Chapter

Bioactive Phenolic Compounds and Biological Activities of Mururé Bark (*Brosimum acutifolium*), a Natural Antioxidant

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Abstract

Brosimum acutifolium is a large tree with high medicinal and pharmacological value, widely used in folk medicine by some communities in South America and northern Brazil, as a potent antirheumatic, antiarthritic and anti-inflammatory, so this work aims to address the chemical composition and biological activities of the bark of the species, reported in the scientific literature in the last 30 years. Information was collected from the databases such as the Google Scholar, Scientific Electronic library online (Scielo), National Library of Medicine (PubMed), Elsevier, institutional repositories and government websites. The bark of the plant species has a variability of compounds in its composition, such as flavonoids, coumarins, phytosterols, alkaloids and lignoids, representing an important source of phenolic bioactives, which makes it a natural antioxidant. In this research, biological activities, such as antibacterial, antifungal, antioxidant, anti-inflammatory, neuroprotective and anticancer activities, were found. The biological properties observed are related to the promotion of human health, and when added to the vast diversity in secondary metabolites present in the bark, it transforms the species into a strong candidate to act as an auxiliary therapeutic alternative in the control and treatment of certain diseases and as an input for the development of bioproducts.

Keywords: *Brosimum acutifolium*, chemical profile, biological activities, natural antioxidant, bioactive compounds

1. Introduction

The Amazon rainforest, known worldwide for its biodiversity, has a variety of plant species that are seen as natural sources of bioactive compounds of high added value and high antioxidant capacity, as is the case of phenolic compounds, which have

the potential to be used as inputs in the formulation of manufactured products of interest to the chemical, food and pharmacological industries [1].

In this context, a huge number of scientific publications have aroused the interest of the scientific community demonstrating the possibility of using plants native to the Amazon region, as is the case of species of the genus *Brosimum*, as potential bioactive agents with pharmacological and biotechnological properties [2, 3].

The species of the genus *Brosimum*, belonging to the *Moraceae* family, are native to the Amazon region and have their economic importance associated, mainly, with the production and sustainable extraction of latex, which is obtained from the tree. However, other potentialities are associated with this genus as is the case of the use of tree bark for medicinal purposes [4].

The species *B. acutifolium*, popularly known as "mururé," is also known by the names of Amapá doce, congona, mururé da terra firme, muirapiranga; urupi, quecho, tamamuri, mercúrio vegetal, amarillo, tamamuri, takini, tauni, congona and typique, nominal variations related to the region of occurrence [5]. It is one of the varieties of this genus and stands out from the other species due to recent scientific discoveries that have revealed potential bioactivities of this species as an antioxidant, anti-inflammatory and neuroprotective [6, 7] due especially to the presence of natural antioxidants, as is the case of secondary metabolites.

Thus, this species is seen as a natural source of antioxidants and with high economic value, despite these advantages it presents, it is still little known about its potential for exploitation, especially about its composition [8].

Considering the productivity potential of the species *B. acutifolium* in terms of its chemical composition and potential bioactivities, the search for knowledge about the bioactive potential of the species is configured as an important strategy to encourage its sustainable exploitation, identify possible potentialities of this species to be used as an input in the development of new drugs and new technologies, in addition to enabling the insertion of this plant species in the economic matrix of natural products of high added value in the Brazilian states of the Amazon region. It is worth mentioning that there is growing demand for natural products obtained from Brazilian biodiversity, as is the case of natural antioxidants extracted from the native plant species of the Amazon rainforest [6–9].

Thus, this article is the first review work in the literature for the species *B. acutifolium* that discusses the bioactive potential of the species through the systematic classification of scientific works published in the last three decades.

2. Methods

This article consists of a review of the scientific literature, using the integrative method. For bibliographic mapping, the following descriptors were used: *B. acutifolium*, Genus *Brosimum*, *Moraceae*, Mururé, profile phytochemical of *B. acutifolium*, biological activity of *B. acutifolium* and morphology, derived from the name of the species, genus or family searched. The procedures for exclusion and inclusion of the studies were based on predefined criteria: dating from 1990 to 2023, languages: English, Portuguese, Spanish and Japanese. The selection and categorization of the scientific contribution occurred through a thorough and complete reading of all the collected works, to identify key information that would fit the predefined topics of this work.

3. Botanical taxonomy

The species has a wide geographic distribution throughout South America, being mostly found in Brazil, French Guiana, Peru and Colombia, as presented in **Table 1**, according to the government website of the Global Biodiversity Information System [10]. It has characteristic habitat of *terra firme* rain forests, with tropical climate, as to its seasonality, covers the period between the months of July and September with flowering, fruiting until the end of October, where its fruits are found ripe and can be harvested. As regards phenology, the species is adept at climates with annual rainfall, medium lighting and clayey soils [11, 12]. *B. acutifolium* is a tree that can reach a height ranging from 15 to 25 m(**Figure 1**), is characterized by the presence of rough branches of grayish color, leaves with stipulae of aspect that resemble spears, acuminate apex with rounded base and slightly wavy margins, and has a glabra ventral face and a tubercular dorsal face. Globose floral receptacle is covered by basal bracts with female flowers. Its fruits are globose and reddish approximately 3 cm in diameter, containing up to five seeds inside. The trunk has horizontal lines on the surface, with bark and root of reddish color, a latex can be extracted through a cut in the stem [13, 14]. **Tables 2** and **3** contain, respectively, the taxonomy of the species and synonymy of the subspecies, as available on the government websites of the Taxonomic Catalog of the Fauna of Brazil and List of the Flora of Brazil 2020 [15].

4. Ethnopharmacology of the species

The bark is one of the main structures of the species used by communities in South America and Northern Brazil for the treatment of ailments involving inflammatory conditions, infectious diseases, rheumatism and arthritis, acts as analgesic, antipyretic, vermicide, antisyphilitic and in respiratory, gastrointestinal and neurological disorders. It is also indicated its use for anemia and allergies as well as appetite stimulator and aphrodisiac. The latex extracted by incision has an initially light coloration that quickly reddens over time. This liquid is also popularly used for the treatment of diseases being also considered antirheumatic, antiarthritic, antisyphilitic, anthelmintic, anti-inflammatory and should be consumed moderately because it can cause intoxication [12].

Countries	Number of occurrences
Brazil	383
Bolivia	45
French Guiana	38
Peru	36
Colombia	26
Ecuador	11
Suriname	8
Guyana	5
Martinique	2

Table 1.
Occurrence of the species B. acutifolium.

Figure 1.
B. acutifolium tree.

Classification	
Kingdom	*Plantae*
Subkingdom	*Tracheobionta*
Phylum	*Tracheophyta*
Class	*Magnoliopsida*
Order	*Rosales*
Family	*Moraceae*
Tribe	*Dorstenieae*
Genus	*Brosimum*
Subgenus	*Brosimum*
Species	*B. acutifolium*
Subspecies	*B. acutifolium* Huber subsp. *acutifolium*
	B. acutifolium subsp. *interjectum* C.C.Berg
	B. acutifolium subsp. *obovatum* (Ducke) C.C.Berg

Table 2.
Taxonomy of the plant species B. acutifolium.

As for the method of preparation, the information found points to the consumption of teas, macerations, bottles, spirits and mixtures. Teas are prepared from the decoction or infusion of the whole or ground bark and the fruits in boiling water, being popularly

Scientific name		Synonymy
Specie	*B. acutifolium* Huber	*Brosimopsis acutifolia* (Huber) Ducke
Subspecies	*B. acutifolium* Huber subsp. *acutifolium*	*Brosimopsis aculifolia* (Huber) Ducke, *Piratinera acutifolia* (Huber) Pittier
	B. acutifolium subsp. *interjectum* C.C.Berg	
	B. acutifolium subsp. *obovatum* (Ducke) C.C.Berg	*Brosimopsis obovata* Ducke, *Brosimum caniceps* Standl.

Table 3.
Synonymy of the species of the subgenus Brosimum.

associated with the treatment of diseases of the digestive tract. Maceration is done by mixing cachaça, wine or brandy with the peel, remaining at rest inside a bottle for 48 h. After this time, a purplish coloration is observed, indicating that the preparation is ready to be used. It can be consumed orally twice a day (in the morning and afternoon before bathing) or by applying the mixture directly to the skin, through frictions and massages, especially in cases of joint pain and inflammation. A few drops of latex can be added to cachaças and drinks, at the beginning of magic rituals. Reports indicate the use of latex for the treatment of syphilis, in preparations with water (4 g of latex and 15 g of water), not exceeding the intake of 8 g of latex per day and should be drunk daily. If there are lesions on the skin, latex can be applied directly to the wound and the sap can be stored for longer if it stays at low temperatures or mixed in alcohol [12].

The bottles are prepared based on peels or together with peels of other species, mixed in water undergoing a decoction treatment or not, the liquid is then separated and packed in glass bottles to then be consumed daily until there is an improvement in the condition of the disease. These preparations are very common to be ingested when you have apathy or muscle fatigue, caused by intense physical activity. The distillates and mixtures were not possible to be described due to the lack of information on the method of preparation. The traditional knowledge attributed to mururé has been confirmed through much research, which attribute its anti-inflammatory, antibacterial and antioxidant character due to the large number of flavonoids present in its chemical composition. Its performance as antianemic and aphrodisiac has no scientific proof, only reports of use [2, 12].

5. Bioactive compounds

Previously in the species, the presence of flavonoids, coumarins, lignoids and phytosterols was observed. There are a vast number of bioactive compounds that have been discovered and isolated in recent decades, mainly polyphenols of the flavonoid class such as flavans and chalcones [3, 13, 14, 16]. In this section, the main classes of secondary metabolites investigated in the bark of the species *B. acutifolium* will be presented. The substances presented were identified and elucidated through high-performance liquid chromatography (HPLC) coupled to mass spectrometry (MS) in the extracts obtained through the maceration technique.

5.1 Flavonoids

Flavonoids are secondary metabolites from plant matrices, found in the bark of the species. Structurally, these compounds have approximately 15 carbon atoms

distributed in a chain of three rings, with nucleus C6-C3-C6, which are units called A, B and C. They can be found in the form of flavones, flavanones, flavonols, flavanols, anthocyanins, isoflavones and chalcones [17, 18], are found oxygenated and much of it is conjugated to sugars [19]. Chalcones are precursors and product of the biosynthesis of flavonoids, are classified as naturally occurring aromatic ketones, whose structure is 1,3-diaryl-2-propen-1-one. They are considered open-chain flavonoids, composed of an α, β-unsaturated carbonyl system responsible for the union of two aromatic rings, called A and B, which constitute their chemical structure [19, 20]. These substances exhibit a vast biological activity found as antidiabetic, antioxidant, protective vessel, anti-inflammatory and antimicrobial, including antiviral, antifungal and antiparasitic [17–22]. The flavonoids identified are gathered and organized in **Table 4**.

The species has a high number of flavonoids, such as: 4′-hydroxy-7,8-(2″,2″-dimethylpyran)flavan, 4′-hydroxy-7,8-(3″-hydroxy-2″,2″-dimethylpyran)flavan, Brosimine A, Brosimine B and 3′,7-dihydroxy-4′-methoxyflavan, which are compounds observed in dichloromethane extracts obtained by cold maceration [2, 4]. Cold methanoic maceration [3, 14] allowed obtaining extracts rich in flavanoids, such as Acutifolins A-F and Brosimacutins A-M. In a study carried out with methanolic extracts [3] to evaluate the cytotoxicity of molecules: Brosimacutins J-L and the chalcone Brosimacutin M, it was found that these molecules showed cytotoxicity against P388 leukemic cells resistant to vincristine (IC50 4.4–19 microg/mL).

Compound	Molecular formula	Yield (%)	Reference
4′-hydroxy-7,8-(2″,2″-dimethylpyran) flavan	$C_{20}H_{19}O_2(OH)$	0.0019	[4]
4′-hydroxy-7,8-(3″-hydroxy-2″,2″-dimethylpyran)flavan	$C_{20}H_{18}O_2(OH)_2$	0.00052	
Brosimine A	$C_{20}H_{22}O_4$	0.00069	[2]
Brosimine B	$C_{20}H_{22}O_3$	0.0035	
Isobavachin	$C_{20}H_{20}O_4$	0.00052	
Isoliquiritigenin	$C_{15}H_{12}O_4$	0.00017	
4-Hydroxyisocordoin	$C_{20}H_{20}O_4$	0.00073	
Liquiritigenin	$C_{15}H_{12}O_4$	0.00017	
4′,7-dihydroxy-8-prenylflavan	$C_{20}H_{22}O_3$	0.000068	[12]
Acutifolin A	$C_{20}H_{22}O_4$	0.001	[13]
Acutifolin B	$C_{22}H_{26}O_3$	0.000087	
Acutifolin C	$C_{21}H_{22}O_3$	0.00019	
Acutifolin D	$C_{20}H_{24}O_5$	0.03	
Acutifolin E	$C_{20}H_{24}O_5$	0.0016	
Acutifolin F	$C_{17}H_{18}O_4$	0.00013	
7,4′-dihydroxyflavan	$C_{15}H_{10}O_4$	0.00017	
7,3′-dihydroxy-4′-methoxyflavan	$C_{16}H_{12}O_5$	0.00032	

Compound	Molecular formula	Yield (%)	Reference
Brosimacutin A	$C_{20}H_{20}O_6$	0.0017	[14]
Brosimacutin B	$C_{20}H_{22}O_6$	0.0012	
Brosimacutin C	$C_{20}H_{22}O_5$	0.000073	
Brosimacutin D	$C_{20}H_{20}O_5$	0.00014	
Brosimacutin E	$C_{20}H_{20}O_5$	0.00031	
Brosimacutin F	$C_{20}H_{20}O_6$	0.00017	
Brosimacutin G	$C_{20}H_{20}O_6$	0.0001	
Brosimacutin H	$C_{20}H_{24}O_6$	0.00055	
Brosimacutin I	$C_{20}H_{24}O_6$	0.00049	
Luteolin	$C_{15}H_{10}O_6$	0.000067	
Liquiritigenin	$C_{15}H_{12}O_4$	0.000067	
Naringenin	$C_{15}H_{12}O_5$	0.00015	
Brosimacutin J	$C_{17}H_{14}O_3$	0.000067	[3]
Brosimacutin K	$C_{20}H_{22}O_5$	0.000093	
Brosimacutin L	$C_{20}H_{24}O_4$	0.00033	
Brosimacutin M	$C_{20}H_{22}O_6$	0.0044	

Table 4.
Flavonoids present in B. acutifolium.

5.2 Phytosterols

Phytosterols are compounds of plant origin, belonging to the triterpene family. They have a tetracyclic structure, formed by four rings, called A, B, C and D, with a branched side chain in the carbon of position 17 of the D ring. They structurally resemble cholesterol, differing from this due to the addition of a methyl or ethyl group in the position of carbon C24, for example [23–26]. There is a vast amount of phytosterols, the most common among which are β-Sitosterol, Campesterol, Stigmasterol, Brassicasterol and Avenasterol [27]. These compounds are related to decreased risk of developing cardiovascular disease and cancer, exhibit numerous other properties, such as antidiabetic, anti-inflammatory, neuroprotective, antimicrobial, and act in the control of low-density lipoprotein (LDL) cholesterol levels [24–29]. The phytosterols isolated and identified in the bark of *B. acutifolium* are β-Sitosterol (0,0013%) and Stigmasterol (0,001%) [2], obtained from methanolic extracts (**Figure 2**). Stigmasterol and β-Sitosterol are structurally similar compounds, with a difference in the double bond located at the position of the C22 carbon, in which the sterol C-22 desaturase is inserted, transforming β-Sitosterol into Stigmasterol [30].

5.3 Coumarins

Coumarins are polyphenols of the benzopyrone family, and they are oxygenated substances with heterocyclic structure, formed by two rings with a carbonyl group in carbon of C2 position. Coumarins (1,2-benzopyrone) and their derivatives are

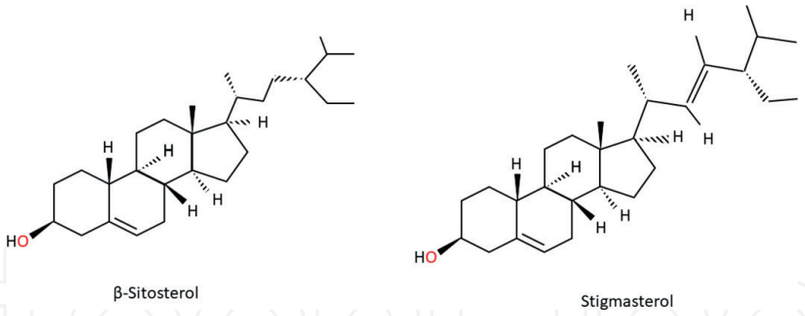

Figure 2.
Phytosterol molecules present in B. acutifolium.

compounds of high biological potential and can be biosynthesized by plants, and some fungi and bacteria. They are classified as simple coumarins, furanocoumarins, pyranocoumarins and pyrone-substituted coumarins [31–33]. Coumarin compounds exhibit a vast pharmacological activity arousing interest in the cosmetic, food and pharmaceutical industries. These bioactive compounds exhibit anti-inflammatory, antibacterial, Alzheimer's disease inhibition, anticonvulsant, anticoagulant, anticancer, antimalarial, antifungal, antiviral, neuroprotective and antihypertensive activity [33–36]. The coumarin substances present in the bark of the species are available and organized in **Table 5**.

5.4 Alkaloids

The alkaloids present in *B. acutifolium* are organic substances found in the latex extracted from the bark of the stem of the species. In this case, the alkaloid 5-hydroxytryptamine (bufotenine) was recorded for the first time in latex-based potions prepared for magical rituals (**Figure 3**) [38]. The bufotenine molecule is derived from the amino acid tryptamine. It has hallucinogenic action, being found in animal organisms, such as frogs, and in Amazonian plants such as the *Moraceae* and *Leguminosae* families. It also has an inhibitory action against the rabies virus and serves as an anti-inflammatory and analgesic [39]. In general, alkaloid molecules have a heterocyclic structure, in which nitrogen atoms are incorporated, which give them basicity [40, 41]. They are produced by fungi, bacteria and plants, and alkaloids are mainly classified into indoles, purines, quinolines, isoquinolines, tropanes, imidazole, pyridines and others [41, 42]. The structural variability of these compounds gives them vast pharmacological activity such as anticancer, antibacterial, analgesic, antifungal, anti-inflammatory, antidiabetic and antimalarial [40–46].

Compound	Molecular formula	Reference
Psoralen	$C_{11}H_6O_3$	[10]
Bergapten	$C_{12}H_8O_4$	
Mururin A	$C_{24}H_{16}O_9$	[37]
Mururin B	$C_{24}H_{16}O_9$	
Mururin C	$C_{20}H_{20}O_7$	

Table 5.
Coumarins identified in B. acutifolium.

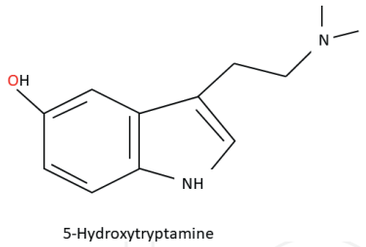

Figure 3.
Alkaloid observed in the latex of mururé bark.

5.5 Lignoids

The molecules identified in the bark of the mururé are Coniferaldehyde and Syringaldehyde (**Figure 4**). Lignoids are aromatic phenolic molecules deposited on the cell wall in plants, accounting for up to 45% of their biomass. They are formed from phenylpropanoic groups (C6-C3)n ("n" the number of atoms interconnected with this configuration),being divided into groups, such as lignans, neolignans, allolignans, oligolignoids and heterolignoids, for example. They express anticancer, antiviral, anti-inflammatory, antimicrobial and antioxidant activity [46–49].

5.6 Recently discovered compounds in the species

In the last 5 years, a study was reported that investigated the phytochemical composition of the species [13], which identified the presence of chalcones until then, not yet seen in *B. acutifolium*. The molecules found in the bark of the mururé are presented in **Table 6**.

6. Biological activities of *B. acutifolium*

B. acutifolium, as can be seen in the previous section, exhibits a vast number of bioactive molecules that are related to pharmacological properties of great interest for improving human health (**Figure 5**). The premise of the studies that investigate the biological potential of mururé is based on the ethnopharmacological report available in the literature, in which, the plant species is used in the treatment of rheumatism, arthritis, lesions and inflammatory conditions [6, 8]. In this topic, research that evaluates biological activity and proves its use reported in folk medicine will be addressed.

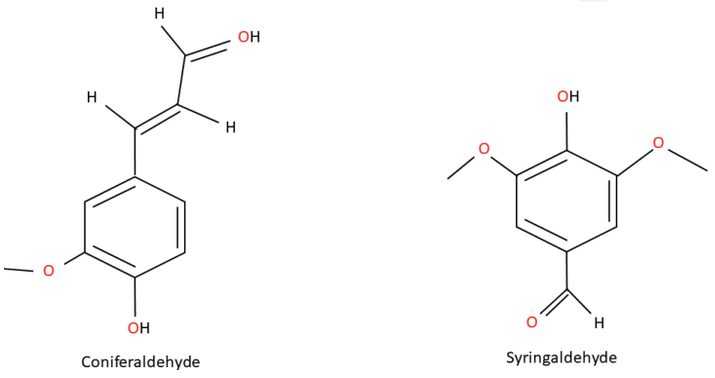

Figure 4.
Lignoids present in the species.

Compound	Molecular formula	Reference
Kanzonol B	$C_{20}H_{18}O_4$	[13]
Kanzonol C	$C_{25}H_{28}O_4$	
Corylifol B	$C_{20}H_{20}O_5$	

Table 6.
Recently discovered compounds in the bark of mururé.

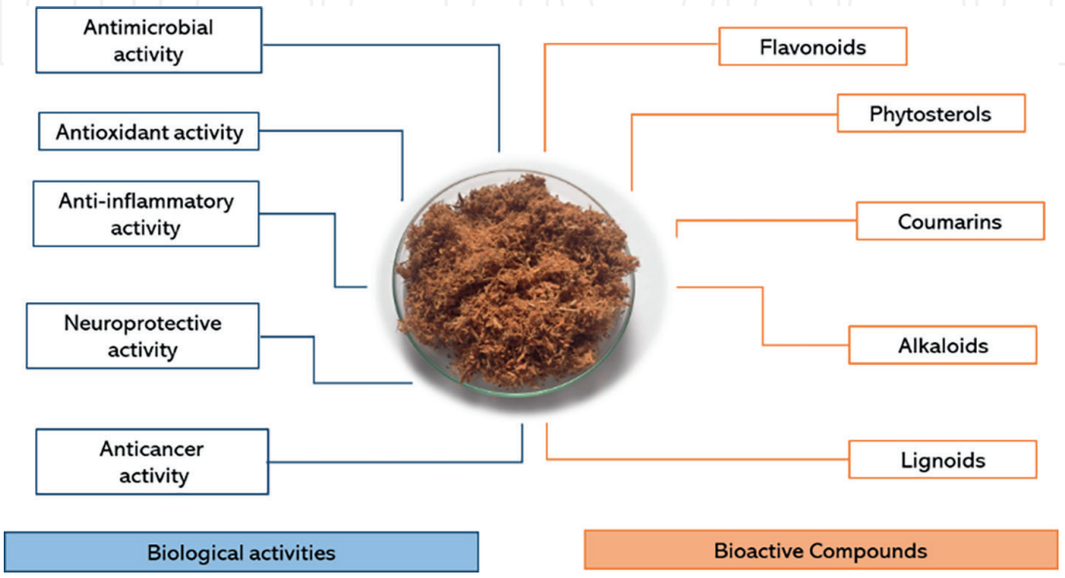

Figure 5.
Bioactive potential of mururé bark.

6.1 Antimicrobial activity

Methicillin-resistant *Staphylococcus aureus* (MRSA) (β-Lactam) is a public health problem that is related to the increase in cases of bacterial resistance to antibiotics worldwide. *S. aureus* is an opportunistic bacterium present in the epidermis and nasal cavities of healthy humans, and most often this pathogen lives in the human microbiota without causing greater harm; however, if this microorganism invades the bloodstream or enters deep into the tissues it can cause very serious infections [49–51]. As a form of drug protection, bacteria can generate biofilms, which are a conglomerate of microorganisms encapsulated by a polymeric compound that protect them from both the antibiotic and the attack of the human immune system [52–55].

A study [56] evaluated the antimicrobial potential of the ethanolic extract of the bark of *B. acutifolium* against seven multidrug-resistant bacteria (*Proteus mirabilis, Klebsiella pneumoniae, Pseudomonas aeruginosa, Escherichia coli, S. aureus, Enterococcus faecalis* and *Streptococcus pneumoniae*) by the Kirby-Bauer method. As a result, activity against *P. aeruginosa* and high inhibitory activity against multidrug-resistant *S. aureus* were observed, with minimum inhibitory concentration (MIC) ranging from 1.25 to 80 mg/L.

An ethnobotanical survey of 59 Amazonian plant species [57] used as local phytotherapics by Amazon riverine population was carried out and antimicrobial activity of their extracts evaluated. Several plant species tested did not show effective antibacterial activity; however, the ethanolic extract of *B. acutifolium* obtained a minimum active inhibitory concentration (150 mg/L) against seven Gram-positive bacteria: *P.*

aeruginosa, *Stenotrophomonas maltophilia*, *Staphylococcus epidermidis*, *Staphylococcus lugdunensis*, *Staphylococcus warneri*, *Corynebacterium striatum* and *Mycobacterium smegmatis*. It was also found to have shown moderately active inhibition (300 mg/L) for Gram-negative bacteria: *K. pneumoniae, Yersinia pseudotuberculosis* and Gram-positive bacteria: *S. aureus*.

More adverse pathogenic bacteria that reach the enterogastric system, *E. coli*, *E. faecalis* and *Salmonella* sp., did not express results for antibacterial activity [56, 57]. The infusion of *B. acutifolium* has not shown an effective antibacterial activity against potential pathogenic bacteria that reach the enterogastric system, *E. coli*, *E. faecalis* and *Salmonella* sp., and consequently compromising the treatment of diseases. However, the most appropriate ethnopharmacological application would be the topical use of disease treatment.

In another study [8], the ability to disrupt biofilms formed by MRSA and antibacterial activity was investigated, using three flavonoids isolated from this species: 4′-hydroxy-7,8-(2″,2″-dimethylpyran)flavan, 4-hydroxy-lonchocarpin and Brosimine B. In this study, the molecules 4′-hydroxy-7,8-(2″,2″-dimethylpyran)flavan and Brosimine B were able to further reduce the viability of this pathogen in the biofilm by a MIC of 50 mg/L. At a concentration of 200 mg/L, Brosimine B was able to reduce bacterial viability by up to 94%, and it was also demonstrated to reduce the biomass of biofilms formed by *S. aureus* by up to 48% at a MIC of 100 mg/L. The flavonoids 4′-hydroxy-7,8-(2″,2″-dimethylpyran)flavan and 4-hydroxy-lonchocarpin were not able to promote the reduction in bacterial biomass. However, the molecule 4-hydroxy-lonchocarpin, at a concentration of 400 mg/L, obtained a reduction in bacterial cell viability close to 43%.

The evaluation of the antifungal actions [58] of extracts of *B. acutifolium* against the standard strain of *Candida albicans* showed an excellent inhibition (MFC = 9.7 mg/L), whereas for the other species, *Candida glabrata* minimum fungicidal concentrations (MFC) = 2500 mg/L and *Candida krusei* (MFC) = 2500 mg/L, there was a weak antifungal activity.

Candidemia is considered an epidemic of opportunistic fungal infection caused by yeasts of the genus *Candida* sp. with high mortality in immunocompromised people and patients hospitalized under severe conditions in a secondary way, during hospital practices. The emergence of infections by opportunistic pathogenic fungi occurs due to the indiscriminate use of synthetic antimicrobials, which act antagonistically to the intestinal bacterial flora, causing exponential growth and causing the weakening of the patient's state of health. Reducing the use of antibiotics or adopting other therapeutic practices is imperative to prevent the emergence of multidrug-resistant fungi and bacteria and coinfections [59].

This research fosters the search for new therapeutic alternatives, which have instigated research on plant drugs with biological potential for the formulation of antibiotics that aim to reduce the development of multidrug-resistant bacterial strains and that can enter the biofilms to cause bacterial death, which is still a barrier to be faced by the pharmaceutical industry and in the medical area [8].

6.2 Antioxidant activity

Plant species in general exhibit antioxidant activity, and this activity is related to the ability to inhibit oxidative stress, being considered natural antioxidants. Oxidative stress can be defined as an imbalance of reactive oxygen species (ROS) responsible for the correct performance of the human organism. The excessive presence of ROS results in an attack on human cells causing the development of several degenerative diseases. Natural antioxidants can neutralize ROS by capturing these free radicals [60–63].

In this sense, some studies have been conducted to evaluate the antioxidant potential of *B. acutifolium*, in which the 2,2-diphenyl-1-picrylhydrazyl (DPPH+) method is the most widely used assay to determine this potential in the extracts of the species [6, 63]. This method is based on the elimination of the organic radical 1,1-diphenyl-2-picryl-hydrazyl (a free and stable molecule) by antioxidants. The reduction of this radical is accompanied by the reduction of absorbance, and the results are expressed mostly using IC50 (half-maximal inhibitory concentration), which indicates the amount of antioxidant needed to sequester 50% of the free radicals of 1,1-diphenyl-2-picrylhydrazyl [64, 65].

The antioxidant activity of the Brosimine B molecule (4′,7-dihydroxy-8-(3,3-dimethylallyl)flavan) present in the species was investigated [7] by the (DPPH+) method obtaining a value of IC50 = 55.16 μM, observing that it has a profile like that of ascorbic acid with IC50 = 36.91 μM. The ethanolic extract of *B. acutifolium* was evaluated [66] by the DPPH+ method finding a value of CI50 = 2.84 ± 0.38 μg. mL^{-1}. In another study [7], the antioxidant activity of the ethanolic extract and three flavonoids isolated from the species (4′-hydroxy-7,8-(2″,2″-dimethylpyran)flavan, Brosimine B and 4-hydroxy-lonchocarpin) was evaluated by the DPPH+ method, out of which only the ethanolic extract and the compounds 4′-hydroxy-7,8-(2″,2″-dimethylpyran)flavan and Brosimine B exhibited antioxidant activity.

When the reaction kinetics were evaluated in comparison with Trolox (IC50 = 3.5 ± 0.2 μg/mL), the ethanolic extract showed a value of IC50 = 4.8 μg/mL and Brosimin B a value of IC50 = 16.6 μg/mL. As can be observed, the antioxidant activity of the species *B. acutifolium* is related to its variability in the chemical composition mainly in the diversity of phenolic compounds [2, 4, 13], which if concentrated may contribute to a greater antioxidant character in this plant species.

6.3 Anti-inflammatory activity

Inflammation is a response of the body caused by a tissue injury or by microbial infections [67]. In general, inflammation develops to repair the events of trauma or microbial infection, but it can suffer a response without being directly related to the events mentioned, which can lead to chronic pathologies, resulting from dysregulated inflammation [68, 69].

An inflammatory response involves the recruitment of innate immune cells, which produce cytokines and chemokines, attracting lymphocytes and then triggering the inflammatory process. A cascade of events occur during this process, and there are many studies that have focused on the use of bioactives with anti-inflammatory actions [70].

Flavonoids are known to have several pharmacological actions, and the anti-inflammatory activity was found in a study in which flavanoid isolate, 4′-hydroxy-7,8-(2″,2″-dimethylpyran)flavan from mururé bark, was evaluated in two *in vivo* experimental models: models of duck edema and air pocket. This study verified the anti-inflammatory activity of this flavonoid, but the mechanism of action was not elucidated [71].

The mechanism of anti-inflammatory action of this flavonoid was investigated in a later study, using murine stimulated macrophages, which are extremely important for the control of inflammation and infections. It is possible to observe the anti-inflammatory action, evidencing the decrease in the proinflammatory cytokine tumor necrosis factor alpha (TNF-α) and indicating a specific mechanism of its action in the proinflammatory pathway [37].

In another study conducted with flavonoids isolated from the species, the substances, called murinin A, murinin B and murinin C, were tested for the inhibitory activity of protein kinases A and C. As a more relevant result, the inhibitory action of

63% for protein kinase C was observed, when using 20 μM of murine A, while murine C did not demonstrate significant inhibitory activity for these proteins [72].

There are few studies published in the literature on the anti-inflammatory activity of mururé. However, the results demonstrated in this review found its medicinal action and that due to the variability of bioactive compounds in its composition [13], the species becomes an interesting candidate in the search for new anti-inflammatory agents.

6.4 Neuroprotective activity

Stroke is one of the main comorbidities in the world, more prevalent in the elderly population, with ischemic (cerebral vascular accident (CVA)) being the most common type of stroke, compromising the metabolic pathways in the central nervous system (CNS) causing severe degeneration in the affected area. The stroke is caused by the interruption in blood flow for some time, causing cell groups to be injured, and its effects last even after the establishment of blood flow, generating an ischemic cascade with a lot of cellular damage [73]. As a consequence, it also causes the temporary blockage of the supply of oxygen, glucose and other nutrients to the CNS, triggering an oxidative stress that culminates in damage to cellular tissues. In the individual, these effects manifest themselves through intense headache, dizziness and imbalance [74].

The Brosimine B molecule obtained from extracts of the species *B. acutifolium* was evaluated for its neuroprotective effect in an *in vitro* experiment, using retinal cells from the chicken embryo subject to hypoxia, with oxygen and glucose deprivation. The molecule has been shown to increase cell viability by combating oxidative stress caused by ROS over a period of 3 to 6 h and protecting the studied cell culture from the hypoxia to which it was subjected [7].

Currently, the treatment for stroke cases is administered through thrombolytic therapies as a measure to prevent the emergence of new ischemic episodes. It is necessary to conduct research involving studies of new therapies that can clarify the mechanism that acts on the death of cells in the affected areas due to ischemia [75]. In this sense, it is essential to find products and therapeutic strategies that act with neuroprotective objective to protect cells from brain lesions.

6.5 Anticancer activity

Glioblastoma is a rare malignant brain tumor that mostly affects males, where the patients affected by the disease generally have a poor prognosis, and in most cases the chances of survival are less than 2 years. Treatment for such cases involves surgery, radiation therapy and chemotherapy. However, these treatments harm healthy cells causing harm to the human body [76].

In a study [6], three flavonoids (4′-hydroxy-7,8-(2″,2″-dimethylpyran)flavan, Brosimine B and 4,2′-dihydroxy-3′,4′-(2″,2″-dimethylpyran)-chalcone) were tested against C6 glioblastoma. The results showed that these flavonoids inhibited the migratory and antiproliferative activity of cell cultures, and act by inducing glioma apoptosis. Of the three species studied, the substance 4′,7-dihydroxy-8-(3,3-dimethylallyl)flavan was the one that presented the best antineoplastic activity acting through the mechanism of apoptosis and autophagy.

Currently, there are many medical treatments that aim to slow the advance of cancer. Natural products, such as those derived from *B. acutifolium*, can slow the proliferation of malignant cancer cells and can act together as a complementary alternative to cancer treatment, delaying tumor development [6, 76].

7. Application and suggestions

Extracts of *Brosimum acutifolium* are among the active principles of two registered cosmetic patents, according to which, they exhibit inhibitory activity of hyaluronidase and interesting response to hair growth, and may, therefore, be a promising species in the production of creams, shampoos, soaps and among others, aimed at this cosmetic industry. In addition to having already been shown to have anti-inflammatory characteristics, it may be an indication that these extracts have great chances of being worked at for the development of bioproducts [11]. It should be noted, however, that many of the mechanisms of action of the molecules present in the plant species are not yet described. Similarly, whether there is a relationship between various features such as the number of rings, hydroxyls or conformations in their form of action is yet to be described. Moreover, it is not yet clear as regards their biophysical characteristics. It is also necessary to evaluate the levels of toxicity of these extracts so that they can be administered with maximum effectiveness and minimum risks. The results of the studies mapped in this chapter to date already ratify the characteristics of this species as an aid in the protection of neurodegenerative processes and in the synthesis or molecular biotransformation, such as steroids.

8. Conclusion

The discovery of plant species with a high content of phenolic compounds is important for numerous sectors such as food, cosmetics and large pharmaceutical industries. The species *B. acutifolium*, an Amazonian tree that represents very well, is premise, since they present a vast number of bioactive compounds, mainly of the class of flavonoids, besides being responsible for the biological activities observed as antimicrobial, antioxidant, anti-inflammatory, anticancer and neuroprotective. These compounds promote human health benefits by improving the quality of life and can be useful in the manufacture of new drugs.

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Declaration of interest statement.

The authors declare no conflict of interest, financial or otherwise.

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