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CIÊNCIAS DA SAÚDE

Medicinal plants used in the treatment of infectious diseases in the state of Paraíba, Brazil: a review of ethnomedicinal evidence and clinical trials

Plantas medicinais utilizadas no tratamento de doenças infecciosas no estado da Paraíba, Brasil*: uma revisão das evidências etnomedicinais e ensaios clínicos*

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ABSTRACT

Infectious diseases are caused by pathogenic microorganisms, mainly bacteria, viruses, parasites and fungi, and represent a threat to public health. In the state of Paraíba, Brazil, several plant species are widely used in traditional medicine to treat infections caused by pathogenic microorganisms. From this perspective, the present study aimed to carry out a bibliographic survey of plants used in the treatment of infectious diseases by local communities and to identify the species that have already been investigated in clinical trials. The scientific documents were retrieved from different databases. A total of 31 species distributed in 22 families are used against infections by traditional communities in different municipalities in Paraíba. However, only 8 species have had their herbal products evaluated in clinical trials. Mouthwashes containing *Aloe vera*, *Anacardium occidentale* and *Punica granatum* have been targeted for dental applications. Considering the urgency in developing broad-spectrum antimicrobials, it is recommended that new randomized clinical trials be developed to investigate the traditional uses of other medicinal plants against infectious diseases reported in this study.

Keywords: Ethnopharmacology; Herbal medicine; *Punica granatum*.

RESUMO

As doenças infecciosas são causadas por microrganismos patogênicos, principalmente bactérias, vírus, parasitas e fungos, e representam uma ameaça à saúde pública. No estado da Paraíba, Brasil, várias espécies de plantas são amplamente utilizadas na medicina tradicional para tratar infecções causadas por microrganismos patogênicos. Nessa perspectiva, o presente estudo teve como objetivo realizar um levantamento bibliográfico de plantas utilizadas no tratamento de doenças infecciosas pelas comunidades locais e identificar as espécies que já foram investigadas em ensaios clínicos. Os documentos científicos foram recuperados de diferentes bases de dados. Um total de 31 espécies distribuídas em 22 famílias são utilizadas contra infecções por comunidades tradicionais em diferentes municípios da Paraíba. Contudo,

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apenas 8 espécies tiveram seus produtos fitoterápicos avaliados em ensaios clínicos. Enxaguantes bucais contendo Aloe vera, Anacardium occidentale e Punica granatum têm sido alvo de aplicações odontológicas. Considerando a urgência no desenvolvimento de antimicrobianos de amplo espectro, recomenda-se que novos ensaios clínicos randomizados sejam desenvolvidos para investigar os usos tradicionais de outras plantas medicinais relatadas no presente estudo contra doenças infecciosas.

***Palavras-chave**: Etnofarmacologia; Fitoterapia; Punica granatum.*

1. INTRODUCTION

Infectious diseases are caused by pathogenic microorganisms, mainly bacteria, viruses, parasites and fungi, and represent a threat to public health (Ortega *et al.,* 2020). The discovery of penicillin (produced by fungi of the genus *Penicillium*) and streptomycin (produced by *Streptomyces griseus*) in 1928 and 1943, respectively, presaged the time when antibiotics became a dominant component for the treatment of infectious diseases (Dhingra *et al.,* 2020). However, microbial resistance to conventional antibiotics has increased significantly across the world in recent decades and thus has led to the end of the current “antibiotic era” (Wang *et al.,* 2020). Antimicrobial resistance occurs when different pathogens mutate over time and no longer respond to any pharmacological agent, making infections resistant to available treatments (Arip *et al.,* 2022).

Despite efforts to control infectious diseases (Pacios *et al.,* 2020), the crisis of antibiotic resistance is global, highlighting the problem of inappropriate drug use by the population and the lack of development of new antimicrobial agents (Eldin *et al.,* 2023). Investigations on plant-based antimicrobials have shown that these natural products act in a similar way to conventional antibiotics (Uddin *et al.,* 2021), as they kill bacteria or limit their development through mechanisms of action related to rupture of the plasma membrane, inhibition of protein synthesis, inhibition of metabolic pathways, interference with cell wall synthesis, inhibition of DNA and RNA synthesis (Álvarez-Martínez *et al.,* 2021). Therefore, extracts obtained from plants and isolated phytochemicals can be used as promising alternatives in the treatment of microbial infections (Wang *et al.,* 2020; Eldin *et al.,* 2023).

In the state of Paraíba, Brazil, ethnobotanical and ethnopharmacological surveys have reported that several plant species are widely used in traditional medicine to treat infections caused by pathogenic microorganisms (Coutinho *et al.,* 2018; Silva *et al.,* 2018; Medeiros *et al.,* 2019; Felix *et al.,* 2019; Ferreira *et al.,* 2021; Maia *et al.,* 2021). Some herbal medicines obtained from these species have been evaluated in clinical trials to verify the effectiveness of their antimicrobial effects. Mouthwashes containing *Aloe vera* (L.) Burm.f., *Anacardium occidentale* L., and *Punica granatum* L., for example, may represent a promising alternative in the treatment of gingivitis and bacterial plaque (Ahuja *et al.,* 2011; Gomes *et al.,* 2016; Sargolzaie *et al.,* 2016; Vangipuram *et al.,* 2016; Sedigh-Rahimabadi *et al.,* 2017; Eltay *et al.,* 2021; Pattnaik *et al.,* 2022).

From this perspective, considering the medicinal potential of the flora of Paraíba, the present study aimed to carry out a survey of the plants used to treat infections by

local communities and identify the species that have already been investigated in clinical trials.

2. METHODS

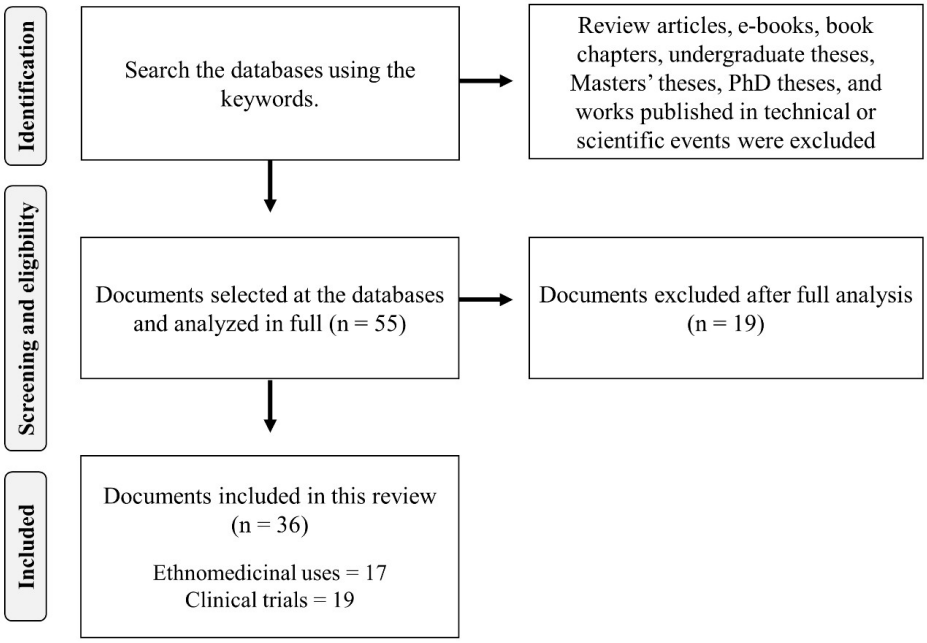
2.1. DATABASES

Scientific documents were retrieved from Google Scholar (https://scholar.google.com/), PubMed® (https://pubmed.ncbi.nlm.nih.gov/), ScienceDirect® (https://www.sciencedirect.com/search), and SciELO (https://search.scielo.org/) databases. The following terms were used as search strategies: “ethnobotany AND infections AND Paraíba”, “medicinal plants AND infections AND Paraíba”, “traditional uses AND infections AND Paraíba”, “antimicrobial OR anti-infective AND medicinal plants AND clinical trial”, and “infectious diseases AND herbal medicine AND clinical trial”.

2.2. INCLUSION AND EXCLUSION CRITERIA

Regarding the inclusion criteria, only scientific articles published in the last 20 years (2003-2023) that reported ethnomedicinal uses of plants in the state of Paraíba and clinical trials of herbal products used to treat infections were selected. Review articles, e-books, book chapters, undergraduate theses, Masters’ thesis, PhD thesis, and works published in technical or scientific events were excluded. Scientific articles that did not provide sufficient ethnopharmacological information about the parts used, preparation mode and/or administration mode of medicinal plants used in the treatment of infectious diseases were also excluded. Finally, a total of 36 articles were included in the present study (Figure 1).

Figure 1 – Flow diagram of selection of scientific documents included in this review.



Source: Elaborated by the author.

2.3. DATA ANALYSIS AND CATEGORIZATION OF INFORMATION

The data extracted from the selected scientific documents were analyzed qualitatively and presented in tables and graphs when necessary. The results were described in two broad categories: 1) Medicinal plants used to treat infections by traditional communities in Paraíba, Brazil, and 2) Clinical trials of medicinal plants used to treat infections in Paraíba, Brazil. The scientific names of all species were checked on the website Flora e Funga do Brasil© (http://floradobrasil.jbrj.gov.br/reflora/).

3. RESULTS AND DISCUSSION

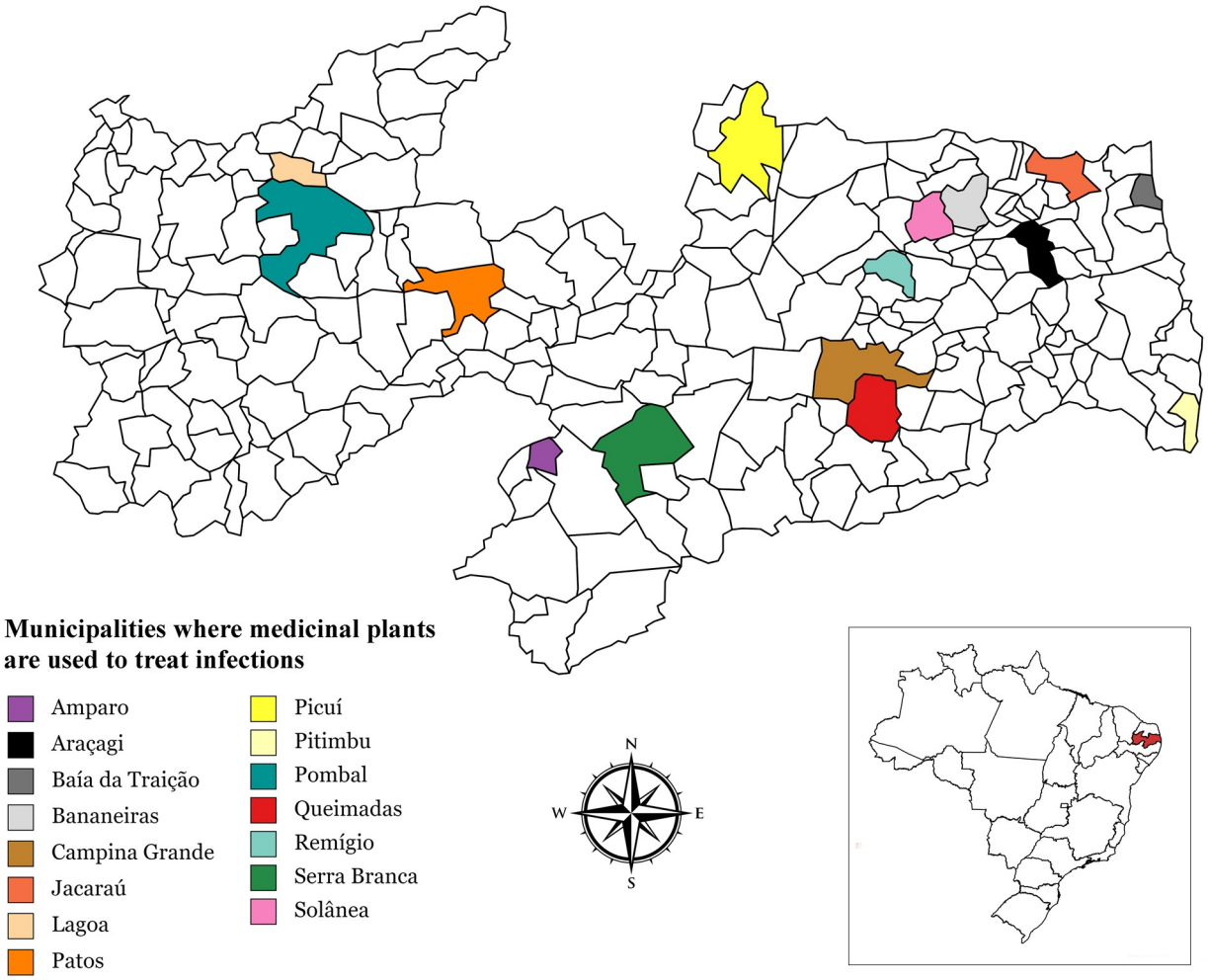
3.1. MEDICINAL PLANTS USED TO TREAT INFECTIONS BY TRADITIONAL COMMUNITIES IN PARAÍBA, BRAZIL

According to the scientific documents analyzed, it was possible to observe that medicinal plants are used to treat infectious diseases in 15 municipalities in the state of Paraíba (Figure 2), including: Campina Grande (Alves *et al.,* 2007; Souza *et al.,* 2013), Queimadas (Barbosa, 2011; Santos *et al.,* 2012), Lagoa (Lucena *et al.,* 2012), Pombal (Andrade *et al.,* 2012), Baía da Traição (Leite; Marinho, 2014), Bananeiras (Cavalcante; SILVA, 2014), Pitimbu (Brito *et al.,* 2015), Solânea (Silva *et al.,* 2015), Picuí (Costa; Marinho, 2016), Amparo (Coutinho *et al.,* 2018), Remígio (Silva *et al.,* 2018), Patos (Medeiros *et al.,* 2019), Serra Branca (Felix *et al.,* 2019), Araçagi (Ferreira *et al.,* 2021), and Jacaraú (Maia *et al.,* 2021).

A total of 31 species distributed in 22 families are used to treat infectious diseases in Paraíba (Table 1). Fabaceae was the family with the largest number of species (5 spp.), followed by Amaranthaceae (2 spp.), Anacardiaceae (2 spp.), Arecaceae (2 spp.), Bignoniaceae (2 spp.), and Lamiaceae (2 spp.). It has been reported that several flavonoids identified in Fabaceae species showed anti-infective potential against pathogenic microorganisms (Abad *et al.,* 2011). According to Ding *et al.* (2014), the Asteraceae, Lamiaceae, and Fabaceae families can be considered as important sources of bioactive compounds for the treatment of inflammatory and infectious diseases. Therefore, the traditional uses of Fabaceae in Paraíba are supported by scientific evidence.

The leaves (29%), bark (27%), and roots (17%) are the parts most used in the preparation of herbal medicines by local populations (Figure 3). In other states in Northeastern Brazil, it was also evident that the leaves are the parts most used to treat diseases caused by pathogenic microorganisms. According to Rêgo et al. (2023), the leaves (22.91%) are commonly recommended against infections by "*raizeiros*" in the public market in Maceió, Alagoas. In an ethnobotanical survey conducted in the municipality of Aracajú, Sergipe, it was reported that leaves (87.8%) are the parts of plants most used for the treatment of parasitic infections (Ribeiro *et al*. 2016).

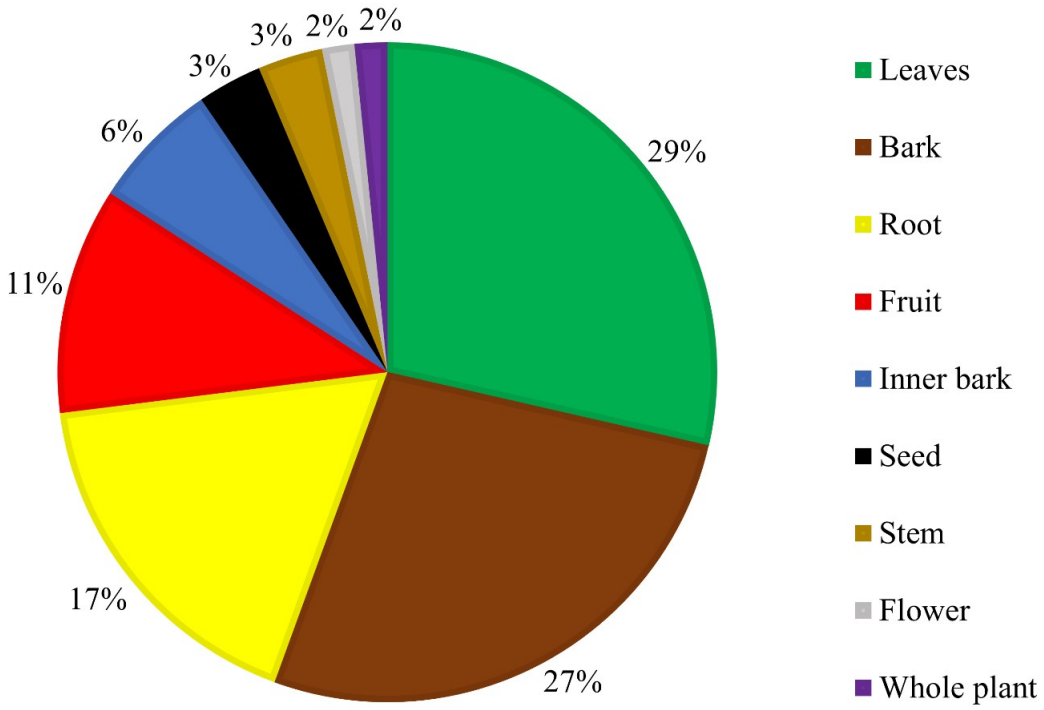
Figure 2 – Geographic distribution of scientific documents with information on the use of medicinal plants to treat infectious diseases in different municipalities of the state of Paraíba, Brazil.



Source: Map elaborated by the author in MapChart©.

Interestingly, different results were observed in the Midwest region of Brazil. In the municipality of Rondonópolis located in the state of Mato Grosso, for example, it was observed that the parts of plants most used to treat infections were the bark (53.33%) and root (20%) (Martins *et al.* 2022). These findings suggest that the use of plant parts for herbal preparations varies according to traditional communities located in different Brazilian regions.

Figure 3 – Parts of plants traditionally used in the treatment of infectious diseases.



Source: Elaborated by the author.

Table 1 – Medicinal plants used to treat infections by traditional communities in Paraíba, Brazil.

Family / Species	Vernacular name	Municipalities	Part used	Mode of preparation	Medicinal use	References
ADOXACEAE						
Sambucus australis Cham. & Schltdl.	Sabugueira	Jacaraú	Flower, root, leaves	Decoction, infusion	Infection in general	Maia *et al.* (2021)
AMARANTHACEAE						
Alternanthera brasiliana (L.) Kuntze	Penicilina	Solânea	Leaves	Tea	Urinary infection	Silva *et al.* (2015)
Dysphania ambrosioides (L.) Mosyakin & Clemants [Syn. *Chenopodium ambrosioides* L.]	Mastruz	Amparo	-	Tea	Infection	Coutinho *et al.* (2018)
		Baía da Traição	Leaves	Infusion, bath, tincture, juice	Tuberculosis	Leite and Marinho (2014)
ANACARDIACEAE						
Anacardium occidentale L.	Cajueiro	Queimadas	Leaves, bark	-	Urinary infection	Barbosa (2011)
		Campina Grande	Bark	Oral use	Urinary infection	Souza *et al.* (2013)
		Araçagi	Bark, inner bark, fruit	Decoction, maceration, juice	Infection	Ferreira *et al.* (2021)

Astronium urundeuva (M.Allemão) Engl. [Syn. *Myracrodruon urundeuva* M. Allemão]	Aroeira	Queimadas	Bark, inner bark	-	Infection	Barbosa (2011)
		Campina Grande	Bark	Tea, topical use	Infection in the vagina	Alves *et al.* (2007)
		Araçagi	Bark, inner bark, leaves	Decoction, "*garrafada*", infusion, syrup, maceration	Infection	Ferreira *et al.* (2021)
ARECACEAE						
Syagrus cearensis Noblick	Coco-catolé	Serra Branca	Root, fruit, Leaves	Maceration, *in natura*	Urinary infection	Felix *et al.* (2019)
Syagrus oleracea (Mart.) Becc.	Coco-catolé	Patos	Root	-	Urinary infection	Medeiros *et al.* (2019)
ASPARAGACEAE						
Aloe vera (L.) Burm.f.	Babosa	Campina Grande	Leaves	Topical use	Furuncle	Souza *et al.* (2013)
		Araçagi	Leaves	Decoction, "*garrafada*", juice, syrup, suppository	Acne, furuncle	Ferreira *et al.* (2021)
ASTERACEAE						
Solidago chilensis Meyen	Arnica	Campina Grande	Bark	Tea	Urinary infection	Alves *et al.* (2007)
BIGNONIACEAE						
Fridericia chica (Bonpl.) L.G.Lohmann [Syn. *Arrabidea chica* (HBK.) Verlot]	Cajuruna	Solânea	Leaves	Tea	Skin infections	Silva *et al.* (2015)
Handroanthus heptaphyllus (Vell.) Mattos [Syn. *Tabebuia avellanedae* (Mart. ex. D.C.) Standl.]	Pau-d'arco-roxo	Queimadas	Bark, inner bark	-	Infection	Barbosa (2011)
CACTACEAE						
Cereus jamacaru DC.	Cardeiro	Campina Grande	Root	Tea	Urinary infection	Alves *et al.* (2007)
		Lagoa	Root	Decoction, sitz bath	Infection	Lucena *et al.* (2012)
CRASSULACEAE						
Kalanchoe pinnata (Lam.) Pers. [Syn. *Bryophyllum calycinum* Salisb.]	Saião, corama	Queimadas	Leaves	-	Infection	Barbosa (2011)
		Picuí	Leaves	Syrup	Infection	Costa and Marinho (2016)
EUPHORBIACEAE						
Cnidoscolus urens (L.) Arthur	Urtiga-branca	Queimadas	Root	Decoction, maceration	Urinary infection	Santos *et al.* (2012)

		Araçagi	Root	Decoction, “*garrafada*”, maceration	Infection	Ferreira *et al.* (2021)
FABACEAE						
Amburana cearensis (Allemão) A.C.Sm.	Cumarú	Araçagi	Bark, seed	Decoction, “*garrafada*”, syrup, powder	Infection	Ferreira *et al.* (2021)
Anadenanthera colubrina (Vell.) Brenan	Angico	Remígio, Solânea	Bark	Decoction, maceration, oral use	Infection	Silva *et al.* (2018)
Copaifera langsdorffii Desf.	Copaíba	Patos	Bark	-	Infection	Medeiros *et al.* (2019)
Hymenaea courbaril L.	Jatobá	Picuí	Bark, fruit	Syrup, tea	Urinary infection	Costa and Marinho (2016)
Stryphnodendron adstringens (Mart.) Coville	Barbatimão	Campina Grande	Bark	Oral use	Urinary infection	Souza *et al.* (2013)
LAMIACEAE						
Mentha arvensis L.	Hortelã-japonesa	Jacaraú	Leaves	Decoction, infusion, *in natura*	Infection in general	Maia *et al.* (2021)
Mentha × *villosa* Huds.	Hortelã-miúda	Picuí	Leaves	Tea, syrup, juice	Intestinal infection	Costa and Marinho (2016)
LYTHRACEAE						
Punica granatum L.	Romã	Queimadas	Fruit, fruit peel, bark, root	-	Throat infection	Barbosa (2011)
		Campina Grande	Bark	Oral use	Pharyngitis	Souza *et al.* (2013)
		Araçagi	Fruit	Decoction, maceration	Throat infection	Ferreira *et al.* (2021)
MALPIGHIACEAE						
Malpighia glabra L.	Acerola	Bananeiras	Fruit	-	Infection	Cavalcante and Silva (2014)
MALVACEAE						
Malva parviflora L.	Malva	Pombal	Leaves	Infusion	Mouth and throat infection	Andrade *et al.* (2012)
OXALIDACEAE						
Averrhoa carambola L.	Carambola	Jacaraú	Leaves	Infusion	Infection in general	Maia *et al.* (2021)
PHYLLANTHACEAE						
Phyllanthus niruri L.	Quebra-pedra	Queimadas	Leaves, root	-	Urinary infection	Barbosa (2011)
RUBIACEAE						
Borreria verticillata (L.) G.Mey.	Vassoura-de-botão	Pitimbu	Whole plant	-	Urinary infection	Brito *et al.* (2015)
SAPOTACEAE						

Sideroxylon obtusifolium (Roem. & Schult.) T.D.Penn. subsp. *obtusifolium* [Syn. *Bumelia sartorum* M.]	Quixabeira	Campina Grande	Bark	Oral use	Urinary infection	Souza *et al.* (2013)
SCHISANDRACEAE						
Illicium verum Hook.f.	Anil-estrelado	Araçagi	Fruit, seed	Decoction, "*garrafada*", infusion	Infection	Ferreira *et al.* (2021)
TURNERACEAE						
Turnera subulata Sm.	Chanana	Queimadas	Leaves, root	-	Urinary infection	Barbosa (2011)
		Picuí	Root, Leaves	Tea, infusion	Urinary infection	Costa and Marinho (2016)
XIMENIACEAE						
Ximenia americana L.	Ameixa	Queimadas	Bark	Maceration	Infection	Santos *et al.* (2012)
		Campina Grande	Bark	Tea, topical use	Urinary infection	Alves *et al.* (2007)

Source: Elaborated by the author.

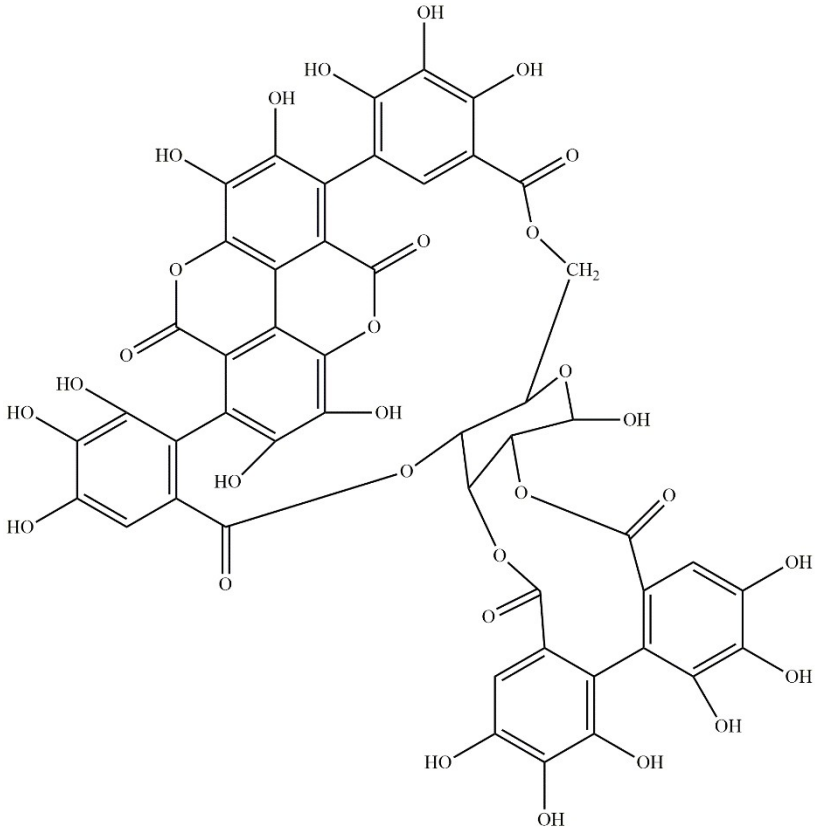
Anacardium occidentale L., *Astronium urundeuva* (M.Allemão) Engl. (syn. *Myracrodruon urundeuva*) and *Punica granatum* L. were the most cited species in ethnobotanical and ethnopharmacological surveys carried out in Paraíba. The traditional communities of Queimadas, Campina Grande, and Araçagi use these plants in the form of tea, "garrafada", syrup, and juice to treat throat infection, pharyngitis, urinary infection, and vaginal infections (Alves *et al.,* 2007; Barbosa, 2011; Souza *et al.,* 2013; Ferreira *et al.,* 2021). Several scientific studies have proven the antimicrobial potential of extracts and phytochemicals isolated from species.

Punica granatum, popularly known as "romã", has been reported for its broad spectrum of activity against pathogenic microorganisms *in vitro* studies (Chen *et al.,* 2020; Qahir *et al.,* 2021; Machado *et al.,* 2022; Valero-Mendoza *et al.,* 2022). Punicalagin (Figure 4) isolated from the fruit pericarp of *P. granatum* showed a minimum inhibitory concentration (MIC) of 61.5 µg/mL against methicillin-resistant *Staphylococcus aureus* strains (Machado *et al.,* 2002). Gosset-Erard et al. (2021) also reported that punicalagin isolated from the fresh peels of the fruits of this species showed antimicrobial activity against gram-negative and gram-positive bacteria, with MIC values ranging between 0.3 and 1.2 µg/mL. According to Nweze *et al*. (2019), the compound *β*-sitosterol isolated from the hexane extract of the stem bark of *P. granatum* was effective against *Salmonella typhi* and *Escherichia coli*, with MIC values of only 6.25 and 12.5 µg/mL, respectively.

Traditionally used to treat infections, *A. occidentale* is another species with scientifically proven antimicrobial potential (Bouttier *et al.,* 2002; Anand *et al.,* 2015; Ribeiro *et al.,* 2021). Bouttier *et al.* (2002) reported that cashew nut shell liquid exhibited potent antimicrobial activity against *Propionibacterium acnes* (1.56 µg/mL), *Corynebacterium xerosis* (6.25 µg/mL), and various strains of *Staphylococcus aureus* (25 µg/mL). According to Anand *et al.* (2015), the ethanolic extract of *A. occidentale*

leaves showed an MIC of 78.12 µg/mL against the pathogenic bacteria *Staphylococcus aureus* and *Staphylococcus mutans*. In a study carried out by Ribeiro *et al.* (2021), it was observed that the bacterial strain most sensitive to the hydroethanolic extract of the bark of *A. occidentale* was *Staphylococcus epidermidis*, with MIC values of only 62.5 µg/mL. These results confirm the ethnomedicinal uses of *A. occidentale* by traditional communities in Paraíba.

Figure 4 – Punicalagin, an ellagitannin from *Punica granatum* with high antimicrobial activity.



Punicalagin

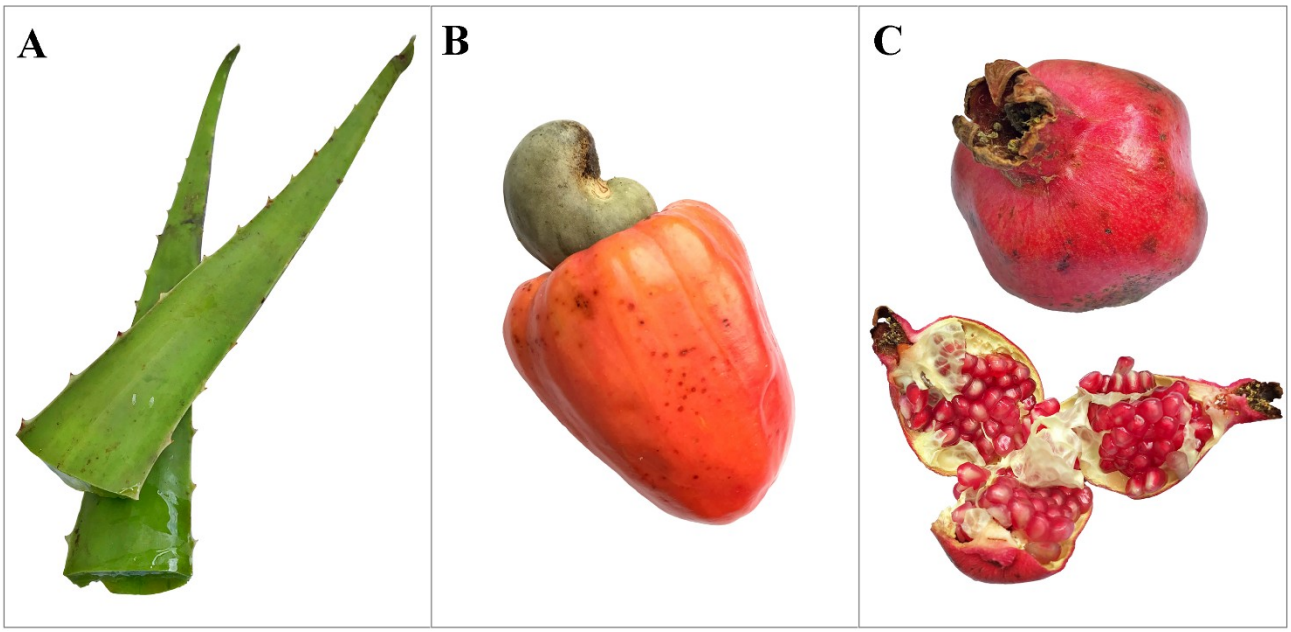
Source: Elaborated by the author in ChemDraw®.

3.2. CLINICAL TRIALS OF MEDICINAL PLANTS USED TO TREAT INFECTIONS IN PARAÍBA, BRAZIL

Of the 31 species used medicinally to treat infections in Paraíba, only 8 were evaluated in clinical trials (Table 2). The results of these studies indicated that herbal medicines based on *Kalanchoe pinnata* (Lam.) Pers. (Torres-Santos *et al.,* 2003), *Phyllanthus niruri* L. (Sarisetyaningtyas *et al.*, 2006; Diarsvitri *et al.,* 2018), *Copaifera langsdorffii* Desf. (Silva *et al.,* 2012; Valadas *et al.,* 2021), *Aloe vera* (L.) Burm.f. (Sargolzaie *et al.,* 2016; Pattnaik *et al.,* 2022), *Anacardium occidentale* L. (Gomes *et al.,* 2016), *Punica granatum* L. (Sedigh-Rahimabadi *et al.,* 2017; Eltay *et al.,* 2021), *Illicium verum* Hook.f. (Assiry *et al.,* 2021; Salem *et al.,* 2023), and *Myracrodruon urundeuva* M. Allemão (Maia *et al.,* 2023) showed potential against several diseases caused by pathogenic microorganisms that affect humans.

Products based on *A. vera, A. occidentale*, and *P. granatum* have been the target of several dental applications (Figure 5). According to clinical evidence, the effectiveness of mouthwashes containing these plants is similar to commercial mouthwashes in controlling bacterial plaque and gingivitis (Ahuja *et al.,* 2011; Gomes *et al.,* 2016; Sargolzaie *et al.,* 2016; Vangipuram *et al.,* 2016; Sedigh-Rahimabadi *et al.,* 2017; Eltay *et al.,* 2021; Pattnaik *et al.,* 2022). Therefore, these herbal products can be a natural alternative to chemically formulated mouthwashes. Furthermore, Prabhakar *et al.* (2015) reported that ethanolic extracts of *A. vera* can be used as effective cavity disinfectants to prevent the appearance of secondary caries, contributing to the long-term success of restoration.

Figure 5 – Medicinal plants evaluated in clinical trials. A) Leaves of *Aloe vera*. B) Pseudo-fruit of *Anacardium occidentale.* C) Fruit of *Punica granatum.*



Source: Elaborated by the author.

Other species also stood out for their potential for dental applications (Valadas *et al*., 2021; Maia *et al*., 2023). The mouthwash containing *M. urundeuva* showed satisfactory results in patients with gingivitis, reducing the plaque index, gingival bleeding index and probing depth, being similar to that of chlorhexidine (Maia *et al*., 2023). In another clinical trial, Valadas *et al.* (2021) reported that *C. langsdorffii* dental varnish demonstrated significant antimicrobial activity against *Streptococcus mutans* for up to 12 months in children at high caries risk.

Clinically, infectious diseases such as cutaneous leishmaniasis, varicella, and HIV (human immunodeficiency virus) have been treated with herbal medicines from *K. pinnata* (courama) and *P. niruri* (quebra-pedra). According to Torres-Santos *et al.* (2003), a 36-year-old man diagnosed with active cutaneous leishmaniasis was treated with *K. pinnata* for 14 days. During treatment, the lesion stopped growing and decreased slightly, demonstrating the effectiveness of this plant. Sarisetyaningtyas *et al.* (2006) reported that *P. niruri* extract administered to children diagnosed with varicella accelerated the appearance and abortion of crusts compared to the placebo

group. In a pilot study carried out with HIV patients, it was observed that the combination of antiretroviral therapy with *P. niruri* extract was more effective in increasing the absolute CD4 cell count compared to the administration of antiretroviral therapy alone (Diarsvitri *et al.,* 2018).

Although some traditional communities in Paraíba use *Cnidoscolus urens* (L.) and *Syagrus cearensis* Noblick to treat urinary infections (Santos *et al.,* 2012; Felix *et al.,* 2019), the anti-infectious potential of these species has been little investigated and reported in the scientific literature. Only two recent studies have evaluated the *in vitro* antimicrobial activity of *S. cearensis* (Farias et al., 2022; Sampaio et al., 2023); while Saraiva *et al.* (2012) and Costa *et al.* (2013) pointed out that extracts and fractions of *C. urens* showed low activity against pathogenic bacteria and fungi. From this perspective, considering the urgency in developing new broad-spectrum antimicrobials, it is necessary to focus on other species that have demonstrated high activity against multidrug-resistant strains *in vitro*, preclinical, and clinical trials.

Table 2 – Clinical trials medicinal plants used in the treatment of infectious diseases in Paraíba, Brazil.

Species	Study design	Patients	Products	Dose	Recommendations	References
Aloe vera (L.) Burm.f.	Randomized controlled clinical trial	Male and female, with a mean aged of 32.7 and 34.9 years	Mouthwash containing *Aloe vera*	5 mL	Mouthwash containing *Aloe vera* can be used to improve oral and dental health.	Sargolzaie *et al.* (2016)
	Randomized, double-blind, placebo-controlled, prospective parallel-arm clinical and microbiological trial	Undergraduate dental students aged 18-25 years, with at least 20 evaluable teeth	Mouthwash containing 20% *Aloe vera*	10 mL	The antiplaque and antibacterial efficacy of the mouthwash containing *Aloe vera* was significantly better than that of the mouthwash containing hydrogen peroxide.	Pattnaik *et al.* (2022)
	Randomized controlled clinical trial	Undergraduate and postgraduate dental students aged 18-40 years	Mouthwash containing *Aloe vera*	10 mL	Mouthwash containing *Aloe vera* showed equal effectiveness as Chlorhexidine. Therefore, it can be used as an alternative product for curing and preventing gingivitis.	Vangipuram *et al.* (2016)
	Randomized clinical trial	Children aged 5–12 years suitable for atraumatic restorative treatment with at least three cavitated dentinal lesions in primary molars	*Aloe vera* extract	-	*Aloe vera* extract can be used as a potential natural disinfecting agent in dental restoration.	Prabhakar *et al.* (2015)
Anacardium occidentale L.	Examiner-blinded, crossover, controlled clinical trial	Male and female, aged 18-32 years	Mouthwash containing *Anacardium occidentale*	10%	Mouthwash containing *Anacardium occidentale* was effective in plaque and gingivitis control, comparable to	Gomes *et al.* (2016)

					chlorhexidine.	
Astronium urundeuva (M.Allemão) Engl. [Syn. *Myracrodruon urundeuva* M. Allemão]	Controlled clinical study	Male and female, aged 18-65 years	Mouthwash containing *Myracrodruon urundeuva*	10%	Mouthwash containing *Myracrodruon urundeuva* showed satisfactory results in plaque index, gingival bleeding index, and probing depth, being similar to that of 0.12% chlorhexidine.	Maia *et al.* (2023)
Copaifera langsdorffii Desf.	Longitudinal, parallel, randomized, double-blind controlled clinical trial	Caries-free children, with 4 erupted primary second molars, aged 36-71 months and of both genders	*Copaifera langsdorffii* oilresin (dental varnish)	1%	*Copaifera langsdorffii* varnish demonstrated significant antimicrobial activity against *Streptococcus mutans* for up to 12 months in children with high risk of caries.	Valadas *et al.* (2021)
	Double-blind, placebo controlled clinical trial	Patients with a clinical diagnosis of type 1 acne lesions	Gel containing *Copaifera langsdorffii* essential oil	1.0%	The gel containing *Copaifera langsdorffii* essential oil might have utility as a topical treatment for mild acne.	Silva *et al.* (2012)
Illicium verum Hook.f.	Randomized clinical trial	Children aged 6-13 years	Mouthwash containing *Illicium verum*	5%, 10%, and 15%	The 15% concentration of *Illicium verum* was the most effective against oral plaque-forming bacteria compared to fluoride.	Salem *et al.* (2023)
	Double-blind randomized clinical trial	Patients aged 18-25 years who had not undergone any oral hygiene sessions previously up to the last 6 months	Mouthwash containing *Illicium verum*	-	The study revealed that the Illicium verum anise has potent antibacterial, anti-inflammatory, and astringent properties.	Assiry *et al.* (2021)
Kalanchoe *pinnata* (Lam.) Pers.	Clinical case study	Male aged 36 years, diagnosed with cutaneous leishmaniasis	Lyophilized aqueous leaf extract	21 mg	*Kalanchoe pinnata* contains substances potentially active and safe for the oral treatment of human cutaneous leishmaniasis.	Torres-Santos *et al*. (2003)
Phyllanthus *niruri* L.	Double-blind randomized controlled clinical trial	Children aged 12-14 years, who experienced varicella without complications, and acquired papules for less than two days	*Phyllanthus niruri* extract (Stimuno®)	25 mg	Clinically, *Phyllanthus niruri* extract accelerates appearing and aborting crust compared to placebo.	Sarisetyaningtyas *et al.* (2006)
	Pilot study	Treatment naïve AIDS patients aged 17 years and over	Capsules *of Phyllanthus niruri* extract	50 mg	The combination of the first line of antiretroviral therapy and *Phyllanthus niruri* extract was more effective in increasing the absolute CD4 cells count compared to the administration of	Diarsvitri *et al.* (2018)

					antiretroviral therapy alone in HIV patients.	
	Double-blind, placebo-controlled, parallel-group clinical trial	Patients aged 18-75 years, diagnosed with chronic hepatitis B virus infection	*Phyllanthus niruri* extract tablets	250 mg	This study does not support the use of *Phyllanthus niruri* for the treatment of chronic hepatitis B.	Baiguera *et al.* (2018)
Punica *granatum* L.	Randomized, controlled, double-blind clinical trial	Children aged 9-12 years	Mouthwash containing *Punica granatum* (6.25%)	10 mL	Mouthwash containing *Punica granatum* was not effective in reducing dental biofilm and gingival inflammation.	Nóbrega *et al*. (2015)
	Double-blind, parallel, randomized controlled clinical trial	Patients with chronic gingivitis aged 18-60 years	*Punica granatum* fruit peel extract	5%	The adjunct effect of a pulsating oral jet containing 5% of *Punica granatum* extract effectively reduced plaque index, gingival bleeding index, and IL-1β levels in chronic gingivitis patients.	Eltay *et al.* (2021)
	Randomized, double-blind clinical trial	Dental students aged 22-28 years	Gel containing *Punica granatum* extract	10%	The gel containing 10% *Punica granatum* extract was not efficient in preventing supragingival dental plaque formation and gingivitis.	Salgado *et al.* (2006)
	Randomized clinical trial	Female and male, aged 14-25 years, with moderate gingivitis	Mouthwash containing *Punica granatum*	10 mL	Mouthwash containing *Punica granatum* is beneficial in improving gingival status due to its profound styptic action, with sufficient reduction in plaque scores.	Ahuja *et al.* (2011)
	Double-blind, randomized comparative clinical trial	Patients aged 20-65 years, diagnosed with diabetes mellitus and having at least 20 teeth	Mouthwash containing *Punica granatum*	10 mL	The use of mouthwash containing *Punica granatum* is a safe and effective modality in the treatment of gingivitis in diabetic patients.	Sedigh-Rahimabadi *et al*. (2017)

Source: Elaborated by the author.

4. CONCLUSION

This is the first study that brings together literature publications on the medicinal potential of Paraíba flora used in the treatment of infectious diseases. A total of 31 species distributed in 22 families are used against infections by traditional communities in different municipalities in this Brazilian state. However, only 8 species had their herbal products evaluated in clinical trials. Mouthwashes based on *Aloe vera, Anacardium occidentale*, and *Punica granatum* have been targets of dental applications to assist in the treatment of bacterial plaque and gingivitis. It is recommended that new randomized clinical trials be developed to investigate the

traditional uses of other medicinal plants reported in the present study against infectious diseases caused by pathogenic microorganisms.

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