antimicrobial-only formulations as an important gap (Versey et al. 2021; Trinh et al. 2022). In this context, the antimicrobial activity of *B. orellana* becomes particularly relevant, as it contributes to infection control while simultaneously supporting regenerative mechanisms.

Technological Prospecting of *Bixa orellana* as an Antimicrobial and Wound Healing Agent

The use of natural products as therapeutic agents for treating diseases caused by microorganisms offers significant advantages over synthetic drugs, as phytotherapy tends to cause fewer adverse effects, both toxicologically and pharmacologically. Based on the findings of this research, which highlight antimicrobial activity as a central property of *B. orellana* and demonstrate its relevance associated with wound healing, it can be inferred that there is significant technological potential for developing multifunctional therapeutic products.

Despite the increasing number of patent applications related to natural products, a significant gap persists between technological development and clinical validation. Although patents reflect innovation potential and efforts to secure intellectual property, it does not indicate that the proposed technologies have undergone rigorous preclinical or clinical evaluation. Moreover, patented inventions may be based on preliminary data, such as *in vitro* assays or limited experimental models, which do not always translate into safety and efficacy in humans (Jiang and Zhang 2025).

This discrepancy highlights a critical problem in the translational process, in which numerous promising compounds fail to progress to more advanced stages of development. Factors such as high costs, regulatory barriers, and the complexity of clinical trials further contribute to this gap (Jiang and Zhang 2025).

In this context, a low number of patent applications utilizing *B. orellana* as an antimicrobial agent were observed, with only two applications in Brazil and two in India. Among the precedents found, two address extraction methods, and two discuss the antimicrobial activity of *B. orellana* extract. Despite the ample evidence found in the literature regarding its antimicrobial properties, this has not been translated into technological applications. In contrast, regarding the wound healing activity, 12 patent applications were found, of which

three use *B. orellana* extract, and nine use its extract associated with polymeric films, which accelerate and improve the healing process.

Thus, although *B. orellana* has a variety of applications, incentives for the development of phytotherapy products remain limited, and greater encouragement is needed for medicinal plants to be transformed into products (Ryan 2010). Moreover, despite there being several pieces of evidence for the use of *B. orellana* as a wound healing and antimicrobial agent, clinical trials, standardized extraction methods, and *in vivo* efficacy assessments are still needed in order to support the development of innovations that effectively result in safe and efficacious therapeutic products.

In addition to the direct use of *B. orellana* extract or oil for antimicrobial evaluation, recent studies have explored its potential as a photosensitizing agent in photodynamic therapy (PDT). Photodynamic therapy is a therapeutic approach that involves the application of a photosensitizer—typically a natural or synthetic compound—which, when activated by light at a specific wavelength, produces reactive oxygen species capable of destroying microbial cells. Derivatives of *B. orellana*, particularly its extract, have demonstrated photosensitizing capacity under blue LED light. In one study, annatto extract combined with blue LED was used in antimicrobial photodynamic therapy (aPDT) to reduce halitosis, showing comparable efficacy to conventional methods like tongue scraping, and even greater effectiveness when both methods were combined (Neto et al. 2020).

In another investigation, Silva-Júnior et al. (2020) evaluated a formulation combining Papacarie Duo™ and *B. orellana* extract, also activated with blue LED. The results indicated no cytotoxicity, preservation of collagen structure, and significant antimicrobial action. These findings support the potential of *B. orellana*-based formulations not only as direct therapeutic agents but also as effective photosensitizers for use in aPDT, particularly in the treatment of oral infections and carious lesions. This potential is further supported by patent BR PI 0921269 A2, which describes a composition combining an oxidizing agent and a photoactivator, suggesting its use in phototherapy involving *B. orellana* to accelerate wound healing (Piergallini et al. 2018).

Quality of Scientific Evidence, Limitations, and Potential Bias Risks

Despite the promising antimicrobial activity reported for *B. orellana*, the available evidence remains limited and markedly heterogeneous, which compromises the robustness and generalizability of the conclusions. One of the main sources of this variability is associated with the different plant parts used (*e.g.*, seeds and leaves). This variability is intrinsic, as different plant tissues exhibit an uneven distribution of secondary metabolites. In this context, leaf extracts tend to

contain higher levels of phenolic compounds and flavonoids, whereas seeds are richer in carotenoids such as bixin and norbixin (Ahmed et al. 2020; Raju et al. 2022). Furthermore, ecological and genetic factors, including geographical variation and reproductive isolation, may significantly alter the metabolic profile of the species, thereby influencing experimental outcomes (Guerrero-Lagunes et al. 2025).

In addition, the diversity of solvents (aqueous, ethanolic, methanolic, chloroform) and extraction techniques (e.g., maceration, decoction) plays a central role in the observed variability, as differences in solvent polarity favor the extraction of specific classes of compounds. For instance, methanolic extracts are generally more efficient in recovering phenolic compounds associated with antimicrobial activity, whereas aqueous extracts may exhibit lower extraction efficiency (Ahmed et al. 2020). However, many studies describe their materials generically as “*Bixa orellana* extract” without adequate characterization, which limits the comparability of findings. Moreover, factors such as drying temperature and fruit maturation stage further influence the stability and concentration of bioactive metabolites (Everton et al. 2020; Oliveira et al. 2022).

Another critical issue is the lack of standardization in antimicrobial assays. The analyzed studies employ different methodologies—including agar diffusion, broth microdilution, and colorimetric assays—with substantial variation in tested concentrations, measurement units, and interpretation criteria, often without reference to internationally recognized guidelines. This methodological inconsistency precludes direct comparison of minimum inhibitory concentration (MIC) values or inhibition zones, thereby hindering the consolidation of robust quantitative evidence.

Finally, there is a clear predominance of *in vitro* studies, with limited investigations in *in vivo* models and a lack of clinical trials, which restricts the extrapolation of findings to therapeutic applications. Therefore, although the available data suggest a promising antimicrobial potential for *B. orellana*, the high methodological heterogeneity and lack of standardization weaken the strength of the evidence and warrant cautious interpretation. Progress in this field depends on the adoption of standardized protocols, rigorous phytochemical characterization, and the advancement of well-designed preclinical and clinical studies.

Future Perspectives

Despite the consistent body of evidence supporting the antimicrobial potential of *B. orellana* synthesized in this integrative review, the translation of these findings into clinically validated therapeutic products will require coordinated progress along four complementary axes.

First, methodological standardization is a prerequisite for cumulative evidence. As demonstrated in Table 1 and discussed in Sect. “Antimicrobial Activity,” future antimicrobial studies on *B. orellana* should adopt internationally recognized protocols—particularly the Clinical and Laboratory Standards Institute guidelines (CLSI 2018) or the European Committee on Antimicrobial Susceptibility Testing breakpoint tables (EUCAST 2024). Standardized broth microdilution should be prioritized over agar diffusion when minimum inhibitory concentration (MIC) values are reported, and bactericidal versus bacteriostatic effects should be systematically distinguished by determining minimum bactericidal concentrations (MBC). Reporting should also include strain provenance, inoculum density, growth media, and the use of quality-control reference strains, enabling cross-study comparison and meta-analytic synthesis—currently precluded by the methodological heterogeneity highlighted earlier in this section.

Second, rigorous phytochemical characterization of the extracts under investigation is essential. As emphasized in this review, the current literature is hindered by generic descriptions such as “*B. orellana* extract” without quantification of bixin, norbixin, geranylgeraniol, tocotrienols, or phenolic content—a limitation that is compounded by the well-documented variability in metabolite distribution between seeds and leaves and across geographical origins (Ahmed et al. 2020; Guerrero-Lagunes et al. 2025). Adoption of validated analytical platforms (HPLC–DAD, LC–MS, and HPLC–PDA) for batch-level fingerprinting would enable meaningful comparisons across studies and allow identification of the active fractions responsible for the observed antimicrobial effects, ultimately supporting reproducibility and quality-control criteria for future phytotherapeutic formulations.

Third, prioritized experimental models should advance the field beyond planktonic *in vitro* susceptibility assays. Of particular relevance are (i) mature biofilm models, given that chronic wound infections and oral infections—two clinical contexts in which *B. orellana* has shown promise in the studies retrieved by this review—are predominantly biofilm-mediated; (ii) *in vivo* wound infection models in rodents, including MRSA-infected excisional wounds in immunocompetent and diabetic mice; (iii) *ex vivo* human skin explant models for translational relevance; and (iv) early-phase randomized controlled trials targeting well-defined clinical scenarios in which standardization is realistic—for example, topical adjuvant therapy for chronic wounds or photodynamic protocols for oral infections, building on the antimicrobial photodynamic therapy evidence mapped in Sect. “Wound Healing Activity” of this review.

Fourth, regulatory and translational pathways should be considered from the earliest stages of product development. The marked gap between patent filings and clinical

validation observed in this review (17 patents identified, none with documented clinical trials) illustrates a broader translational bottleneck that affects natural-product research globally. In the Brazilian context, early alignment with ANVISA RDC 26/2014 for herbal medicines and RDC 318/2019 for stability requirements would streamline future registration; internationally, equivalent frameworks such as the European Medicines Agency monographs on herbal medicinal products and the FDA Botanical Drug Development guidance provide additional reference standards for translational planning. Greater integration between academic research groups, INPI-protected technology developers, and the pharmaceutical innovation ecosystem will be decisive for converting the demonstrated experimental potential of *B. orellana* into accessible, evidence-based phytotherapeutic and biomaterial-based solutions.

Conclusion

According to the results obtained, it was verified that Brazil not only is a major producer of annatto but also has been increasingly investing in research, development, and innovation. This reflects notable progress in the intellectual property field, with Brazil registering the highest number of patent applications involving *B. orellana* as an antimicrobial and wound healing agent. The findings confirm that, beyond its extensive use as a food coloring agent, annatto extracts offer multiple pharmacological applications, demonstrating potential antioxidant, antimicrobial, and regenerative properties. Its ability to be incorporated into polymeric formulations further expands its applicability across various biomedical fields.

Building upon this scientific foundation, recent studies have further highlighted the pharmacological diversity of *B. orellana*. Its antimicrobial activity, effective against a broad spectrum of Gram-positive and Gram-negative bacteria, as well as fungi, is attributed to compounds such as bixin, norbixin, and tocotrienols. Moreover, the plant exhibits significant anti-inflammatory potential by modulating key pathways through the action of geranylgeraniol, lutein, and procyanidins. These effects work synergistically to enhance its wound healing capacity, reducing oxidative stress, stimulating fibroblast proliferation, and supporting tissue reepithelialization.

Bixa orellana demonstrates significant antimicrobial and wound healing potential, with growing evidence supporting the integration of these properties in therapeutic and technological applications—particularly in biomaterials for wound management. At the same time, the species exemplifies how biodiversity-based research can generate socioeconomic and innovation opportunities when scientific knowledge is translated into products. To realize this potential, however,

standardized experimental protocols, robust preclinical models, and well-designed clinical studies are required to validate safety and efficacy and to support regulatory approval and commercialization. Addressing these translational gaps will be essential to move *B. orellana* from promising experimental evidence to effective, evidence-based phytotherapeutic and biomaterial solutions.

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Declarations

Conflict of Interest The authors declare no competing interests.

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